www.btvb.org

The Official Journal of the
Italian Society for the Study of Hemostasis and Thrombosis
SISET
Società Italiana per lo Studio dell'Emostasi e della Trombosi

BLEEDING, THROMBOSIS AND VASCULAR BIOLOGY

XIX Convegno Triennale sugli Aspetti Clinici e Sociali dell'Emofilia

Verona | 15, 16, 17 e 18 ottobre 2026

btvb

pagepress

Bleeding, Thrombosis and Vascular Biology

EDITORIAL BOARD

SISET President
Giancarlo Castaman, *Firenze*, *Italy*

AICE President
Rita Carlotta Santoro, *Catanzaro*, *Italy*

Editor-in-Chief
Giovanni de Gaetano, *Istituto Neurologico Mediterraneo Neuromed*, *Pozzilli (IS)*, *Italy*

Assistant Editor-in-Chief
Chiara Cerletti, *Istituto Neurologico Mediterraneo Neuromed*, *Pozzilli (IS)*, *Italy*

Section Editors
Francesco Bernardi, *Ferrara*, *Italy*
Giancarlo Castaman, *Firenze*, *Italy*
Raimondo De Cristofaro, *Roma*, *Italy*
Licia Iacoviello, *Pozzilli and Casamassima*, *Italy*
Domenico Prisco, *Firenze*, *Italy*
Anna Randi, *London*, *United Kingdom*

Deputy Section Editors
Emilia Antonucci, *Bologna*, *Italy*
Alessio Branchini, *Ferrara*, *Italy*
Simona Costanzo, *Pozzilli*, *Italy*
Silvia Della Bella, *Milano*, *Italy*
Stefano Lancellotti, *Roma*, *Italy*
Silvia Linari, *Firenze*, *Italy*

Board Members

Walter Ageno, *Italy*
Lina Badimon, *Spain*
Stefano Barco, *Switzerland*
Marina Camera, *Italy*
Caterina Casari, *France*
Alessandro Casini, *Switzerland*
Sergio Coccheri, *Italy*
Valerio De Stefano, *Italy*
Augusto Di Castelnuovo, *Italy*
Giovanni Di Minno, *Italy*
Maria Benedetta Donati, *Italy*
Anna Falanga, *Italy*
Karin Fijnvandraat, *the Netherlands*
Massimo Franchini, *Italy*
Alessandro Gialluisi, *Italy*
Paolo Gresele, *Italy*
Paula James, *Canada*
Andrew D. Johnson, *USA*
Wolfgang Koenig, *Germany*
Maria Elisa Mancuso, *Italy*
Pier Mannuccio Mannucci, *Italy*
Lorenzo Mantovani, *Italy*
Rossella Marcucci, *Italy*
Maurizio Margaglione, *Italy*
Francesco Marongiu, *Italy*
Juan Melero-Martin, *USA*
Angelo Claudio Molinari, *Italy*
Mariasanta Napolitano, *Italy*
Vittorio Pengo, *Italy*
Nicola Pozzi, *USA*
Paolo Prandoni, *Italy*
Alireza Rezaie, *USA*
Marc Righini, *Switzerland*
Bianca Rocca, *Italy*
Francesco Rodeghiero, *Italy*
Luigi Sironi, *Italy*
David Smadja, *France*
Alessandro Squizzato, *Italy*
Saverio Stranges, *Canada*
Hugo TenCate, *the Netherlands*
Alberto Tosetto, *Italy*
Elena Tremoli, *Italy*
Armando Tripodi, *Italy*
Ezio Zanon, *Italy*

Managing Editor
Emanuela Fusinato, *Italy*

The Official Journal of the
Italian Society for the Study of Hemostasis and Thrombosis
SISET
Società Italiana per lo Studio dell'Emostasi e della Trombosi

SISET - Società Italiana per lo Studio dell'Emostasi e della Trombosi

CONSIGLIO DIRETTIVO

Presidente
Giancarlo Castaman, *Firenze*, *Italy*

Vice Presidente
Elvira Grandone, *San Giovanni Rotondo (FG)*, *Italy*

Past President
Valerio De Stefano, *Roma*, *Italy*

Consiglieri
Loredana Bury, *Perugia*, *Italy*
Antonio Coppola, *Parma*, *Italy*
Marina Marchetti, *Bergamo*, *Italy*
Angelo Porfidia, *Roma*, *Italy*

Segretario
Silvia Linari, *Firenze*, *Italy*

XIX CONVEGNO TRIENNALE SUGLI ASPETTI CLINICI E SOCIALI DELL'EMOFILIA



VERONA

15, 16, 17 e 18 OTTOBRE 2026

Camera di Commercio di Verona

Presidente AICE
Dr.ssa Rita Carlotta SANTORO

AICE
Associazione Italiana Centri Emofilia

IDENTIFICATION OF NOVEL HYPERACTIVE RFVIIA BYPASSING MOLECULES INFERRED BY ANCESTRAL SEQUENCE RECONSTRUCTION APPROACH

M.F. Testa, I. Passerini, P. Santos, A. Benazzo, S. Ghirotto, F. Bernardi, A. Branchini, M. Pinotti, D. Balestra

Dep. of LSB, University of Ferrara, Italy

Background and Aims. Recombinant activated factor VII (rFVIIa) is the most common by-passing agents (BPA) licensed for the treatment of HA and HB patients with inhibitors, and it has proven to be safe and efficacious, but its dosing remains problematic. In this view, a hyperactive and/or longer acting rFVIIa variant is highly desirable. Here, we propose novel rFVIIa variants with improved specific activity.

Materials and Methods. We collected FVII homologues of a broad range of species from sequence databases (n=5000), used to perform multiple-sequence alignments. Through the GRASP tool, we inferred a phylogenetic tree considering all species, namely Ancestral Sequence Reconstruction (ASR) approach, mapping the evolutionary relationships among FVII homologs. F7 sequences were restricted to species (n=61) whose evolutionary context suggests potential favored coagulation system. Selected rFVIIa sequences (n=20) were transiently expressed in HEK293 lines, and protein levels analyzed by ELISA and PT/FXa generation assays.

Results. The rFVIIa variants were selected (n=20) from phylogenetic trees composed by 61 contemporary F7 sequences and 59 ASR sequences based on i) structural features (n=12) and ii) ASR-derived sequences (n=8), considering basal and divergency nodes among species. Among expression data of contemporary rFVIIa variants, we identified four out of 12 (var3 FVII:C 148% of WT, var6 FVII:C 66%, var9 FVII:C 360% and var10 FVII:C 110%) showing remarkable higher coagulant activity (3-fold) in PT assays. Evaluation of antigen levels of novel variants (var3 FVII:Ag 123% of WT, var6 FVII:Ag 36%, var9 FVII:Ag 300%, var10 FVII:Ag 59%) clearly demonstrated significantly higher (var3 Sp.Ac:2.0; var6 3.1; var9 2.0;var10 3.2) specific activity compared to rFVIIa WT (1.6). These data were further confirmed by the highly sensitive FXa generation assay resulting in comparable fold (ratio Sp.Ac. variants/Sp.Ac. rFVIIa WT) with PT. Data obtained from expression of ASR variants showed 5 out of 8 nodes with marked coagulant hyperactivity (N10, N11, N18, N28; N30) and significantly higher specific activity compared to rFVIIa WT. Interestingly, we found out that the F7 sequences that one exist in the past with hyperactive features ensue from a basal node between carnivores and cetaceans or primates. In-silico immunogenicity studies are ongoing.

Conclusions. Our data, through the innovative ASR approach, revealed hidden FVII variants with improved features that once existed in the past and promises to redefine the landscape of hemophilia treatment. Importantly, the development of novel rFVIIa variants will enable the exploration of new molecular insights, considering the FVII involvement in several hemostatic pathways.

XIX CONVEGNO TRIENNALE
VERONA
15, 16, 17 e 18 OTTOBRE 2026
Camera di Commercio di Verona
AICE Associazione Italiana Centri Emofilia

XIX Convegno Triennale sugli Aspetti Clinici e Sociali dell'Emofilia ABSTRACT N. BEST-02

3.01 Von Willebrand Factor and von Willebrand Disease

PERIOPERATIVE BLEEDING IN CHILDREN WITH LOW VON WILLEBRAND FACTOR UNDERGOING ADENOID AND TONSIL SURGERY: A 15-YEAR SINGLE-CENTER EXPERIENCE

T. Martini[1], B. Borsellino[1|2], B. Pollio[1]

[1]Haemophilia Centre, Immune-Haematology and Transfusion Medicine, University Hospital "Città della Salute e della Scienza", Torino, Italy; [2]Department of Biomedicine and Prevention, PhD in Immunology, Molecular Medicine and Applied Biotechnology, University of Rome Tor Vergata, Roma, Italy

Background and Aims. Low VWF (von Willebrand Factor) subjects have VWF antigen or activity levels 0.30–0.50 IU/mL; its perioperative significance is, mainly in children, uncertain. Adenoid and tonsil surgery (ATS) represents a clinically relevant model, as bleeding risk may reflect systemic hemostatic impairment, local surgical and fibrinolytic mechanisms. We aimed to evaluate incidence, timing, predictors and management of perioperative bleeding in children with low VWF undergoing ATS, comparing outcomes with a large healthy pediatric controls cohort.

Methods. We conducted a retrospective single-center study including 138 children with low VWF and 1.152 healthy pediatric controls, derived from institutional databases collected between 2010 and 2025 in Regina Margherita Hospital. Collected variables: age, sex, surgery type, family bleeding history, ISTH-BAT (International Society of Thrombosis and Haemostasis Bleeding Assessment Tool) score, VWF:RCo (VWF Ristocetin Cofactor), VWF:Ag (VWF antigen), FVIII (factor VIII), aPTT (activated partial thromboplastin time) ratio and platelet function analyser (PFA) closure times, hemostatic treatment. Primary outcome was intra- and post-operative bleeding (early: 0–48 h; late: day 7–14). Continuous variables were analysed using Mann–Whitney U test, categorical variables with Fisher's exact test.

Results. Low VWF cohort (n=138) was comparable to controls for age and sex. ISTH-BAT≥1 was 8.1% for low VWF (vs 3.9%, p=0.185); family history 15.3% vs 1.1% (p<0.001). Major perioperative bleeding occurred in 5.8% vs 3.0% (p=0.125). In low VWF cohort, no baseline clinical or laboratory parameter predicted bleeding. Bleeding showed bimodal temporal distribution: 70.0% within 48 h, 23.3% day 7–13, 6.7% not defined. Tranexamic Acid (TXA) was the most used hemostatic treatment, ± concentrate or Desmopressin; bleeding incidence does not significantly differ between treatments (table 1). VWF:Ag and VWF:RCo were the main determinants in treatments choice (p<0.05), ISTH-BAT and family history show non-significant tendency.

Conclusions. Low VWF children undergoing ATS show relevant increase of surgical bleeding risk supporting at least having VWF concentrate available in the operating room; bleeding temporal pattern supports coexistence of systemic and local mechanisms (eschar falling). Despite higher prevalence of baseline bleeding phenotype, no clinical or laboratory parameter predicted surgical bleeding; VWF levels were the treatment choice main determinants, together with ISTH-BAT and family history (even if not statistically significant). Despite updated guidelines, the management of VWF deficiency remains a diagnostic and therapeutic challenge, warranting particular caution in pediatric patients.

Treatment	Patients no. (%)	Bleeding no. (%)	Major bleeding no. (%)	Major bleeding p
TXA alone	42 (30.4)	9 (21.4)	3 (7.1)	0.699
TXA+DDAVP	27 (19.6)	5 (18.5)	0 (0)	0.355
TXA+concentrate	44 (31.9)	12 (27.2)	4 (9.1)	0.266
TXA+concentrate on standby	19 (13.7)	5 (26.3)	1 (5.2)	1.000
No treatment	3 (4.4)	1 (33.3)	0 (0)	1.000
Treatment unknown	3 (4.4)	0 (0)	0 (0)	1.000

Table 1. Haemostatic treatments in low VWF patients. TXA: Tranexamic Acid; DDAVP: Desmopressin; concentrate: von Willebrand factor/factor VIII concentrate

XIX CONVEGNO TRIENNALE
VERONA
15, 16, 17 e 18 OTTOBRE 2026
Camera di Commercio di Verona
AICE Associazione Italiana Centri Emofilia

XIX Convegno Triennale sugli Aspetti Clinici e Sociali dell'Emofilia ABSTRACT N. BEST-03

2.07 Novel therapeutic products and approaches (including gene therapy)

CRISPR-CAS9 CORRECTION IN SEVERE HEMOPHILIA A

A. Benetti[1], C.M. Radu[1], M. Trevisan[2], C. Samà[1], C. Simion[1], E. Campello[1], P. Simioni[1]

[1]First Chair of Internal Medicine and Thrombotic and Haemorrhagic Diseases Unit, Department of Medicine, Padova University Hospital, Italy; [2]Department of Molecular Medicine, University of Padua, Italy

Background and Aims. Haemophilia A (HA) is a rare X-linked recessive bleeding disorder caused by variants in the *F8* gene, which encodes coagulation Factor VIII (FVIII). HA is characterized by FVIII deficiency, leading to impaired haemostasis and spontaneous bleeding episodes. In patients with HA, increasing FVIII activity above 2–5% can significantly improve quality of life. The aim of the study is to correct *F8* variant and to restore FVIII expression in a male patient with Severe Haemophilia A through CRISPR–Cas9 Base Editing in Liver Sinusoidal Endothelial Cells (LSECs).

Materials and Methods. Peripheral blood stem cells were isolated and reprogrammed into induced pluripotent stem cells (iPSCs) after transduction with a non-integrative Sendai virus system. The clones obtained were stabilized and their pluripotency was characterised by specific markers such as Oct4, Sox2, Klf4 and Nanog. Gene correction of HA-iPSCs was performed using CRISPR-Cas9 DNA base editing technology targeting the *F8* variant NM_000132.4: c.6967C>T. Following editing, cells were differentiated into LSECs using an optimised differentiation protocol and FVIII expression was assessed by immunofluorescence (IF) and real-time PCR (RT-qPCR).

Results. HA-iPSCs were positive for alkaline phosphatase staining, and IF validated the expression of pluripotency markers. The differentiated LSECs were positive for FCGR2B expression, as assessed by both IF and RT-qPCR. Furthermore, embryoid bodies formation were performed, demonstrating the expression of markers from all three germ layers. FVIII expression in HA-derived LSECs was evaluated before and after gene editing using IF, RT-qPCR, and western blot. The gene correction was confirmed, resulting in approximately 70% restoration of FVIII levels (*Figure 1*).

Conclusions. The iPSCs derived from the severe HA patient were successfully edited, highlighting the potential of CRISPR–Cas9 technology for future patient-specific correction of pathogenic variants. Furthermore, differentiation into LSECs proved to be a relevant and robust in vitro model for evaluating FVIII restoration in HA patients. In conclusion, given the limitations of current treatments, gene therapy may provide a promising and personalized therapeutic approach for these patients.

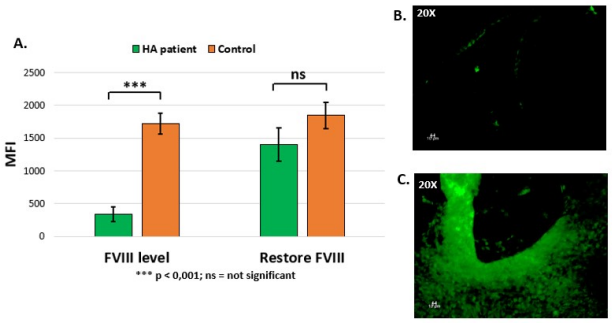


Figure 1: Expression of FVIII before and after base editing. A. IF quantification of FVIII level in HA patient *vs* Control. B. IF HA patient before editing C. IF HA patient after editing.

MAJOR ORTHOPAEDIC SURGERY WITH EMICIZUMAB: A SERIES OF 22 PATIENTS (40 PROCEDURES) WITH A MID TERM FOLLOW-UP

G. Daniele[1], C. Carulli[1], S. Linari[2], L. Pieri[2], G. Castaman[2]

[1]Clinica Ortopedica, Azienda Ospedaliero-Universitaria Careggi, Università degli Studi di Firenze, Italy; [2]Centro Malattie Emorragiche e della Coagulazione, Azienda Ospedaliero-Universitaria Careggi, Firenze, Italy

Introduction. Persons with Haemophilia (PWH) needing orthopaedic surgery have been managed effectively for a long time by a prophylaxis with specific recombinant factors. Recently, emicizumab was introduced for the prophylaxis in PWH with and without inhibitors. However, major orthopaedic surgeries with this regimen have been occasionally performed in very few centers. PURPOSE The aim of the present study is the report of the experience on major orthopaedic surgery with emicizumab at a single Haemophilia center with a mid-term follow-up.

Materials and Methods. Between 2018 and 2026, 22 PWH (10 with high titre inhibitors, 12 without inhibitors) underwent 40 orthopaedic surgeries: two above-the-knee amputations, sixteen Total Knee Arthroplasty (TKA); five Total Hip Arthroplasty (THA); five revision knee arthroplasty (rTKA), two revision hip arthroplasty (rTHA); two pseudotumor excisions; one knee fusion; five partial knee revisions; a knee manipulation under anaesthesia. The mean age of patients was 54.5 years at the time of each procedure (range: 29-69). Prophylaxis consisted in the association of weekly subcutaneous injections of emicizumab and peri-/post-operative boli of rFVIIa (PWH and inhibitors) or rFVIII (PWH without inhibitors). Clinical parameters of evaluation were: VAS, Haemophilic Joint Health Score (HJHS), dedicated imaging. Follow-up was conducted at 1, 3, 6 months, and then yearly.

Results. All patients were successfully treated without any complications during surgery. In the postoperative period, three complications were recorded: a patient, affected by a septic complication two months after his pseudotumor excision, underwent an above-the-knee amputation. Another patient, few days after the TKA, underwent a manipulation under anesthesia for a persisitent knee flexion contracture. Finally, one patient required two blood transfusions for a post-operative anemia after a hip revision. The mean follow-up was 38.86 months (range:3-99). No adverse events were recorded related to the haematological prophylaxis and all patients were regularly rehabilitated and then discharged. The mean hospital stay was 16.55 days (range: 7-46). All patients reported satisfaction, for pain reduction and improved joint and global function, as VAS and HJHS improved scores after surgery confirmed.

Conclusions. Prophylaxis regimen with emicizumab and factor replacement in PWH undergoing major surgery has proved to be safe, ensuring an effective bleeding control and good postoperative clinical outcomes at mid-term follow-up.

XIX CONVEGNO TRIENNALE
VERONA
15, 16, 17 e 18 OTTOBRE 2026
Camera di Commercio di Verona
AICE Associazione Italiana Centri Emofilia

XIX Convegno Triennale sugli Aspetti Clinici e Sociali dell'Emofilia ABSTRACT N. BEST-05

2.01 Hemophilia - clinical and treatment issues

LONG-TERM EMICIZUMAB PROPHYLAXIS IN PEOPLE WITH HEMOPHILIA A: REAL-WORLD EXPERIENCE ACROSS ALL AGES

A. Colombo[1], I. Quaglia[1], M.R. Fasulo[1], C. Lodigiani[1], M.E. Mancuso[1|2]

[1]Center for Thrombosis and Hemorrhagic Diseases, IRCCS Humanitas Research Hospital, Rozzano, Milano, Italy; [2]Department of Biomedical Sciences, Humanitas University, Pieve Emanuele, Milano, Italy

Background and Aims. Emicizumab has provided people with haemophilia A (PwHA) stable bleed protection across inhibitor status and age groups. Nevertheless, a subset of patients continues to experience bleeding despite adequate treatment exposure. This study aimed to evaluate long-term laboratory and clinical outcomes in a real-world setting.

Materials and Methods. All PwHA receiving emicizumab prophylaxis regularly followed up at our Haemophilia Centre were included. Clinical data included type and number of bleeds and physical activity before and after emicizumab start. Physical activity was categorized as: no activity, light-, and moderate/high-impact physical activity. Laboratory data included emicizumab plasma concentration (r2 Diagnostics Inc., South Bend, Indiana, USA) and FVIII-like activity measured by chromogenic assay with human reagents (BiophenTM FVIII:C, Hyphen BioMed, Neuville-sur-Oise, France).

Results. Forty PwHA (97.5% severe; 40% with inhibitors; 30% children) received emicizumab prophylaxis for a median of 5.7 years (IQR 4.4–7.6). During follow-up, 12 patients (30%) were bleed-free, while 28 experienced 121 bleeding episodes (84, 69% joint bleeds; 77, 63% spontaneous). Blood samples were drawn after a median of 5 days since the last emicizumab administration (IQR 2–7; range 1-21). Median emicizumab plasma concentration was 49 µg/mL (IQR 43–59), with a corresponding median FVIII-like activity of 19.6 IU/dL (IQR 16–24). Median emicizumab concentration and FVIII-like activity were similar between bleeders and non-bleeders (47 vs 50.6 µg/ml and 20 vs 19.9 IU/dL, respectively). During emicizumab prophylaxis, the proportion of patients who performed moderate/high-impact activity increased from 15 to 33% and that of sedentary patients decreased from 48 to 25%. Overall, 15 (38%) patients reported increased physical activity intensity after switching to emicizumab.

Conclusions. In this cohort of patients followed-up for a median of 6 years, emicizumab concentration remained consistently within the therapeutic range with a median FVIII-like activity well beyond the threshold of mild haemophilia range. Only 30% of patients remained bleed free, confirming persistent heterogeneity in clinical phenotype and suggesting that emicizumab concentration and/or FVIII-like activity levels do not reflect the haemostatic potential of the drug and cannot be used to inform level of protection against bleeds. Switching to emicizumab favoured increased physical activity suggesting an important impact on patients' lifestyle and functional confidence. Further studies are warranted to investigate how individual haemostatic potential, joint status and lifestyle changes may contribute to improve treatment and monitoring individualization in PwHA on emicizumab.

Abstracts printing tool powered by pagepress.org

XIX CONVEGNO TRIENNALE
VERONA
15, 16, 17 e 18 OTTOBRE 2026
Camera di Commercio di Verona
AICE Associazione Italiana Centri Emofilia

XIX Convegno Triennale sugli Aspetti Clinici e Sociali dell'Emofilia

ABSTRACT N. BEST-06

2.02 Laboratory issues

OPTIMIZING LABORATORY MONITORING OF EFANESOCTOCOG ALFA: IMPACT OF APTT REAGENTS AND CHROMOGENIC ASSAYS ON DIAGNOSTIC ACCURACY

A. Strangio, A. Ierardi, M. Leotta, L.C. Elia, M. Falbo, C. Condina, G. Procopio, R.C. Santoro

Hemophilia Hemostasis and Thrombosis Unit, Azienda Ospedaliero Universitaria Renato Dulbecco, Catanzaro, Italy

Background. Efanesoctocog alfa (FVIII-ULTRA) represents a paradigm shift in hemophilia A treatment as a first-in--class recombinant factor VIII engineered for high, sustained activity. Due to its unique structural modifications—including the fusion of the D'D3 domain of von Willebrand factor and XTEN polypeptides—the molecule presents significant diagnostic challenges. Precise laboratory monitoring is mandatory to validate its pharmacokinetic profile and ensure clinical safety; however, its structural complexity necessitates a rigorous validation of standard laboratory assays to prevent therapeutic misinterpretation.

Methods. FVIII-ULTRA activity was comprehensively evaluated at a 100% nominal concentration and across a six-step dilution series (ranging from 50% down to 5%), using HemosIL Factor VIII deficient plasma (Werfen) as the matrix. Measurements were conducted on a Werfen instrumentation platform employing three distinct analytical methodologies: two one-stage clotting assays (OSA) utilizing SynthASil (SYS) and Synthafax (SFX) reagents, and a chromogenic substrate assay (CA) using the Coamatic reagent. Accuracy was quantified by calculating the percentage deviation from nominal values, supported by a robust statistical analysis of mean deviations and 95% Confidence Intervals (CI) derived from two independent, high-throughput datasets.

Results. The study revealed critical, reagent-specific variations that could impact clinical decision-making. SFX emerged as the most accurate reagent for the high-to-intermediate therapeutic range (10%–100%), demonstrating a negligible mean deviation of only -2.0% at the 50% activity level. In contrast, SYS significantly underestimated activity at higher concentrations, showing a negative deviation of up to -42%. Interestingly, SYS proved superior in precision at the 5% trough level, with a minimal deviation of +6.0%. Notably, the CA consistently and markedly overestimated FVIII activity across the entire spectrum, with deviations reaching a staggering +160%, rendering it potentially unreliable for routine monitoring without specific calibration.

Conclusions. For clinical laboratories utilizing the Werfen platform, SFX is the most reliable reagent for standard therapeutic monitoring where trough levels remain $\ge 10\%$. Conversely, SYS provides a more accurate assessment for lower-range troughs (approx. 5%), which is particularly critical for tailoring prophylaxis in the pediatric population. The dramatic overestimation observed with the CA underscores the urgent need for standardized, reagent-specific protocols. Establishing these guidelines is essential to prevent over--dosing or under-dosing, ensuring the safe and effective long-term management of patients treated with efanesoctocog alfa. For laboratories utilizing the Werfen platform, SFX is the most reliable reagent for standard therapeutic monitoring (trough levels ≥10%). However, SYS may offer a more accurate assessment for lower trough levels (approx. 5%), which are particularly relevant in the pediatric population. The significant overestimation by the chromogenic assay highlights the critical need for reagent-specific protocols to ensure the safe and effective management of patients treated with efanesoctocog alfa.

DATA	FVIII/SYS %	FVIII/SFX %	CROM %
1.	75 (-25%)	99,7(-0,9)	192 (+92%)
2.	30 (-40%)	48 (-4%)	97 (+94%)
3.	14 (-44%)	23 (-8%)	48 (+92%)
4.	11 (-45%)	19 (-5%)	32 (+60%)
5.	9 (-28%)	14 (+12%)	28 (+124%)
6.	8,5 (-15%)	13 (+30%)	15 (+50%)
7.	5,5 (+10%)	6,8 (36%)	10 (+200%)
1.	70 (-30%)	100,5 (+0,5%)	187 (+87%)
2.	31 (-38%)	50 (0%)	99 (+98%)
5.	15 (-40%)	24 (-4%)	57 (+128%)
4.	9 (-55%)	21 (+5%)	39 (+95%)
5.	7 (-44%)	13,7 (+9%)	29 (+132%)
6.	8 (-20%)	11,5 (+15%)	16 (+60%)
7.	5,1 (+2%)	7 (+40%)	11 (+120%)

TAB 1

Initial nominal concentration 100

1. Diluition 1:2 (50%)
2. Diluition 1:4 (25%)
3. Diluition 1:5 (20%)
4. Diluition 1:8 (12,5%)
5. Diluition 1:10 (10%)
6. Diluition 1:20 (5%)

ULTRASOUND EVALUATION AND JOINT SCORING IN MILD HEMOPHILIA A: A SINGLE-CENTER CASE SERIES FOR THE IDENTIFICATION OF SUBCLINICAL ARTHROPATHY

M. Leotta, A. Strangio, R.C. Santoro

Hemophilia Hemostasis and Thrombosis Unit, Azienda Ospedaliero Universitaria Renato Dulbecco, Catanzaro, Italy

Background. Mild Hemophilia A (FVIII 5–40%) is often underestimated, yet patients remain at risk for chronic arthropathy due to subclinical bleeds and trauma. Since the HJHS (physical exam) often misses early damage, this study uses Point-of-Care Ultrasound (POCUS) to detect early synovial and osteochondral changes. The goal is to correlate clinical data, including Body Mass Index (BMI), with ultrasound findings to better assess true joint health.

Materials and Methods. A cross-sectional analysis was conducted on a series of patients with mild hemophilia followed at our Institution in the last year. For each patient, the primary target joints (elbows, knees, and ankles) were evaluated. The HJHS was administered to quantify functional joint impairment. BMI was recorded for all participants to evaluate the impact of body weight on joint health. POCUS scans were performed using the HEAD-US (Hemophilia Early Arthropathy Detection with Ultrasound) protocol. Correlation was assessed between baseline clotting factor levels, BMI, HJHS, and the total HEAD-US score.

Results. A total of 36 mild patients are currently followed at our center; 23 male patients underwent HJHS and HEAD--US within the last 12 months. The median age was 40.6 years (range 12–65) and the mean BMI was 25.73 kg/m^2. The median baseline factor level was 10% (range 5-24%).The median ABR was remarkably low (0.4). The median HJHS score was 7.23 (range 0–16). HEAD-US scoring revealed structural abnormalities in 56.5% of the evaluated patients (13 pz). Notably, within a subgroup of 13 patients particularly susceptible to joint changes, 4 (33.3%) presented both osteostructural alterations and a BMI >25 kg/m^2. Mild synovial hypertrophy was detected in 23% of cases, and significant cartilage thinning was observed in 69% of subjects.

Discussion. Our findings demonstrate that mild hemophilia does not preclude chronic arthropathy, which is more accurately detected by HEAD-US than by HJHS. The significant correlation between age and HEAD-US scores, alongside the impact of BMI >25 on structural damage, suggests that mechanical stress and cumulative trauma, rather than factor deficiency alone, are the primary drivers of joint degradation in this cohort. Consequently, the presence of osteostructural damage in overweight patients emphasizes the critical role of weight management. Integrating routine ultrasound into clinical follow-up allows for a more personalized therapeutic approach.

Conclusions. Systematic HEAD-US evaluation facilitates pre-clinical arthropathy diagnosis in mild hemophilia. Monitoring should integrate periodic imaging and metabolic assessments, such as BMI, to ensure a proactive, personalized strategy that preserves long-term quality of life.

XIX CONVEGNO TRIENNALE
VERONA
15, 16, 17 e 18 OTTOBRE 2026
Camera di Commercio di Verona
AICE Associazione Italiana Centri Emofilia

XIX Convegno Triennale sugli Aspetti Clinici e Sociali dell'Emofilia

ABSTRACT N. BEST-08

3.02 Rare bleeding disorders

PERIOPERATIVE MANAGEMENT OF CHILDREN WITH MILD FACTOR VII DEFICIENCY UNDERGOING SURGERY: A RETROSPECTIVE COHORT STUDY

B. Borsellino[1], T. Martini[1], I. Ricca[2], B. Pollio[1]

[1]Haemophilia Centre, Immune-Haematology and Transfusion Medicine, University Hospital "Città della Salute e della Scienza", Torino, Italy; [2]Transfusion Medicine, Ivrea Hospital, Ivrea, Italy

Background and Aims. Perioperative bleeding risk assessment in children with mild factor VII (FVII) deficiency remains challenging because bleeding history is often uninformative and laboratory parameters correlate poorly with clinical phenotype. Consequently, the optimal use of prophylactic recombinant activated FVII (rFVIIa) before surgery remains uncertain and management varies across centres. We evaluated perioperative bleeding outcomes in children with mild FVII deficiency (FVII activity 20–40%) undergoing surgery and explored factors associated with prophylactic treatment.

Materials and Methods. We retrospectively analyzed 64 consecutive pediatric patients who underwent surgery at Regina Margherita Children's Hospital, Turin, Italy, between January 2017 and February 2020. Procedures included adeno-tonsillar surgery (59.3%), urological surgery (21.9%) and other specialties (18.8%). Patients were managed either with a watch-and-wait strategy, with rFVIIa immediately available in the operating room if abnormal bleeding occurred (n=41), or with prophylactic preoperative rFVIIa administration (n=23). Bleeding phenotype was assessed using the ISTH Bleeding Assessment Tool (BAT): BAT score 0 in 85.9%, 1 in 7.8%, 2 in 4.7% and 3 in 1.6%. Multivariable analyses were performed to identify factors associated with prophylaxis use and perioperative bleeding.

Results. Perioperative bleeding occurred in 3/41 patients (7.3%) managed without prophylaxis, whereas no bleeding events occurred among patients receiving prophylactic rFVIIa (0/23), although the difference did not reach statistical significance (p=0.29). Overall perioperative bleeding prevalence was 4.7% (3/64). Lower baseline FVII activity and lower haemoglobin concentration were independently associated with the decision to administer prophylaxis. Mean FVII activity was significantly lower in the prophylaxis group than in the non-prophylaxis group (30.9±6.4% vs 40.5±6.5%; p<0.0001), as was mean haemoglobin concentration (12.1±1.3 vs 13.0±1.2 g/dL; p=0.03). No independent predictor of perioperative bleeding was identified.

Conclusions. The overall perioperative bleeding prevalence in this cohort was 4.7% (3/64), confirming the insidiousness of FVII deficiency. Both strategies: having rFVIIa immediately available intraoperatively and administering preventive rFVIIa, were effective and safe in children with FVII levels between 20% and 40%. Although the difference in bleeding incidence between strategies did not reach statistical significance, bleeding events occurred only in the untreated group. These findings suggest that a prophylactic approach may be preferable for patients with FVII values below approximately 31%, but confirmation in larger, prospective studies is warranted.

Table 1. Patients' characteristics

	Pts not undergoing FVII prophylaxis (n=41)	Pts undergoing FVII prophylaxis (n=23)
Age range (years)	6.0 ± 3.5	5.7 ± 3.1
Gender (male/female)	26/15	16/7
Type of surgery, no (%):		
• adenoid and tonsil surgery	23 (56.1)	15 (65.2)
• urological surgery	11 (26.8)	3 (13)
• general surgery	1 (2.4)	2 (8.7)
• neurosurgery	2 (4.9)	1 (4.3)
• heart surgery	1 (2.4)	0 (0)
• high airway surgery	1 (2.4)	1 (4.3)
• toracic surgery	0 (0)	1 (4.3)
• ortopedic surgery	2 (4.9)	0 (0)
ISTH-BAT, no (%):		
• 0	37 (90.2)	18 (78.3)
• 1	3 (7.3)	2 (8.7)
• 2	1 (2.4)	2 (8.7)
• 3	0 (0)	1 (4.3)
Perioperative bleeding, no (%)	3 (7.3)	0 (0)

Abstracts printing tool powered by pagepress.org

XIX CONVEGNO TRIENNALE
VERONA
15, 16, 17 e 18 OTTOBRE 2026
Camera di Commercio di Verona
AICE Associazione Italiana Centri Emofilia

XIX Convegno Triennale sugli Aspetti Clinici e Sociali dell'Emofilia ABSTRACT N. BEST-09

2.04 Inhibitors

IMMUNOGENIC IMPLICATIONS OF TRANSLATIONAL READTHROUGH MODULATE THE ASSOCIATION OF F8 NONSENSE MUTATIONS WITH INHIBITORS IN HEMOPHILIA A

D. Balestra[1], M.F. Testa[1], M. Pinotti[1], A. Branchini[1], M.E. Mancuso[2], F. Bernardi[1]

[1]Department of Life Sciences and Biotechnology and LTTA Center, University of Ferrara, Italy; [2]IRCCS, Humanitas Research Hospital, Center for Thrombosis and Hemorrhagic diseases, Milano, Italy

Introduction. In Hemophilia A (HA), nonsense mutations introducing premature termination codons (PTCs) in the F8 gene are a major determinant of inhibitor development, yet they exhibit a wide and often unexplained variation in clinical risk. Translational readthrough (Rdthr) is a molecular mechanism that can override PTCs, producing traces of full-length factor VIII (FVIII). This process may result in the synthesis of either wild-type (WT-Rdthr) or missense proteins, potentially modulating the patient's immune tolerance toward therapeutic FVIII (tFVIII).

Aims. The study aimed to classify F8 nonsense mutations based on their propensity for translational readthrough and to investigate how the predicted protein output and its affinity for HLA-DRB alleles influence the risk of inhibitor formation in HA patients.

Materials and Methods. A total of 335 unique PTCs from 1048 patients in the EAHAD database were analyzed. PTCs were categorized by inhibitor status (from PTCinh=0 to PTCinh≥3). In silico predictions were used to identify PTCs capable of WT-Rdthr (re-insertion of the original amino acid). For PTCs without WT-Rdthr, the binding affinity of predicted missense peptides to 26 common HLA-DRB alleles was calculated using NetMHCII and compared to tFVIII. Experimental validation was performed using recombinant FVIII-luciferase constructs to measure readthrough output in vitro.

Results. WT-Rdthr was significantly more frequent in patients without inhibitors (PTC inh=0, 20.1%) compared to those with inhibitors and was entirely absent in PTCs detected in three or more inhibitor-positive cases (PTC inh≥3, 0%; p=0.0001). PTCs in the light chain (A3-C1-C2 domains) showed lower WT-Rdthr rates and a higher association with inhibitors. Furthermore, for PTCs where only missense variants are produced, the mean differential affinity for HLA-DRB alleles was significantly higher in inhibitor-positive patients than in inhibitor-free cases (p<0.0001). This difference became more pronounced as the number of patients with inhibitors for a specific PTC increased.

Conclusions. The study provides a novel genetic classification for HA nonsense mutations. It demonstrates that both the qualitative nature of readthrough (presence of WT-FVIII) and the immunogenicity of predicted missense variants (HLA-DRB affinity) are critical modulators of inhibitor risk. These findings improve the prediction of personalized inhibitor risk and may be applicable to other genetic diseases caused by PTCs.

XIX CONVEGNO TRIENNALE
VERONA
15, 16, 17 e 18 OTTOBRE 2026
Camera di Commercio di Verona
AICE Associazione Italiana Centri Emofilia

XIX Convegno Triennale sugli Aspetti Clinici e Sociali dell'Emofilia

ABSTRACT N. BEST-10

2.05 Musculoskeletal issues

CHANGES IN HYPERTROPHIC SYNOVIUM STATUS IN ADULT PATIENTS WITH SEVERE HEMOPHILIA A RECEIVING EMICIZUMAB PROPHYLAXIS: THE RESOLVE STUDY

I.L. Calcaterra[1], M. Di Minno[1], E. Baldacci[2], G. D'Errico[1], C. Santoro[2], A. Strangio[3], S. Sorella[2], M. Leotta[3], R.C. Santoro[3]

[1]Department of Clinical Medicine and Surgery, Federico II University, Napoli, Italy; [2]Haematology, University Hospital Policlinico Umberto I, Roma, Italy; [3]Hemostasis and Thrombosis Centre, Azienda Ospedaliero Universitaria Renato Dulbecco, Catanzaro, Italy

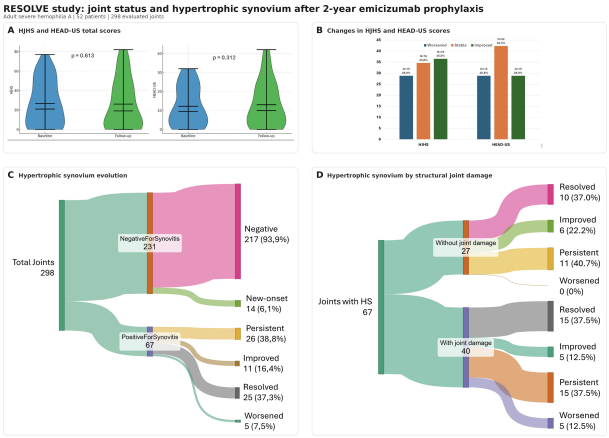
Background. Evidence on the impact of emicizumab on joint health, particularly hypertrophic synovium, remains limited.

Objectives. To evaluate changes in joint status, with a specific focus on HS, using point-of-care ultrasound and clinical examination in PwH switching from replacement therapy to emicizumab.

Methods. The RESOLVE study is a retrospective observational, multicenter cohort study including adults with severe hemophilia A (FVIII <1%), with and without anti-FVIII inhibitors, who started a treatment with emicizumab and were followed for at least 2 years. Clinical data, annualized bleeding rates (ABR, AjBR), HJHS, and HEAD-US assessments were collected during replacement therapy and after ≥2-year emicizumab. HS was graded according to the HEAD-US protocol. Changes in HS represented the primary outcome.

Results. Fifty-two PwH (mean ± SD age: 37.9±12.1years) were enrolled, with data on 298 joints. Emicizumab prophylaxis resulted in a significant reduction in ABR and AjBR compared with replacement therapy, with an increase in patients achieving ABR zero and AjBRzero. At baseline, HS was present in 22.5% of joints. After ≥2-year-emicizumab, HS was improved/resolved in 53.7% of affected joints, while it persisted in 38.8% and worsened in 7.5% of joints. New-onset HS was developed in 6.1% of previously unaffected joints. Baseline structural joint damage was strongly associated with the presence and persistence of HS.

Conclusions. In this real-world setting, emicizumab provides bleeding protection and is associated with reduction/resolution of HS in more than 50% of affected joints. In case of persistent HS, a tailored approach to joint health management may be needed to fully prevent or reverse HS.



XIX CONVEGNO TRIENNALE
VERONA
15, 16, 17 e 18 OTTOBRE 2026
Camera di Commercio di Verona
AICE Associazione Italiana Centri Emofilia

XIX Convegno Triennale sugli Aspetti Clinici e Sociali dell'Emofilia ABSTRACT N. CO-01

1.01 Epidemiology and databases of congenital bleeding disorders

BLEEDING EVENTS IN MILD HEMOPHILIA A AND VON WILLEBRAND DISEASE TYPE 1 YEARLY TREATABLE WITH DESMOPRESSIN IN ITALY

A. Gringeri[1|2], P.M. Mannucci[3], G.C. Castaman[4], F. Peyvandi[3|5]

[1]Fondazione Charta, Milano, Italy; [2]Centro di Sanità Solidale, Lucca, Italy; [3]Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Angelo Bianchi Bonomi Hemophilia and Thrombosis Center and Fondazione Luigi Villa, Milano, Italy; [4]Centre for Bleeding Disorders and Coagulation, Careggi University Hospital, Firenze, Italy; [5]Department of Pathophysiology and Transplantation, Università degli Studi di Milano, Italy

Background. Subcutaneous and intranasal desmopressin is safe and effective in type 1 VWD, and particularly convenient for pediatric use and home treatment. Thus, it can reduce in-hospital admissions and inherent costs, favor adherence and the prompt control of bleeding. Nevertheless, it is often underused or unavailable. We aimed to establish how many patients with mild hemophilia A and VWD type 1 and how many bleeding episodes can potentially benefit from it in Italy.

Methods. The reference population of Italian patients with mild hemophilia A and type 1 VWD was that reported in the National Registry of congenital bleeding disorders. Report 2023 of Istituto Superiore di Sanità (ISS). We reviewed the literature to estimate the bleeding incidence in patients with mild hemophilia A and type 1 VWD. We adopted the rate of responsiveness to desmopressin in VWD type 1 as reported in the metanalysis of Laan et al. (Blood 2025; 145:1814): 0.89 (confidence interval, CI, 0.83-0.93). The rate of DDAVP responsiveness was estimated to be about 80%.

Results. The ISS Report 2023 gave details on 2,085 patients with hemophilia A, of whom 938 had mild severity defects, and on 2,422 patients with VWD, of whom 2069 with type 1. Based on these figures, data on bleeding rates and desmopressin response, we estimated 188 yearly bleeding events in mild hemophilia A and 6,156 in type 1 VWD; of these 5,840 events are represented by heavy menstrual bleeding in 608 women in fertile age (15-49 years). Overall, mild hemophilia A and VWD type 1 patients would successfully be treated with desmopressin for at least 150 and 4,925 yearly bleeding events, respectively.

Conclusions. More than 5,000 bleeding episodes can benefit from desmopressin treatment. This number of bleeding events is based on the number of patients with type 1 VWD and mild hemophilia A reported in the National Registry of Congenital Bleeding Disorders, which collected data from 71% of Italian hemophilia centers only. Consequently, it can be expected that the number of bleeding episodes treatable with desmopressin might be higher. With a higher availability of intranasal and subcutaneous desmopressin a huge number of bleeding events in VWD type 1 can be treated successfully, safely and economically, thus reducing the use of costly replacement therapies. It has been an estimated (Gringeri & Castaman: Italian resource use in mild hemophilia A and type 1 von Willebrand disease. 2026: this abstract book) an overall annual expenditure of 29.6 million € for the procurement of 61 million IU FVIII concentrates. These figures include use of desmopressin for diagnosis, surgery, childbirth, the preemptive use for trauma or bleeding prophylaxis, in addition to the bleeding episodes that we considered.

XIX CONVEGNO TRIENNALE
VERONA
15, 16, 17 e 18 OTTOBRE 2026
Camera di Commercio di Verona
AICE Associazione Italiana Centri Emofilia

XIX Convegno Triennale sugli Aspetti Clinici e Sociali dell'Emofilia ABSTRACT N. CO-02

1.02 Genetics of congenital bleeding disorders (including prenatal diagnosis)

NEONATAL GENOMIC SCREENING ENABLES PRE-SYMPTOMATIC DIAGNOSIS AND PREVENTIVE MANAGEMENT OF HEMOPHILIA

B. Borsellino[1], B. Pollio[1], P. Quarello[2|3], T. Martini[1], C. Linari[4], M. Carabotta[5], C. Cagnazzo[2], S. Minucci[6], F. Fagioli[2|3]

[1]Paediatric Haemophilia Centre, Immune-Haematology and Transfusion Medicine, University Hospital "Città della Salute e della Scienza", Torino, Italy; [2]Paediatric Onco-Hematology, Stem Cell Transplantation and Cellular Therapy Division, Regina Margherita Children's Hospital, Torino, Italy; [3]Department of Paediatric and Public Health Sciences, University of Turin, Italy; [4]Department of Laboratory Medicine, Azienda Ospedaliera Universitaria Città della Salute e della Scienza, Torino, Italy; [5]Department of Pediatrics, G. d'Annunzio University, Chieti, Italy; [6]Italian Institute for Genomic Medicine, IRCCS, Candiolo, Italy

Background and Aims. Haemophilia A and B are X-linked bleeding disorders caused by factor VIII or IX deficiency. In newborns without a known family history, diagnosis is often delayed until a bleeding event occurs, exposing infants to potentially severe complications, including intracranial haemorrhage. Although genomic newborn screening programmes are rapidly expanding, evidence regarding their role in inherited bleeding disorders remains limited. We evaluated the feasibility, diagnostic yield and clinical impact of including haemophilia in a population-based neonatal genomic screening programme.

Materials and Methods. Newborns born at Sant'Anna Hospital (Turin, Italy) between October 2023 and July 2024 were prospectively enrolled in the NeoGen study (IRB 278/2023). Whole-exome sequencing (WES) was performed on DNA extracted from dried blood spots. Infants carrying pathogenic or likely pathogenic variants in F8 or F9 underwent haematological assessment, genetic counselling, coagulation testing, molecular confirmation and family segregation studies. Parental psychological outcomes were evaluated using validated questionnaires.

Results. Among 4,054 screened newborns, 11 carried pathogenic or likely pathogenic variants in F8 or F9 (5 males, 6 females). Seven variants involved F8 and four F9. All three males carrying F9 variants were confirmed to have haemophilia B, including one infant with severe disease diagnosed before symptom onset who started primary prophylaxis before any major bleeding event. Two males carrying F8 variants had normal factor VIII levels and their variants were subsequently reclassified as variants of uncertain significance. All assessed female infants remained asymptomatic. Two premature twin boys with severe haemophilia A were not identified by WES but were investigated after prolonged bleeding following heel-prick sampling and subsequently diagnosed with F8 intron 1 inversion, a structural variant not detectable by short-read sequencing. Parents reported moderate distress but high levels of understanding of the information provided.

Conclusions. Neonatal genomic screening can identify children with haemophilia before clinical presentation and enable earlier preventive management. To our knowledge, this is the first reported case in which neonatal genomic screening led to initiation of primary prophylaxis before any major bleeding event. Our findings also highlight the limitations of short-read sequencing for detecting recurrent structural F8 rearrangements. Combining genomic screening with coagulation testing, targeted molecular analyses and emerging long-read sequencing technologies may overcome these limitations and improve diagnostic yield, supporting a shift from reactive to preventive haemophilia care.

XIX CONVEGNO TRIENNALE
VERONA
15, 16, 17 e 18 OTTOBRE 2026
Camera di Commercio di Verona
AICE Associazione Italiana Centri Emofilia

XIX Convegno Triennale sugli Aspetti Clinici e Sociali dell'Emofilia ABSTRACT N. CO-03

1.02 Genetics of congenital bleeding disorders (including prenatal diagnosis)

BEYOND CONVENTIONAL TESTING: NANOPORE LONG-READ SEQUENCING FOR RECURRENT F8 INVERSIONS IN HEMOPHILIA A

A. Taiani[1|2], F. Riccardi[1], L. Cozzuto[4], A. Delgado[4], S. Busciglio[1|2], G. Quintavalle[1], A. Matichecchia[1], I. Tassoni[1], B.M. Roccon[1], I. R. Cannizzaro[2], A. Luberto[2], J. Ponomarenko[4], A. Percesepe[3], V. Barili[2], A. Coppola[1]

[1]Regional Hub Center for Hemophilia and Congenital Bleeding Disorders, University Hospital of Parma, Italy; [2]Medical Genetics, Department of Medicine and Surgery, University of Parma, Italy; [3]Medical Genetics, University Hospital of Parma, Italy; [4]Centre Genomic Regulation, CRG, Barcelona, Spain

Background and Aims. Haemophilia A is an X-linked bleeding disorder caused by pathogenic variants in F8. In severe disease, recurrent inversions involving intron 22 and intron 1 represent major molecular defects, but their detection and characterization remain challenging because of homologous repeated sequences and the structural complexity of the F8 locus. Conventional assays may have limited reproducibility and do not directly resolve the genomic architecture of the region. This pilot study aimed to validate an Oxford Nanopore Technologies long-read sequencing workflow for the direct characterization of recurrent F8 inversions. The project was developed with the support of the "Idee Giovani per la Ricerca Ed. 2025" award, with the goal of exploring long-read sequencing as a flexible approach for molecular diagnosis in Haemophilia A.

Materials and Methods. Three male patients with clinical Haemophilia A and recurrent F8 inversions were analyzed, including two cases carrying the intron 22 inversion and one case carrying the intron 1 inversion. Genomic DNA from peripheral blood was quality assessed and used for long-read library preparation. Sequencing was initially performed on MinION and subsequently optimized on PromethION using adaptive sampling. A dedicated Oxford Nanopore long-read analysis pipeline was developed and optimized for this study. Following Dorado basecalling, reads were aligned to the GRCh38 reference genome using minimap2. Structural variants were detected with Sniffles2 and SNVs/indels were called with Clair3. Variant annotation was performed using AnnotSV and ANNOVAR, while structural rearrangements were validated through manual breakpoint inspection in IGV.

Results. The workflow successfully resolved the molecular defect in all three patients. In the two intron 22 inversion cases, long-read sequencing confirmed the rearrangement, showed concordance with conventional molecular methods and enabled discrimination of the molecular inversion subtype. In the intron 1 inversion case supported direct interpretation of the affected genomic region. Overall, long-read sequencing allowed direct inspection of the F8 locus, supporting reconstruction of the rearranged architecture and orientation of the involved regions providing a comprehensive molecular assessment of the locus.

Conclusions. This pilot study demonstrates the feasibility of Nanopore long-read sequencing for the molecular diagnosis of Haemophilia A. The workflow enabled direct detection and characterization of recurrent F8 inversions, including intron 22 and intron 1 inversions, highlighting its added value over conventional approaches. This strategy provides a starting point for extending long-read sequencing to other forms of haemophilia and genetically complex inherited bleeding disorders.

XIX CONVEGNO TRIENNALE
VERONA
15, 16, 17 e 18 OTTOBRE 2026
Camera di Commercio di Verona
AICE Associazione Italiana Centri Emofilia

XIX Convegno Triennale sugli Aspetti Clinici e Sociali dell'Emofilia ABSTRACT N. CO-04

1.02 Genetics of congenital bleeding disorders (including prenatal diagnosis)

INTEGRATING EXPERTISE: IMPLEMENTATION OF A MULTIDISCIPLINARY PATHWAY FOR GENETIC TESTING AND COUNSELLING IN INHERITED BLEEDING DISORDERS

E. Zacchi[1|2], L. Piscitelli[1], C. Manzi[1], L. Godino[2], F. Riccardi[3], A. Vaisfeld[2|4], L. Valdrè[1]

[1]Inherited Bleeding Disorders Unit, IRCCS AOUBO, Bologna, Italy; [2]Medical Genetics Unit, IRCCS AOUBO, Bologna, Italy; [3]Regional Hub Centre for Hemophilia and Inherited Bleeding Disorders, University Hospital of Parma, Italy; [4]Department of Medical and Surgical Sciences, University of Bologna, Italy

Background. the growing availability of genetic testing has expanded its use across many genetic diseases, including inherited bleeding disorders (IBDs), beyond diagnostic confirmation to prenatal, pre-implantation and preconception settings. Patient and family awareness has also increased, leading to greater demand for genetic evaluation. This scenario increasingly requires integration of the expertise of IBDs clinicians and clinical and laboratory geneticists to optimize test indication, interpretation and counselling.

Aims. to describe a multidisciplinary pathway for genetic testing and counselling in IBDs and preliminary results from its implementation in a single center.

Materials and Methods. retrospective descriptive evaluation of the integrated pathway instituted since 2023. The project started with meetings involving medical and nursing staff from the IBDs Unit and the Medical Genetics Unit to identify practical needs, clinical and organizational issues, to define a shared workflow, later formalized as an institutional procedure.

Results. access to genetic testing is provided through dedicated weekly appointments within the Medical Genetics Unit for patients referred by the IBDs Unit clinicians. A shared digital repository was created for document sharing. At first genetic appointment, pedigree reconstruction, informed consent and sample collection are performed. Molecular analyses are centralized to the regional hub reference laboratory. Results are discussed within the multidisciplinary team and returned in a post-test counselling led by a medical geneticist, also enabling identification and referral of at-risk relatives. Dedicated slots are available for specific indications such as preconception counselling. To date, about 85 probands with hemophilia, von Willebrand disease (VWD) or rare bleeding disorders have been managed. Results are so far available for 61. Pathogenic or likely pathogenic variants were identified in 40 cases, allowing diagnostic confirmation or redefinition (e.g. differential diagnosis between VWD and mild hemophilia in 3 cases). In 9 patients no variants were found, while 12 showed variants of unknown significance (VUS), with challenging clinical interpretation. Twenty-six relatives were evaluated: 15 in families with pathogenic variants, for diagnostic confirmation or mainly for potential hemophilia carrier detection, and 11 for segregation studies, together with coagulation assessment, to support VUS interpretation and possible reclassification.

Conclusions. this experience highlights the value of a structured approach to genetic testing and counselling. Close collaboration among specialists improved organization of diagnostic workflow and enhanced integration of expertise, supporting shared clinical and counselling management.

XIX CONVEGNO TRIENNALE
VERONA
15, 16, 17 e 18 OTTOBRE 2026
Camera di Commercio di Verona
AICE Associazione Italiana Centri Emofilia

XIX Convegno Triennale sugli Aspetti Clinici e Sociali dell'Emofilia ABSTRACT N. CO-05

1.02 Genetics of congenital bleeding disorders (including prenatal diagnosis)

IN SILICO ANALYSIS THROUGH A NEWLY GENERATED FACTOR VIII MODEL SUPPORTS TOLERANCE OF B DOMAIN TO MULTIPLE AMINO ACID SUBSTITUTIONS LIMITING THE LOCAL IMPACT OF MISSENSE VARIANTS

A. Branchini[1], M.F. Testa[1], M. Pinotti[1], R. De Cristofaro[2|3]

[1]Department of Life Sciences and Biotechnology, University of Ferrara, Italy; [2]Department of Translational Medicine and Surgery, Catholic University of the Sacred Heart, Roma, Italy; [3]Center for Hemorrhagic and Thrombotic Diseases, Foundation University Hospital "A. Gemelli" IRCCS, Roma, Italy

Background and Aims. Missense variants, a relevant haemophilia A (HA) cause, are scarcely reported in the large factor VIII (FVIII) B domain (3%) that, among FVIII domains, remains the least-characterized and structurally unresolved. Here, to provide insights into the impact of multiple amino acid substitutions in B domain at a single-residue scale, we performed systematic *in-silico* analyses through a newly generated FVIII model ($FVIII_{IT}$) with assembled B domain.

Methods. Generation of the $FVIII_{IT}$ model by the I-TASSER tool and integrated *in-silico* analysis through DDmut (protein stability) and REVEL (variant pathogenicity) tools.

Results. HA missense variants are mainly reported in FVIII A1-A2-A3-C1-C2 (A1-A3, 77%; C1-C2, 20%; hereafter A1-C2), particularly those associated with severe HA as highlighted by frequency normalized per domain size (A1-C2, 0.36-0.49; B, 0.02). The newly generated $FVIII_{IT}$ model was first validated for resolved A1-C2 domains towards reference structures by an alanine scanning approach, showing minor impact when extended to B domain. Noticeably, a mutational scanning at a single-residue scale mimicking all possible single-nucleotide changes resulting in missense variants (total >15,000; >6,0000 in B domain) showed significant differences ($p<0.0001$) between B and A1-C2 domains, with lower predicted impact for a high proportion (~90%) of B-domain variants. Single-nucleotide changes are also associated with clinically relevant nonsense mutations, causing premature termination codons (PTCs), whose suppression by the so-called translational readthrough (TRT) may result in full-length proteins bearing subsets of amino acid substitutions. A three-level and progressively refined analysis, validated in relation to experimentally obtained data, revealed significantly higher values for B-domain TRT-deriving missense variants arising from i) either possible (n=2439) or HA (n=1094) PTCs, corresponding to 2439/1094 (B, n=1007/396) predicted missense variants, ii) possible (n=457) or HA (n=190) PTCs, corresponding to 1371/570 (B, n=651/228) predicted missense variants, at which TRT-mediated re-insertion of the original amino acid is not predicted, and iii) PTCs at tryptophan positions (possible/HA, n=35/31) at which missense changes (n=114/105; B, n=27) are expected to be detrimental, as in A1-C2 domains, while overlapping missense changes are not reported in B domain.

Conclusions. Altogether, these original insights, obtained by rational $_{\text{in-silico}}$ analyses through the newly generated FVIII-IT model, may contribute evidence toward the hypothesis that B domain is tolerant to multiple amino acid changes, supporting potential underestimation of HA-associated B-domain missense variants due to limited local impact of amino acid substitutions.

1.03 Health and social economics, organizational issues

ENHANCING SHARED DECISION-MAKING IN INHERITED BLEEDING DISORDERS: A SINGLE-CENTER QUALITY IMPROVEMENT INITIATIVE

C. Manzi, L. Piscitelli, E. Zacchi, V. Caldi, L. Valdrè

Inherited Bleeding Disorders Unit IRCCS AOU, Bologna, Italy

Background. Shared Decision-Making (SDM) is a collaborative process in which healthcare professionals and patients jointly make decisions based on clinical evidence and patient preferences. Adequate patient knowledge is essential for effective SDM. However, even in specialized Inherited Bleeding Disorders Centers, patients may have limited understanding of their condition and treatment, reducing active participation in care.

Aims. To describe a single-center quality improvement (QI) initiative aimed at improving patient participation through structured written informational materials supporting clinician–patient discussions and disease awareness.

Materials and Methods. A multidisciplinary team of physicians and nurses identified the need for improved patient education and developed a formal QI initiative. During a 4-month preparatory phase (January–April 2026), patient informational needs were assessed and materials drafted, reviewed, validated, and integrated into the institutional documentation system. A 2-year implementation phase followed (May 2026–May 2028). The initiative was approved by the Forensic Medicine Service. Outcome measures include percentage of available materials for each bleeding disorder and proportion of patients receiving them during visits.

Results. Twenty informational documents were developed covering hemophilia A and B, hemophilia carriers, von Willebrand disease and subtypes, rare bleeding disorders and platelet disorders. Documents include information on disease characteristics, treatment options, daily-life recommendations, management in surgical or emergency settings, drugs to avoid and follow-up schedules. Materials also encourage patient participation in SDM, include a section for patient notes or questions, and provide final signatures from patient and physician to formalize shared understanding. Materials are delivered at diagnosis or at follow-up visits, with distribution recorded in the medical record and copies archived in a dedicated repository. During the first month of implementation, 16 patients received the materials. Limitations include the short observation period and absence at present of a standardized tool planned to assess effects on patient empowerment.

Conclusions. This initiative highlights the value of structured informational tools in supporting SDM in inherited bleeding disorders. Nurse involvement was essential during both development and implementation, underlying a central role in patient education, facilitation of understanding, promotion of adherence, and communication with the team. A multidisciplinary approach in developing informational materials is a feasible strategy to improve patient awareness and participation in care, and may facilitate SDM in the clinical practice.

XIX CONVEGNO TRIENNALE
VERONA
15, 16, 17 e 18 OTTOBRE 2026
Camera di Commercio di Verona
AICE Associazione Italiana Centri Emofilia

XIX Convegno Triennale sugli Aspetti Clinici e Sociali dell'Emofilia ABSTRACT N. CO-07

1.03 Health and social economics, organizational issues

ITALIAN RESOURCE USE IN MILD HEMOPHILIA A AND TYPE 1 VON WILLEBRAND DISEASE

A. Gringeri[1|2], G.C. Castaman[3]

[1]Fondazione Charta, Milano, Italy; [2]Centro di Sanità Solidale, Lucca, Italy; [3]Centre for Bleeding Disorders and Coagulation, Careggi University Hospital, Firenze, Italy

Introduction. Hemophilia A and von Willebrand disease (VWD) are the most common inherited bleeding disorders, resulting from low or dysfunctional factor VIII (FVIII) and von Willebrand factor (VWF), respectively. The purpose of the following analysis is to quantify the potential savings through desmopressin (DDAVP) use in terms of pharmaceutical costs alone (costs for concentrates) , specifically for the treatment of those forms of von Willebrand disease (VWD) and hemophilia with high rates of DDAVP responsiveness, namely type 1 VWD and mild Hemophilia A. In fact, treatment of these disorders has relied mostly on desmopressin, which use however has been significantly reduced over the recent years due to reduced production and supply.

Methods. This analysis is based on official 2023 data of the Italian Registry of Congenital Bleeding Disorders (Registry), published in 2025by the Italian National Blood Center (CNS) and by the National Reports on Medicines use in Italy on medicine expenditure referring to 2024 of the Italian Agency of Medicine (AIFA) OsMed.

Results. In Italy, CNS reported an annual consumption in 2023 of 536 million IU of FVIII concentrates, which includes toll fraction concentrates. A total expenditure in 2024 of 310 million € corresponding to 497 million IU has been reported by AIFA. Of these, 83% are recombinant FVIII products used by patients with hemophilia A only. The remaining 17% is represented by pure plasma FVIII (8%), FVIII/VWF products (8%) and pure VWF products (1%). Mild hemophilia A patient treatment represents 7.4% of overall factor consumption, predominantly recombinant products (97%), with an estimated overall expenditure of 22.9 million €. Type 1 VWD patient treatment includes 3% of overall factor consumption, that is 29% of plasma-derived products with an estimated expenditure of 6.7 million €.

Discussion. Current care of mild hemophilia A and type 1 VWD (4,800 estimated patients in Italy) relies largely on the use of intravenous concentrates, with an estimated annual expenditure of 29.6 million € to cover the consumption of 61 million IU (with an average cost of 0.48 €/IU). Improved access to subcutaneous and intranasal desmopressin (DDAVP) and guideline-concordant first-line use in eligible patients could optimize management in responders (reported response rate >80%) and reduce concentrate use and related increased costs. Moreover, it can reduce other direct and indirect costs due to the need to access outpatient clinic for IV infusion and potentially improve quality of life through home treatment.

Abstracts printing tool powered by pagepress.org

XIX CONVEGNO TRIENNALE
VERONA
15, 16, 17 e 18 OTTOBRE 2026
Camera di Commercio di Verona
AICE Associazione Italiana Centri Emofilia

1.03 Health and social economics, organizational issues

IMPLEMENTING A HUB-AND-SPOKE MODEL FOR HEMOPHILIA DIAGNOSIS AND CARE IN BURKINA FASO THROUGH TRAINING OF "HEALTH ASSISTANTS"

C. Gorio[1], E. Kafando[2], A. Buzzi[3]

[1]Oncohematology Unit ASST Spedali Civili Brescia, Italy; [2]Centre Hospitalier Universitaire Charles de Gaulle, Italy; [3]Fondazione Paracelso ETS, Milano, Italy

Background. While haemophilia care has advanced in high-income countries via prophylaxis, multidisciplinary management, and individualized therapies, low-resource settings still face major barriers to access, care coordination, and diagnosis. Burkina Faso is one of the countries classified by the World Bank as a low-income economy (most of them located in Africa)

Aims. to implement and describe a context-adapted model to expand disease awareness, improve case finding, and structure care pathways for haemophilia in Burkina Faso.

Materials and Methods. Training "health assistants", focal points at peripheral Health Centers, often located in remote villages. Developing pictorial educational materials accessible to populations with high illiteracy rates. Community sessions at Health Centers to recognize bleeding symptoms (e.g., excessive bleeding after circumcision) Hub-and-spoke pathway: referral of suspected cases to the nearest spoke hospital for first-line testing; if abnormal/suspected, referral to the HUB (Charles De Gaulle Hospital, Ouagadougou) for specific diagnostics and care initiation; subsequent follow-up at spoke centers with semi-annual then annual visits; ongoing HUB–spoke collaboration to enable care near patients' homes.

Results. Following implementation and increased availability of diagnostic supplies, 13 new patients with haemophilia A were diagnosed between December 2025 and April 2026.

Conclusions. Training proximal health personnel within a hub-and-spoke framework, supported by pictorial education and reliable access to diagnostic kits, enhances case detection and care for haemophilia in low-resource settings. Sustained resource allocation for diagnostics is essential for consolidation and scale-up.

XIX CONVEGNO TRIENNALE
VERONA
15, 16, 17 e 18 OTTOBRE 2026
Camera di Commercio di Verona
AICE Associazione Italiana Centri Emofilia

XIX Convegno Triennale sugli Aspetti Clinici e Sociali dell'Emofilia ABSTRACT N. CO-09

1.03 Health and social economics, organizational issues

THE POSSIBLE ROLE OF THE PSYCHOLOGIST IN THE MANAGEMENT OF PATIENTS WITH CONGENITAL BLEEDING DISORDERS: THE EXPERIENCE OF A SINGLE HEMOPHILIA CENTER

D. Meneghini[1], E. Tosi[1], B. Pernice[2], L. Del Piccolo[2], M. Bodini[1], A.C. Giuffrida[1]

[1]Transfusion Medicine Dep., Integrated University Hospital, Verona, Italy; [2]Dep. of Neurosciences, Biomedicine and Movement Sciences, University of Verona, Italy

Background and Aims. Patients with Congenital Bleeding Disorders (CBDs) face numerous challenges throughout their lives: the management of bleeding episodes and prophylaxis, which, despite considerable progress, still requires continuous psychological engagement in daily life. Additional challenges include adapting to the different life stages, from childhood to old age, and maintaining participation in social activities. Psychological support therefore becomes crucial, however requiring ongoing specialist education and development for practice in the field of bleeding disorders. A psychologist could also be of benefit to healthcare professionals within the team, in particular physicians and nurses, by helping them to manage chronic conditions and enabling them to provide optimal support to both patients and caregivers.

Materials and Methods. In 2025 the University Hospital of Verona implemented a psychological support service for healthcare professionals working within the HC, with several objectives including group training in the communication with patients and caregivers. Following an initial meeting between the medical director and the psychologist assigned to the HC, a second meeting involved all physicians and nurses dedicated to the care of people with CBDs. Subsequently, monthly meetings were specifically organized to discuss issues related to selected patients with CBDs.

Results. During the first two meetings, the congenital bleeding disorders managed at the HC, treatment-related challenges and the difficulties experienced by patients in their daily lives, were explored. Simultaneously, the needs expressed by healthcare professionals in coping with congenital bleeding disorders and addressing patients' needs were discussed. In particular, the need emerged to identify tailored strategies for dealing with the different personalities and behavioural patterns displayed by patients. Over three dedicated sessions, 5 patients (4 with severe hemophilia and 1 with mild FVII deficiency) were discussed. The discussions focused on how patients presented themselves to the HC team, and on the needs that emerged in relation to their disease. The psychologist also highlighted the feelings experienced by professionals towards patients, including anger (for example in case of therapeutic non-adherence) or difficulty relating to the patient. Finally, the group work identified potential strategies to improve the relationship between the team and patients, as well as the individualized patient management.

Conclusions. The psychologist represents a key member of the multidisciplinary HC, supporting patients and their caregivers in disease management, and promoting the education of the team, with the aim of optimizing communication with patients and caregivers.

Abstracts printing tool powered by pagepress.org

XIX CONVEGNO TRIENNALE
VERONA
15, 16, 17 e 18 OTTOBRE 2026
Camera di Commercio di Verona
AICE Associazione Italiana Centri Emofilia

XIX Convegno Triennale sugli Aspetti Clinici e Sociali dell'Emofilia ABSTRACT N. CO-10

1.03 Health and social economics, organizational issues

APPLICATIONS OF ARTIFICIAL INTELLIGENCE IN HEMOPHILIA MANAGEMENT: INNOVATIONS AND FUTURE PERSPECTIVES

A. Ierardi, M. Leotta, A. Strangio, S. Prejanò, R.C. Santoro

UO Hemophilia, Hemostasis and Thrombosis. Azienda Ospedaliero Universitaria Renato Dulbecco, Catanzaro, Italy

Background. Hemophilia care requires a highly personalized paradigm. Despite EHL products, individual PK variability and bleeding phenotypes remain challenging. AI integration now enables a shift from reactive management to a predictive, precision-based clinical strategy. This study hypothesis intends to examine the transformative role and possible applications of AI within the multidisciplinary management of hemophilia, focusing on the optimization of prophylaxis, prevention of joint damage, and enhancement of therapeutic adherence. and its possible applications.

Methods and Areas of Application. *Predictive Analytics and Risk Stratification.* The use of supervised learning algorithms enables the analysis of complex datasets integrating clinical history, baseline factor levels, bleeding phenotypes, and physical activity. Developing predictive models allows for the early identification of patients at higher risk of breakthrough bleeding, facilitating targeted preventive interventions. *Clinical Pharmacokinetics and Personalization.* AI-based systems transcend the limitations of classical pharmacokinetic models by allowing for the dynamic modulation of infusion regimens. Through continuous monitoring, AI facilitates real-time dosage adjustments, optimizing factor consumption while ensuring maximal hemostatic protection. AI-Enhanced Joint Ultrasonography and Structural Damage Assessment The integration of AI into point-of-care ultrasound allows for a standardized and objective evaluation of joint health, even when performed at the patient's home. Beyond detecting synovial hypertrophy and early effusions, advanced AI algorithms can accurately quantify cartilage degeneration (thinning and loss of homogeneity) and identify early subchondral bone damage (erosions and osteophytes). By automating the interpretation of these parameters, AI eliminates operator subjectivity with high precision. *Digital Health and Patient Engagement.* Advanced mobile apps and AI interfaces streamline the collection of Patient-Reported Outcomes (PROs). AI chatbots and virtual assistants enhance treatment adherence through smart reminders and real-time educational support, effectively reducing the psychological burden of disease management.

Results. AI-guided protocols significantly reduce Annualized Bleeding Rates (ABR) and chronic arthropathy. This improves Quality of Life (QoL) by increasing patient autonomy and reducing the uncertainty of unforeseen bleeding events.

Conclusions. Artificial Intelligence is not a substitute for clinical judgment but rather a powerful ally in the multidisciplinary team's decision-making process. Future perspectives include the integration of genomic data and digital biomarkers to foster a hemophilia care model that is increasingly personalized, safe, and sustainable for healthcare systems.

Abstracts printing tool powered by pagepress.org

XIX CONVEGNO TRIENNALE
VERONA
15, 16, 17 e 18 OTTOBRE 2026
Camera di Commercio di Verona
AICE Associazione Italiana Centri Emofilia

XIX Convegno Triennale sugli Aspetti Clinici e Sociali dell'Emofilia ABSTRACT N. CO-11

1.03 Health and social economics, organizational issues

MAPPING THE COMPETENCIES OF NURSES IN ITALIAN HEMOPHILIA CENTRES (HCS): CURRENT STATUS AND PERSPECTIVES FOR THE IDENTIFICATION OF NURSE-SENSITIVE OUTCOMES

M.V. Puliga[1], A.C. Ferrini[2], C. Manzi[3], D. Meneghini[4], E. Tosi[4], P. Berto[5], M. Amelotti-Botta[6], E. Quercio[6], M.E. Mancuso[7], R.C. Santoro[8]

[1]SODc Malattie Emorragiche e della Coagulazione, AOU Careggi, Firenze, Italy; [2]SSI Malattie Emorragiche e Tromboemboliche, Osp. Bufalini, Cesena, Italy; [3]SSD Malattie Emorragiche Congenite, IRCCS Policlinico Sant'Orsola, Bologna, Italy; [4]Centro Emofilia e UOC Medicina Trasfusionale, AOU Integrata, Verona, Italy; [5]Centro Emofilia Hub, AO di Padova, Italy; [6]SSD Emostasi e Coordinamento Malattie Rare, AO SS. Antonio e Biagio, Alessandria, Italy; [7]UOC Centro Trombosi e Malattie Emorragiche, IRCCS Humanitas Research Hospital, Rozzano, Milano, Italy; [8]UOD Emofilia, Emostasi e Trombosi, AOU Renato Dulbecco, Catanzaro, Italy

Background and Aims. Congenital Bleeding Disorders (CBDs) require a multidisciplinary approach in which nurses play a key role in patients' clinical, educational, and organisational management. Despite significant therapeutic and healthcare advances in haemophilia care, scientific evidence regarding specialist nursing competencies and nurse-sensitive outcomes remains limited. The AICE Nursing Working Group analysed the current nursing organisation within Italian HCs by investigating nursing skills and activities.

Materials and Methods. In 2024, the AICE Nursing Working Group distributed a national survey to the directors of Italian HCs. The questionnaire collected data on centre organisation, the presence (or absence) of dedicated nurses, training pathways, professional experience, and the main nursing activities performed.

Results. Thirty centres throughout Italy responded to the survey: 17 HCs (56.7%) cared for patients of all ages, 7 (23.3%) mainly adults, and 4 (13.3%) mainly children; data were missing for two centres. Twenty-one HCs (70%) reported nurses simultaneously caring for other patient groups during the same shift, while 3 (10%) reported the presence of nurses exclusively dedicated to CBDs. In 14 HCs (46.7%), nurses were not subject to periodic rotation, contributing to greater continuity of care. In terms of professional experience, 10 HCs (33.3%) reported nursing experience of 5–15 years, while six (20%) reported experience exceeding 15 years. Nursing activities were broad and multidisciplinary: 13 HCs (43.3%) reported nurse involvement in appointment scheduling and agenda management; 12 (40%) in the administrative management of clinical documentation and healthcare-related telephone support; 18 (60%) in monitoring pharmaceutical stock; and 18 (60%) in providing education to patients and caregivers. Collaboration with hospital pharmacies was reported in 16 centres (53.3%). Regarding training pathways, competencies were acquired primarily "on the job" in 15 HCs (50%); only 2 (6.7%) reported exclusively specialist training dedicated to CBDs, while 9 (30%) combined both approaches. In 15 HCs (50%), a specific training programme was available for newly recruited staff. Participation in internal educational courses dedicated to CBDs was reported in 14 HCs (46.7%), and the same proportion reported participation in specialised external courses.

Conclusions. Nurses play a fundamental role within the multidisciplinary teams of Italian HCs. This survey confirms their strategic importance and highlights the need to define specific competencies, dedicated educational pathways, and measurable nurse-sensitive outcomes.

Table 1. National survey conducted in Italian Haemophilia Centres

	No. of HCs (%)		
Total No. of nurses involved in HC activities (including occasional staff)	< 5 nurses: 18 (60%)	5-10 nurses: 5 (16.7%)	> 15 nurses: 1 (3.3%)
No. of nurses dedicated to the HC	1 nurse: 3 (10%)	2 nurses: 5 (16.7%)	3 nurses: 1 (3.3%)
Is there a planned periodic rotation of nurses assigned to the HC?	No: 14 (46.7%)	Yes: 8 (26.7%)	Occasionally: 4 (13.3%)
Years of experience in HC activities	< 5 Years: 3 (10%)	5-15 Years: 10 (33.3%)	> 15 Years: 6 (20%)
Activities carried out by HC nurses	Appointment scheduling and agenda management		13 (43.3%)
	Management of clinical documentation and healthcare-related telephone support		12 (40%)
	Monitoring pharmaceutical stock		18 (60%)
	Patient and caregiver education		18 (60%)
	Coordination with the hospital pharmacy		16 (53.3%)
Nurse Training and Education	Competencies acquired "on the job": 15 (50%)	Specific training on CBDs: 2 (6.7%)	Both: 9 (30%)
	Participation in in-house training courses: 14 (46.7%)		
	Participation in specialised external courses: 14 (46.7%)		
	Specialised training for new employees: 15 (50%)		

HCs: Haemophilia Centres; CBDs: Congenital Bleeding Disorders

XIX CONVEGNO TRIENNALE
VERONA
15, 16, 17 e 18 OTTOBRE 2026
Camera di Commercio di Verona
AICE Associazione Italiana Centri Emofilia

XIX Convegno Triennale sugli Aspetti Clinici e Sociali dell'Emofilia ABSTRACT N. CO-12

1.03 Health and social economics, organizational issues

BEYOND CLOTTING FACTORS: NURSING AS A CORNERSTONE OF LIFELONG HEMOPHILIA CARE

M.V. Puliga[1], C. Manzi[2], A. Besagni[3], S. Linari[1], C. Carulli[4], M. Morfini[5]

[1]SODc Malattie Emorragiche e della Coagulazione, AOU Careggi, Firenze, Italy; [2]SSD Malattie Emorragiche Congenite, IRCCS Policlinico Sant'Orsola, Bologna, Italy; [3]Indipendente, Italy; [4]Clinica Ortopedica, Università di Firenze, SOD Ortopedia, AOU Careggi, Firenze, Italy; [5]Associazione Italiana Centri Emofilia, AICE, Milano, Italy

Background and Aims. Haemophilia is a rare inherited bleeding disorder requiring specialised, multidisciplinary, lifelong care. Despite major therapeutic advances, optimal outcomes depend on coordinated healthcare delivery, patient education, psychosocial support, and regular follow-up. Within Haemophilia Centres, nurses play a key role in education, care coordination, and treatment adherence. This study analysed the clinical, organisational, educational, and psychosocial aspects of comprehensive haemophilia care across the lifespan, focusing on nursing contributions and their potential impact on patient outcomes.

Materials and Methods. A narrative review of the literature and organisational practices adopted in specialised Haemophilia Centres was conducted. The analysis explored haemophilia management during childhood, adolescence, adulthood, and older age. Areas examined included nursing interventions, patient and family education, communication, treatment adherence, multidisciplinary collaboration, home care, psychosocial support, and the Italian legislative framework for rare diseases. Findings were synthesised to identify the main domains of nursing practice in haemophilia care.

Results. Comprehensive haemophilia management requires continuous, individualised care from diagnosis onwards. During childhood and adolescence, family education, promotion of autonomy, safe physical activity, and prevention of complications were key elements of care. During the transition to adulthood, communication with healthcare professionals, self-management, and adherence to prophylaxis become increasingly important. Older adults often present with age-related comorbidities requiring more complex multidisciplinary management. The analysis identified major nursing domains, including therapeutic education, support for self-management and adherence, coordination of care pathways, psychosocial support, monitoring of complications, and facilitation of communication between patients, families, and healthcare professionals. Electronic communication tools and integrated care models may further improve continuity of care and patient engagement.

Conclusions. Haemophilia management extends beyond replacement therapy and requires a holistic, patient-centred approach integrating clinical, educational, psychological, and organisational aspects of care. Nurses are essential members of the multidisciplinary team, supporting patients and families throughout the disease course while promoting self-management, adherence, and quality of life. The identified domains may provide a basis for developing nurse-sensitive outcomes and strengthening specialised nursing practice within Haemophilia Centres.

Table 1. Nursing contributions and potential nurse-sensitive outcomes in lifelong haemophilia care.

Nursing domain	Key nursing activities	Potential nurse-sensitive outcomes
Therapeutic education	Education of patients and caregivers on disease, treatment, bleeding recognition, and prevention strategies	Increased disease knowledge, improved treatment adherence
Self-management support	Development of autonomy, self-infusion skills, and home treatment management	Greater patient empowerment, increased independence
Care coordination	Coordination among Haemophilia Centre professionals, community services, and family caregivers	Improved continuity of care, enhanced care integration
Adherence promotion	Monitoring and reinforcement of prophylactic treatment adherence	Higher adherence rates, reduced treatment discontinuation
Psychosocial support	Assessment of emotional and social needs, counselling support, referral to specialists when required	Improved coping strategies, enhanced quality of life
Communication facilitation	Promotion of effective communication between patients, families, and healthcare professionals	Increased patient engagement, improved shared decision-making
Monitoring and early intervention	Identification of bleeding episodes, treatment-related issues, and age-related complications	Earlier management of complications, improved clinical stability
Transitional care	Support during transfer from paediatric to adult services	Better continuity of care, sustained long-term engagement
Healthy lifestyle promotion	Encouragement of safe physical activity and preventive health behaviours	Improved physical functioning, reduced risk of disability

Abstracts printing tool powered by pagepress.org

XIX CONVEGNO TRIENNALE
VERONA
15, 16, 17 e 18 OTTOBRE 2026
Camera di Commercio di Verona
AICE Associazione Italiana Centri Emofilia

XIX Convegno Triennale sugli Aspetti Clinici e Sociali dell'Emofilia ABSTRACT N. CO-13

1.04 Psychosocial and quality of life issues

USE OF THE MULTIDIMENSIONAL HEMOPHILIA PAIN QUESTIONNAIRE IN PATIENTS WITH SEVERE HEMOPHILIA A TREATED WITH EMICIZUMAB: A PILOT CROSS-SECTIONAL, SINGLE-CENTRE STUDY

I.L. Calcaterra, S. Donnarumma, G. D'Errico, C. De Luca, C. Caputo, P. Ciciola, E. Cimino, M. Di Minno

Università Federico II di Napoli, Italy

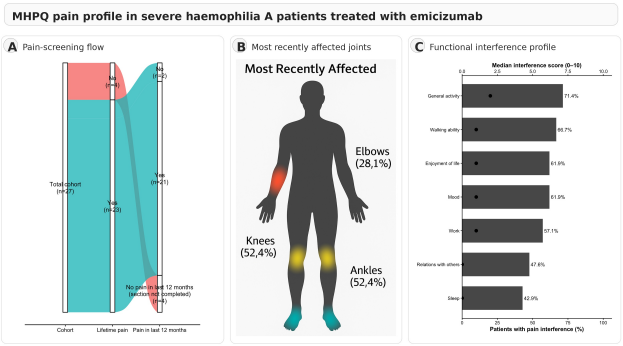
Background. Despite effective bleed prevention with emicizumab, pain remains a relevant clinical burden in adults with severe haemophilia A (sHA). A multidimensional assessment is needed to better characterize contemporary haemophilia-related pain.

Objectives. To evaluate the prevalence, characteristics, and functional impact of pain in adults with sHA receiving emicizumab prophylaxis using the Multidimensional Haemophilia Pain Questionnaire (MHPQ).

Methods. In this single-centre, cross-sectional pilot study, 27 adults with sHA on emicizumab prophylaxis completed the MHPQ. Pain localization, frequency, triggering factors, intensity, and interference across life domains were assessed descriptively.

Results. Lifetime haemophilia-related pain was reported by 85.2% of participants, and 77.8% experienced pain within the previous 12 months. Pain most frequently involved ankles (52.4%), knees (52.4%), and elbows (28.6%). All patients with recent pain reported pain during bleeding episodes; however, movement-related triggers, including accidental movements (66.7%) and physical activity (54.2%), were also common. Pain intensity was generally mild-to-moderate, with the highest median scores observed after accidental movements (median 4, IQR 2–6). Pain interfered predominantly with general activity (71.4%), walking ability (66.7%), mood (61.9%), and enjoyment of life (61.9%). Arthropathy was documented in 70.4% of patients.

Conclusions. In the non-factor prophylaxis era, pain remains prevalent and functionally relevant in adults with sHA despite effective bleed control. These findings suggest that haemophilia-related pain is not exclusively bleeding-driven and highlight the importance of structured, multidimensional pain assessment in routine haemophilia care.



Abstracts printing tool powered by pagepress.org

XIX CONVEGNO TRIENNALE
VERONA
15, 16, 17 e 18 OTTOBRE 2026
Camera di Commercio di Verona
AICE Associazione Italiana Centri Emofilia

XIX Convegno Triennale sugli Aspetti Clinici e Sociali dell'Emofilia ABSTRACT N. CO-14

1.04 Psychosocial and quality of life issues

BEYOND BLEEDING: NARRATIVE MEDICINE AS A METHODOLOGICAL TOOL FOR INVESTIGATION AND CARE IN CONGENITAL BLEEDING DISORDERS

V. Grippa[1], S. Riva[2], A. Gringeri[3]

[1]Centro Malattie Emorragiche Salerno, Italy; [2]St. Mary's University, London, UK; [3]Fondazione Charta, Milano, Centro di Solidarietà Solidale, Lucca, Italy

The approach to congenital bleeding disorders (CBDs) cannot be limited solely to biological parameters and therapeutic outcomes in clinical practice. Alongside the pathophysiological dimension of disease, there is also an experiential dimension involving quality of life, relationships, identity, body perception, treatment adherence, and emotional experience. This highlights the need to integrate Evidence-Based Medicine (EBM) with tools capable of rigorously and systematically exploring the subjectivity of the illness experience. Within this perspective, the Academy of Narrative Medicine for Congenital Bleeding Disorders was established with the aim of promoting Narrative-Based Medicine (NBM) as a qualitative, methodological, and educational approach in the field of CBDs. NBM is not conceived in opposition to EBM, nor as a merely communicative or testimonial practice, but rather as a complementary and integrative dimension of clinical knowledge. EBM and NBM represent two epistemologically convergent approaches: the former oriented toward the interpretation of biological and clinical evidence, the latter aimed at understanding the lived experience of illness. Both contribute to the development of more appropriate, personalized diagnostic and therapeutic pathways that better reflect the complexity of the individual. The Academy applies NBM through structured and scientifically grounded methodologies for the collection, analysis, and interpretation of narratives from patients, caregivers, and healthcare professionals. Narratives are considered qualitative data suitable for systematic interdisciplinary analysis, with the aim of identifying unmet needs, care-related challenges, therapeutic barriers, psychosocial vulnerabilities, and dimensions of illness that cannot be detected through conventional clinical tools. Through narrative workshops, educational activities, interdisciplinary research, and collaborations with Hemophilia Centers, the Academy promotes an integrated model of care in which clinical and narrative data mutually contribute to a deeper understanding of disease. In this sense, NBM emerges as a qualitative investigative tool capable of broadening the clinical perspective without replacing it, thus contributing to the evolution of healthcare models that are increasingly person-centered and aligned with the principles of precision medicine. The Academy therefore seeks to propose an innovative approach to CBDs, in which listening to illness narratives is not considered an accessory element, but rather an essential component of the care process, capable of integrating scientific evidence and lived experience within a single healthcare paradigm.

Abstracts printing tool powered by pagepress.org

XIX CONVEGNO TRIENNALE
VERONA
15, 16, 17 e 18 OTTOBRE 2026
Camera di Commercio di Verona
AICE Associazione Italiana Centri Emofilia

XIX Convegno Triennale sugli Aspetti Clinici e Sociali dell'Emofilia

ABSTRACT N. CO-15

1.04 Psychosocial and quality of life issues

HEMOPHILIA AND PHYSICAL ACTIVITY: A SURVEY ON THE CURRENT STATUS OF SPORTS ACCESSIBILITY IN THE ITALIAN POPULATION

L. Laterza[1], M. Attanasi[1], C. Cassone[2], P. Giordano[3], G. Lassandro[3]

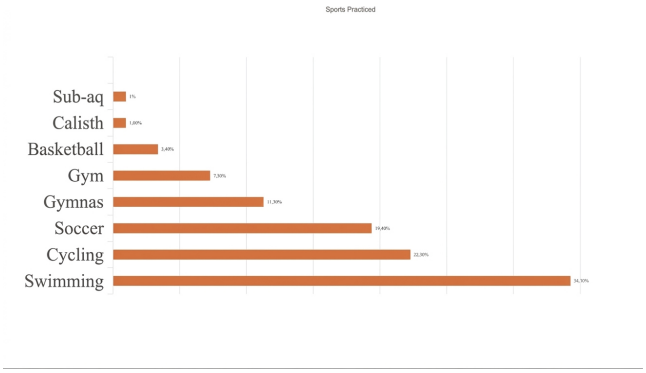
[1]University of Bari "Aldo Moro", Interdisciplinary of Medicine, Bari, Italy; [2]Fedemo, Milano, Italy; [3]Pediatric Haemophilia Center - AOUC Pol. Giovanni XXXIII, University of Bari "Aldo Moro", Italy

Background and Aims. Hemophilia is a congenital, X-linked bleeding disorder, characterized by a high risk of spontaneous and post-traumatic intra-articular hemorrhages. Historically, people with hemophilia (PWH) were advised to restrict their participation in physical activity to avoid bleeding. Recently, the introduction of personalized prophylactic therapies has significantly improved musculoskeletal well-being, ensuring better hemostatic protection. In this newly scenario, physical exercise is recognized not only as a preventive tool against chronic hemophilic arthropathy but also as an essential element to improve quality of life and social inclusion in pediatric and young adult patients. The aim of this study is to analyze the current landscape regarding accessibility and participation in sports activities within a national cohort of PWH. The survey aims to analyze frequency of practiced sports, perceived benefits and any remaining athletic barriers that still limit full patient engagement in physical activities.

Materials and Methods. An observational study was conducted by administering, with the support of the Italian Federation of Hemophilia Associations (Fedemo), an online questionnaire to Italians with hemophilia A and B, of all severities. The 11-item questionnaire collected demographic, clinical and sports accessibility data.

Results. A total of 35 responses were collected, evenly distributed across the national territory (27% in Northern, 28% in Central and 45% in Southern Italy). Of the sample, 47% were under 40 years of age, and 90% of respondents were on a prophylactic regimen. Regarding physical activity, 56.2% had never engaged in it, while 43.8% currently practice or have previously practiced it. Among the latter, 62.76% engage in organized sports, whereas 27.4% lack medical clearance for competitive or non-competitive sports. The most common disciplines were swimming, cycling, soccer, and gymnastics/fitness. Additionally, 33.3% engage in physical activity for at least 2 hours per week.

Conclusions. This is the first survey on sport participation in Italian PWH. The results confirm that physical activity is not an perceived barrier but is becoming an essential component of disease management. However, there is a clear need to develop standardized protocols for the safe integration of physical exercise, thereby supporting patients in accessing sports activities and streamlining the medical certification process



VIRTUAL EVALUATIONS OF JOINT HEALTH USING WEARABLE SENSORS IN PERSONS WITH HEMOPHILIA: THE VESPA STUDY PROTOCOL

S. Riva, R. Mahaffey

St. Marys University London, UK

Virtual Evaluations of joint health using wearable Sensors in Persons with haemophilia (VESPA) is a mixed-methods feasibility study exploring the use of wearable and video-based technologies to remotely monitor joint health and rehabilitation outcomes in adults with haemophilia. The intervention combines a home-based exercise programme with mobile motion capture technology to assess joint range of motion, pain, and quality of life over an eight-week period. Participants attend two laboratory sessions at St Mary's University, during which lower-limb joint movement is assessed using markerless motion capture systems including Sony cameras, The ia modelling software, and the Quantum Mobile App. Between these visits, participants complete weekly home exercise sessions while recording movement data using their own smartphones. The intervention is designed to evaluate whether wearable and mobile technologies can provide clinically meaningful assessments of hip, knee, and ankle function outside laboratory settings. The study integrates several assessment tools, including remote video-based movement analysis, the Haemophilia Joint Health Score, pain questionnaires, quality-of-life measures, exercise logs, and semi-structured interviews. Quantitative measures are used to evaluate joint range of motion, pain intensity, physical function, and rehabilitation adherence, while qualitative interviews explore participants' experiences, barriers, and facilitators associated with remote monitoring technologies. The intervention emphasises digital rehabilitation and remote monitoring within haemophilia care, aiming to improve accessibility and provide real-time feedback to patients and clinicians without requiring frequent hospital attendance. The study also explores the usability, acceptability, and feasibility of integrating mobile health technologies into routine rehabilitation and long-term joint health management.

EMBODIED SELF-MANAGEMENT IN HEMOPHILIA: PSYCHOSOMATIC EFFECTS OF A SUPERVISED PHYSICAL ACTIVITY PROGRAM

F. Valeri[1], M. Miniotti[2], M.G. Bailon[2], C. Dainese[1], B. Bruno[3], P. Leombruni[2], A. Borchiellini[1]

[1]Regional Centre for Haemorrhagic and Thrombotic Disease, Hematology Division, AOU Città della Salute e della Scienza, Torino, Italy; [2]Departement of Neurosciences Rita Levi Montalcini, University of Turin, Italy; [3]Division of Hematology, AOU Città della Salute e della Scienza, Department of Molecular Biotechnology and Health sciences, University of Turin, Italy

Background and Aims. In hemophilia patients (HPs), physical activity has traditionally been limited by fears of bleeding and joint damage, with psychosomatic consequences including reduced body confidence, somatization, type-A behavior and alexithymia. While controlled exercise programs are increasingly recognized as safe, their impact on psychosocial outcomes remains underexplored. This exploratory mixed-method study aimed to investigate the psychosomatic effects of a supervised physical activity program in HPs, integrating clinical outcomes with subjective experiences.

Methods. Nine HPs, on stable prophylaxis, participated in a 12-month physical activity program planned according to individual pharmacokinetic profiles and delivered by trained exercise professionals under medical supervision. Physical safety, joint status, and functional performance were assessed at baseline, 6, and 12 months. After program completion, a psychologist-led focus group was performed to explore participants' subjective experience.

Results. Quantitative data conJrmed the safety of the program, with no increase in bleeding events and maintenance/improvement of joint and functional outcomes over time. Qualitative analysis identified five core themes: Motivation, Symptom management, Relationship with healthcare professionals, Relational engagement, and Program limitations. Participants reported increased body awareness, self-efficacy, and adherence to prophylaxis, reflecting enhanced self-management. Improvements in social quality of life was not consistently reported, and group-based activity did not foster a sense of belonging or relational bonds.

Conclusions. Supervised physical activity may act as a psychosomatic intervention promoting embodied self-efficacy and self-management rather than social integration in HPs. These findings suggest that exercise-based programs should incorporate psychological and relational components to fully address the psychosocial needs of HPs.

XIX CONVEGNO TRIENNALE
VERONA
15, 16, 17 e 18 OTTOBRE 2026
Camera di Commercio di Verona
AICE Associazione Italiana Centri Emofilia

XIX Convegno Triennale sugli Aspetti Clinici e Sociali dell'Emofilia ABSTRACT N. CO-18

2.01 Hemophilia - clinical and treatment issues

PSYCHOMETRIC ASSESSMENT OF PATIENT REPORTED EXPERIENCES WITH ARTIFICIAL INTELLIGENCE TOOLS IN HEMOPHILIA CARE

G. Sottilotta [1|2] , G. Praticò [1] , D. Megalizzi [1] , M. Hart [2] , C. Komar [2] , F. Luise [3]

[1] UOSD Centro Microcitemie - Servizio Emostasi e Trombosi. Grande Ospedale Metropolitano di Reggio Calabria, Italy; [2] Save One Life Inc., USA; [3] Laboratorio Analisi. Grande Ospedale Metropolitano di Reggio Calabria, Italy

Introduction. Artificial intelligence (AI) is increasingly integrated into everyday life and is expected to influence clinical practice by supporting tasks traditionally performed by healthcare professionals. People with haemophilia (PWH) have historically shown a strong interest in understanding scientific, diagnostic, and therapeutic advances related to their condition, often seeking information through conferences, online platforms, and, more recently, AI based applications. As AI tools become more accessible, evaluating how PWH perceive the quality and reliability of AI generated medical information is essential.

Aims. The study aimed to assess patient reported satisfaction with AI generated responses to haemophilia related questions, focusing on clarity, accuracy, and perceived usefulness through a psychometric evaluation.

Materials and Methods. A 10-item questionnaire was developed from questions proposed directly by PWH, addressing innovative therapies, emerging treatment strategies, and future perspectives in haemophilia care. Twelve adults male with haemophilia (mean age 49.2, range 19–65) submitted the same questionnaire to five AI tools: ChatGPT®, Gemini®, Copilot®, DeepSeek®, and Perplexity®. Participants evaluated each set of responses using a Likert-type psychometric scale, generating a total satisfaction score ranging from 0 to 50 for each AI system.

Results. All AI applications achieved medium to high satisfaction scores, with a mean value of 37.9 (range 33.8–39.6), corresponding to an average rating of 3.8 on a 1–5 scale. Participants generally considered the information provided to be clear, relevant, and aligned with their expectations. The use of patient generated questions ensured accessibility and avoided excessive technical complexity, supporting the applicability of AI tools for non professional users. Detailed results are summarised in Table 1.

Conclusions. PWH expressed overall appreciation for the quality of AI generated answers. These findings suggest that AI systems may already serve as valuable resources for patient education in haemophilia, particularly in settings with limited access to specialised haemophilia centres or insufficient availability of trained healthcare personnel. Nonetheless, AI generated information must always be interpreted under medical supervision to prevent misunderstandings or inappropriate self management. Continued monitoring and evaluation of AI tools remain essential to ensure accuracy, safety, and alignment with evolving standards of haemophilia care

Table 1: Patients characteristics and Artificial Intelligence (AI) applications scores

Type of Hemophilia	Age	CHAT GPT	PERPLEXITY	COPILOT	GEMINI	DEEPSEEK
A Severe	41	48	40	30	40	30
A Severe	53	40	40	30	40	47
A Severe with Inhibitor	58	36	38	39	40	39
A Moderate	53	39	35	37	43	47
A Moderate	55	45	45	44	42	40
A Severe	38	30	40	35	42	20
B Severe	19	30	35	30	23	36
A Severe	35	45	40	30	45	35
A Severe with Inhibitor	59	45	45	30	45	50
A Severe	64	46	44	32	42	30
A Severe	65	33	36	37	36	35
A Severe	50	38	34	32	36	38
AI Average rating		39.6	39.3	33.8	39.5	37.2

XIX CONVEGNO TRIENNALE
VERONA
15, 16, 17 e 18 OTTOBRE 2026
Camera di Commercio di Verona
AICE Associazione Italiana Centri Emofilia

XIX Convegno Triennale sugli Aspetti Clinici e Sociali dell'Emofilia ABSTRACT N. CO-19

2.01 Hemophilia - clinical and treatment issues

A CASE OF LOSS OF EFFICACY OF EMICIZUMAB AFTER 6 YEARS OF REGULAR USE

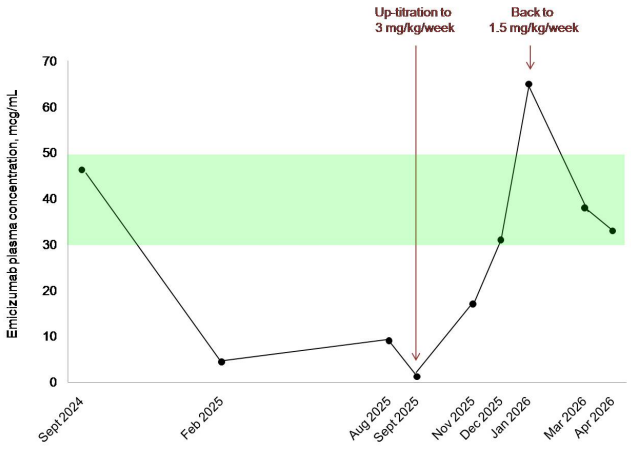
M.R. Fasulo[1], I. Quaglia[1], A. Colombo[1], C. Lodigiani[1], M.E. Mancuso[1|2]

[1]Center for Thrombosis and Hemorrhagic Diseases, IRCCS Humanitas Research Hospital, Rozzano, Milano, Italy; [2]Department of Biomedical Sciences, Humanitas University, Pieve Emanuele, Milano, Italy

Background. Anti-drug antibodies (ADAs) against emicizumab can reduce treatment efficacy by neutralizing drug function or accelerating its clearance. They are rare and usually develop within the first 25 weeks of exposure. We report a case of loss of efficacy likely due to ADAs development after 6 years of regular use.

Case Report. A 24-year-old man with congenital severe hemophilia A who developed high-responding inhibitors at 1 year of age and failed multiple courses of immune tolerance induction including association with immunosuppressive therapy with steroids and cyclosporine. In 2018, after many years of on demand treatment with bypassing agents for recurrent joint bleeds, he started prophylaxis with emicizumab (dosing regimen: 1.5 mg/kg/week). From 2018 to October 2024 he had no breakthrough bleeds and received recombinant activated factor VII (rFVIIa) only for an elective surgical procedure (pilonidal cyst removal). From November 2024, he reported a significant increase in his bleeding tendency with 6 bleeding episodes over 10 months: 1 subcutaneous hand hematoma, 1 episode of hematuria and 4 elbow bleeds with evidence of synovial hypertrophy at point-of-care musculoskeletal ultrasound examination. All these bleeding events were spontaneous and treated with rFVIIa. Regular check of emicizumab plasma concentration allowed us to detect a significant reduction in concomitance with the worsened bleeding phenotype. In fact, levels dropped from 46.3 mcg/mL to 1.2 mcg/mL (Figure 1). Adequate adherence to treatment regimen and drug storage were confirmed, therefore suggesting the development of ADAs with neutralizing potential against emicizumab. To overcome the neutralizing effect of those ADAs and considering that they could be transient, emicizumab dose was up-titrated to 3 mg/kg/week with favorable clinical and laboratory outcomes. A significant improvement of the bleeding phenotype was observed with no further events and progressive improvement of synovial hypertrophy. In parallel, emicizumab plasma concentration increased up to 65 mcg/mL as of January 2026, when he resumed his previous dosing regimen (1.5 mg/kg/week) maintaining emicizumab plasma concentration levels around 35 mcg/mL without bleeds thereafter (Figure 1).

Conclusions. This report demonstrates that clinically significant ADAs can occur even after several years of continuous regular use of emicizumab and supports the evidence that drug plasma concentration is a valid indicator of their presence as well as a useful tool to monitor the effect of treatment tailoring. Additionally, this case confirms that emicizumab up-titration could be considered as a strategy to overcome the effect of ADAs and restore a good protection against bleeds.



XIX CONVEGNO TRIENNALE
VERONA
15, 16, 17 e 18 OTTOBRE 2026
Camera di Commercio di Verona
AICE Associazione Italiana Centri Emofilia

XIX Convegno Triennale sugli Aspetti Clinici e Sociali dell'Emofilia ABSTRACT N. CO-20

2.01 Hemophilia - clinical and treatment issues

REAL WORLD EXPERIENCE ON THE MANAGEMENT OF MILD HEAD INJURY IN A COHORT OF CHILDREN WITH HEMOPHILIA A WITH AND WITHOUT INHIBITORS TREATED WITH EMICIZUMAB

B. Pollio[1], B. Borsellino[1|2], T. Martini[1]

[1]Haemophilia Centre, Immune-Haematology and Transfusion Medicine, University Hospital "Città della Salute e della Scienza", Torino, Italy; [2]Department of Biomedicine and Prevention, PhD in Immunology, Molecular Medicine and Applied Biotechnology, University of Rome Tor Vergata, Roma, Italy

Background and Aims. Children with haemophilia have a significantly increased risk of intracranial haemorrhage (ICH) compared to the normal population; newborn have the highest risk of ICH, estimated to be 33-fold higher than general population (2,1% vs 0,062% per 100 live births); the great majority of ICH occur <2 years of age. Trauma is the main risk factor for ICH in children with haemophilia: mild head trauma is a common occurrence in this population, and there is a lack of data regarding its management. This work represents the experience of Turin paediatric haemophilia Centre in the management of mild head trauma.

Materials and Methods. We retrospectively collected from medical records of our patient in prophylaxis with Emicizumab, data about: age at the time of trauma, severity of head trauma, medical treatment. Mild head trauma is defined by a Glasgow Coma Scale (GCS) 14-15; GCS together with PECARN rules allow to distinguish children with mild head trauma in low, intermediate and high risk. Following PECARN rules, in children <2 years very low risk head trauma is defined by: GCS 15, no loss of consciousness, no severe mechanism of injury (fall >0,9 m; head struck by high impact object; motor vehicle collision with potent ejection, death of another passenger, or rollover; pedestrian or bicyclist without helmet struck by a motorized vehicle), no non-frontal scalp hematoma, no palpable skull fracture, and normal behaviour per caregiver. In children ≥2 years, very low risk requires: GCS 15, no loss of consciousness, no severe mechanism, no vomiting, no severe headache, and no signs of basilar skull fracture. Low risk patients (GCS 15 and no PECARN findings) can be discharged without a CT scan; for intermediate risk patients (only 1 PECARN findings) clinical observation is required; high risk patients (≥2 PECARN findings) CT scan is recommended.

Results. From February 2020 to April 2026, we observed 18 consecutive mild head traumas in 12 children (including 2 patients with inhibitor). All these events were managed with the collaboration of Emergency Department and Haemophilia Centre. Median age at time of trauma is 4 years old, with 8 events occurring <2 years of age. Only one patient required a CT scan for the presence of neurological symptoms. In 9 cases the high impact dynamics of trauma needed the administration of factor VIII concentrate. All the 18 traumas had a favourable outcome (table 1).

Conclusions. We managed the high impact traumas with factor VIII concentrate administration, while low impact traumas did not require replacement treatment. No ICH were reported in 18 mild head traumas. The synergic cooperation of Emergency Department and Haemophilia Centre plays a key role in the effective management of these events.

Table 1. Mild head injury during Emicizumab prophylaxis

Head injury number	Patient	Age at time of trauma	Inhibitor	Severe mechanism of injury	Head CT	Replacement therapy/bypassing agent	ICH
1	1	2	Yes	No	No	No	No
2	1	3	Yes	No	No	No	No
3	2	3	Yes	No	No	No	No
4	3	8	No	No	No	No	No
5	3	8	No	Yes	Yes	Yes	No
6	4	4	No	Yes	No	Yes	No
7	5	2	No	Yes	No	Yes	No
8	5	2	No	No	No	No	No
9	6	2	No	Yes	No	Yes	No
10	7	8	No	No	No	No	No
11	8	2	No	Yes	No	Yes	No
12	8	3	No	No	No	No	No
13	8	4	No	No	No	No	No
14	9	13	No	Yes	No	Yes	No
15	10	0,9	No	No	No	No	No
16	11	2	No	No	No	Yes	No
17	11	2	No	Yes	No	Yes	No
18	12	4	No	Yes	No	Yes	No

Abstracts printing tool powered by pagepress.org

XIX CONVEGNO TRIENNALE
VERONA
15, 16, 17 e 18 OTTOBRE 2026
Camera di Commercio di Verona
AICE Associazione Italiana Centri Emofilia

XIX Convegno Triennale sugli Aspetti Clinici e Sociali dell'Emofilia ABSTRACT N. CO-21

2.01 Hemophilia - clinical and treatment issues

FUSION 2: VALIDATION AND CLINICAL PERFORMANCE OF AN INTEGRATED ULTRASOUND–FUNCTIONAL ASSESSMENT SYSTEM IN HEMOPHILIA

M.E. Susi[1], E.A. Boccalandro[2], A. Giuffrida[3], I. Ricca[4], P. Imazio[5], E. Bonetti[6], I. Nichele[7] B. Pollio[8], E. Zanon[9], E. Baldacci[10], C. Santoro[10], G. Delios[4], S. Ligia[10], M. Biglietto[10], I. Calcaterra[11], M. Napolitano[12], M. Bodini[2], C. Simion[9], B. Borsellino[8], G. Pasta[13], M.N.D. Di Minno[11], C. Martinoli[14|15]

[1]DIMES, Department of Experimental Medicine, University of Genoa, Italy; [2]Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Angelo Bianchi Bonomi Hemophilia and Thrombosis Center and Fondazione Luigi Villa, Milano, Italy; [3]Hemophilia Center, Borgo Roma Hospital, Integrated University Hospital of Verona, Italy; [4]Immunology and Transfusion Medicine Service, Hemophilia Center, Ivrea Hospital, Local Health Authority TO4, Ivrea, Italy; [5]Rehabilitation and Functional Recovery Service, Pediatric Orthopedics Unit, Regina Margherita Children's Hospital, City of Health and Science University Hospital of Turin, Italy; [6]Pediatric Oncohematology Unit, Borgo Trento Hospital, Integrated University Hospital of Verona, Italy; [7]Haemophilia and Thrombosis Center, Haematology Department, San Bortolo Hospital, Vicenza, Italy; [8]Transfusion Medicine and Immunohematology Service, Regina Margherita Children's Hospital, City of Health and Science University Hospital of Turin, Italy; [9]Coagulation Disorders and Hemophilia Center, University Hospital of Padova, Italy; [10]Unit of Special Diagnosis and Therapy of Hemostasis and Thrombosis, Hematology Department, Policlinico Umberto I, Sapienza University of Rome, Italy; [11]Department of Clinical Medicine and Surgery, Regional Reference Centre for Coagulation Disorders, Federico II University, Napoli, Italy; [12]Dipartimento PROMISE, Università degli Studi di Palermo and UOC Ematologia e Malattie Rare, PO "Cervello", Palermo, Italy; [13]Orthopedics and Traumatology Clinic, IRCCS Policlinico San Matteo Foundation, Pavia, Italy; [14]DISSAL, Department of Health Sciences, University of Genoa, Italy; [15]UOC Emergency and Musculoskeletal Radiology, IRCCS AOM San Martino Hospital, Genova, Italy

Background and Aims. FUSION (Functional & Ultrasound Integrated Observation in Hemophilia) is an integrated musculoskeletal assessment framework combining point-of-care ultrasound (HEAD-US) with a simplified functional evaluation. While ultrasound and clinical joint scores provide complementary information, the extent to which functional performance contributes independent information beyond established tools remains unclear. This study aimed to validate the FUSION composite score and investigate whether its functional component captures clinically relevant dimensions not explained by HEAD-US or Hemophilia Joint Health Score (HJHS) 2.1 alone.

Materials and Methods. We conducted a prospective multicenter cross-sectional study including 121 patients with hemophilia A, hemophilia B, or von Willebrand disease undergoing integrated assessment with HEAD-US, HJHS 2.1, and FUSION. The FUSION score combines HEAD-US evaluation of elbows, knees, and ankles with a weighted simplified functional score (F×4) derived from six standardized motor tasks. Convergent validity was assessed using Spearman correlation and Steiger's z-test. Variance decomposition and residual analyses were performed to identify the proportion and nature of information uniquely captured by FUSION.

Results. FUSION showed strong convergent validity with HJHS(ρ=0.764, $p<0.001$), comparable to the correlation observed between HEAD-US and HJHS (ρ=0.776, $p<0.001$; Steiger p=0.82). However, addition of the functional component significantly increased explained variance beyond HEAD-US alone (ΔR^2=0.070, $p<0.001$), supporting an independent contribution of functional assessment. Variance decomposition demonstrated that 25.5% of the variance captured by FUSION was not explained by HJHS. Notably, 43.1% of the variance of the functional component (F×4) remained unexplained by HJHS, indicating that FUSION captures a substantial non-overlapping functional domain. Discordance analyses further supported the complementary role of FUSION. Among patients with HJHS=0, FUSION identified abnormalities in 53.8% of cases. In patients with HEAD-US=0, FUSION detected abnormalities in 55.0% versus 30.0% with HJHS alone (p=0.013), with all additional detections driven by the functional component.

Conclusions. FUSION preserves strong alignment with established hemophilia joint assessment tools while simultaneously identifying a substantial and clinically relevant functional domain not captured by HJHS or structural ultrasound evaluation alone. These findings support the concept of a multidimensional structural-functional assessment model and suggest that current joint-focused scores may underestimate global biomechanical and compensatory impairment in hemophilia.

XIX CONVEGNO TRIENNALE
VERONA
15, 16, 17 e 18 OTTOBRE 2026
Camera di Commercio di Verona
AICE Associazione Italiana Centri Emofilia

XIX Convegno Triennale sugli Aspetti Clinici e Sociali dell'Emofilia ABSTRACT N. CO-22

2.01 Hemophilia - clinical and treatment issues

CLINICAL FEATURES IN PATIENTS WITH NON-SEVERE HEMOPHILIA A: THE DISCOVERY SCORE PROPOSAL FOR PROPHYLAXIS PRESCRIPTION

M.N.D. Di Minno[1], E. Baldacci[2], C. Biasoli[3], A. Borchiellini[4], F. Daniele[5], P. Di Gregorio[6], C. Gorio[7], G. Malcangi[8], E. Marchesini[9], I. Ricca[10], R. Santoro[11], S. Siragusa[12], M.R. Villa[13], E. Zanon[14], A. Tagliaferri[15], A. Coppola[15]

[1]Hub Centre for Thrombotic and Hemorrhagic Disorders, Federico II University Hospital, Napoli, Italy; [2]Haematology, University Hospital Policlinico Umberto I, Roma, Italy; [3]Interdepartmental Simple Structure for the Management of Hemorrhagic and Thromboembolic Diseases, M. Bufalini Hospital, Cesena, Italy; [4]Regional Centre for Hemorrhagic and Thrombotic Diseases, AOU Città della Salute e della Scienza, Torino, Italy; [5]Haemostasis and Thrombosis Service, Ospedale Civile dell'Annunziata, Cosenza, Italy; [6]Transfusion Medicine Department, "SS. Annunziata" Hospital, Chieti, Italy; [7]Pediatric Onco-Hematology Unit, Children's Hospital, ASST-Spedali Civili, Brescia, Italy; [8]Haemophilia and Thrombosis Center, University Hospital Policlinico-Giovanni XXIII, Bari, Italy; [9]Hemophilia Centre, SC Vascular and Emergency Department, University of Perugia, Italy; [10]Centro Emofilia, Città della Salute e della Scienza, Torino, Italy; [11]Hemostasis and Thrombosis Unit, Azienda Ospedaliero Universitaria Dulbecco, Catanzaro, Italy; [12]Centro di Riferimento Regionale per le Emocoagulopatie Congenite, Palermo, Italy; [13]Hematology Unit, Ospedale Santa Maria di Loreto, Napoli, Italy; [14]Hemophilia and Thrombosis Center, University Hospital of Padua, Italy; [15]Hemophilia and Thrombosis Center, Azienda Ospedaliera di Parma, Italy

Background. In non-severe hemophilia A (HA), classification based exclusively on factor VIII (FVIII) activity does not fully reflect bleeding phenotype heterogeneity. Consequently, some patients with clinically relevant bleeding manifestations may remain undertreated and prophylaxis may be underused. We aimed to identify clinical characteristics associated with prophylaxis indication and to develop a phenotype-driven clinical score to support treatment decision-making.

Methods. This retrospective real-world study included consecutive patients with non-severe HA (FVIII 1% to <40%) managed at Italian hemophilia centers. Clinical, bleeding, joint-related, and treatment-related variables were collected and compared between patients receiving physician-indicated prophylaxis and those managed on demand. Candidate predictors associated with prophylaxis indication were identified through univariate analyses and least absolute shrinkage and selection operator (LASSO) penalized logistic regression. Predictors retained in the final parsimonious multivariable model were converted into an integer-based risk score.

Results. Seventy-three patients were included (50.7% moderate and 49.3% mild HA); 67.1% received indication to prophylaxis. Compared with patients treated on demand, those receiving prophylaxis had significantly higher annual bleeding rate (ABR) and annual joint bleeding rate (AjBR), earlier age at first bleed, higher prevalence of severe bleeding history, more problem joints, and more frequent synovial hypertrophy. Following prophylaxis initiation, median ABR decreased from 2.76 to 0.57 and median AjBR from 2.12 to 0.16 (both $p<0.001$). The DISCOVERY score included five predictors: AjBR ≥2 (+3), synovial hypertrophy (+2), history of severe bleeding (+2), antithrombotic therapy (+4), and ABR ≥2 (+1), for a total score range of 0–12. The model showed good discrimination, with an area under the curve of 0.84 (95% CI 0.70–0.96). A threshold ≥4 provided the best balance between sensitivity (75.5%) and specificity (75.0%), whereas higher thresholds increased specificity up to 100%.

Conclusions. A substantial proportion of patients with non-severe HA exhibit a clinically relevant bleeding phenotype that may warrant prophylaxis despite residual FVIII levels above the severe range. The DISCOVERY score integrates bleeding burden, joint disease activity, and treatment-related risk factors into a simple phenotype-driven tool that may support individualized prophylaxis decisions. External prospective validation is warranted.

Abstracts printing tool powered by pagepress.org

XIX CONVEGNO TRIENNALE
VERONA
15, 16, 17 e 18 OTTOBRE 2026
Camera di Commercio di Verona
AICE Associazione Italiana Centri Emofilia

XIX Convegno Triennale sugli Aspetti Clinici e Sociali dell'Emofilia ABSTRACT N. CO-23

2.01 Hemophilia - clinical and treatment issues

PERIOPERATIVE MANAGEMENT OF MILD-TO-MODERATE HEMOPHILIA: A COMPARATIVE STUDY OF EXTENDED HALF-LIFE VERSUS STANDARD HALF-LIFE CONCENTRATES ON CLINICAL OUTCOMES AND FACTOR CONSUMPTION

M. Capetta[1|2|3], F. Valeri[1|2], C. Dainese[1|2], S. Bergonzi[1|2|3], G. Murante[1|2|3], A. Valpreda[4], R. Pastorino[1|3], F. Bocchi[1|3], B. Bruno[2|3], A. Borchiellini[1|2]

[1]Regional Centre for Hemorrhagic and Thrombotic Diseases, AOU Città della Salute e della Scienza, Torino, Italy; [2]Division of Hematology, AOU Città della Salute e della Scienza, University of Turin, Italy; [3]Department of Molecular Biotechnology and Health Sciences, University of Turin, Italy; [4]Central Laboratory Baldi and Riberi, AOU Città della Salute e della Scienza, University of Turin, Italy

Background and Aims. In recent years, extended half-life concentrates (EHLs) have become an effective alternative to standard half-life concentrates (SHLs) in hemophilia, offering improved pharmacokinetics and reduced infusion frequency. These features make EHLs particularly attractive for perioperative management. While their efficacy and safety in surgery have been confirmed in severe or moderate-severe hemophilia, evidence remains scarce for mild-to-moderate hemophilia. The aim of this study was to confirm perioperative safety and hemostatic efficacy of EHLs and to evaluate the reduction of factor consumption and number of infusions of EHLs compared to SHLs in patients with mild-to--moderate hemophilia A (HA) or B (HB).

Materials and Methods. We retrospectively analyzed 191 patients with mild-to-moderate HA or HB and collected data from 27 EHLs-managed surgeries (14 major, 13 minor) performed at our center between 2018 and 2026 on 22 patients (20 mild, 2 moderate). Two patients underwent the same surgery with both SHLs and EHLs, allowing an intra-patient comparison. Data were also compared with published literature for the same procedures (direct comparison of major surgeries was not possible due to the lack of comparable literature data). Preoperative PK studies guided dosing strategies in 16 procedures (59%), maintaining mean trough levels of 55% (24h) and 31% (72h); two emergency major surgeries precluded PK analysis. Regarding patients with HA, 11 procedures were performed using turoctocog alfa pegol, 4 with rurioctocog alfa pegol, 1 with damoctocog alfa pegol. Among patients with HB, nonacog beta pegol was utilized in 6 cases, eftrenonacog alfa and albutrepenonacog alfa in 2 cases each.

Results. In both comparisons we observed a reduction in the number of infusions (Table 1a) and total factor consumption (Table 1a, Table 1b). All 27 surgeries were managed with a single preoperative infusion. Postoperative infusions were administered once daily, whereas the literature reports twice-daily infusions when using SHLs. The sole exception in our cohort was a patient with mild HA undergoing cardiac surgery, who required more frequent infusions within the first 24 hours post-surgery before early transition to a single daily infusion. No patients developed inhibitors; a single bleeding event was due to poor hemostasis.

Conclusions. EHLs appear safe and effective for surgery in mild-to-moderate hemophilia, offering clinical advantages over SHLs across all analyzed populations, particularly in HB. While not statistically significant due to the limited cohort, these findings demonstrate a clinical advantage, despite the absence of baseline factor levels for literature-based cases. For HA, further improvements are expected with the advent of newer molecules.

	Patient 1	Patient 2
Type of hemophilia	HB mild	HB moderate
% of basal factor	11%	2%
Type of surgery	Major	Major
N° of infusions with SHLs	5	15
Total factor consumption with SHLs	200 IU/Kg	925 IU/Kg
N° of infusions with EHLs	2	10
Total factor consumption with EHLs	67 IU/Kg	650 IU/Kg

1a

Type of surgery	Source	Patient	Peri-operative consumption	Bleeding treatment
Colonoscopies with biopsies	Literature with SHLs	Patient 1 - HA mild	142 IU/Kg	293 IU/Kg
		Patient 2 - HA mild	115 IU/Kg	
		Patient 3 - HB mild	283 IU/Kg	
		Patient 4 - HA mild	77 IU/Kg	
		Patient 5 - HA moderate	149 IU/Kg	32 IU/Kg
		Patient 6 - HA moderate	49 IU/Kg	393 IU/Kg
		Patient 7 - HB mild	270 IU/Kg	360 IU/Kg
	Local experience with EHLs	Patient 1 - HB mild	41 IU/Kg	
		Patient 2 - HA mild	45 IU/Kg	
		Patient 3 - HA mild	100 IU/Kg	
		Patient 4 - HA mild	66 IU/Kg	67 IU/Kg + 134 IU/Kg of SHLs + 2 blood transfusions
		Patient 5 - HA mild	34 IU/Kg	
Dental impiant placement	Literature with SHLs	Patient 1 - HA moderate	100 IU/Kg + tranexamic acid	
	Local experience with EHLs	Patient 2 - HA mild	36 IU/Kg	

1b

Table 1: intra-patient comparison (1a) and literature comparison (1b).

Abstracts printing tool powered by pagepress.org

XIX CONVEGNO TRIENNALE
VERONA
15, 16, 17 e 18 OTTOBRE 2026
Camera di Commercio di Verona
AICE Associazione Italiana Centri Emofilia

XIX Convegno Triennale sugli Aspetti Clinici e Sociali dell'Emofilia ABSTRACT N. CO-24

2.01 Hemophilia - clinical and treatment issues

BALANCING BLEEDING AND THROMBOSIS: SAFETY OF LOW-MOLECULAR-WEIGHT HEPARIN THROMBOPROPHYLAXIS IN PATIENTS WITH HEMOPHILIA UNDERGOING MAJOR SURGERY

S. Bergonzi[1|2|3], G. Murante[1|2|3], M. Capetta[1|2|3], F. Valeri[1|2], C. Dainese[1|2], A. Valpreda[3|4], R. Pastorino[3|4], F. Bocchi[3|4], B. Bruno[2|3], A. Borchiellini[1|2]

[1]Regional Centre for Hemorrhagic and Thrombotic Diseases, AOU Città della Salute e della Scienza, Torino, Italy; [2]Division of Hematology, AOU Città della Salute e della Scienza, University of Turin, Italy; [3]Department of Molecular Biotechnology and Health Sciences, University of Turin, Italy; [4]Central Laboratory Baldi and Riberi, AOU Città della Salute e della Scienza, University of Turin, Italy

Background and Aims. In patients with hemophilia, the risk of venous thromboembolism (VTE) is traditionally considered low, but may become clinically relevant in the setting of major surgery, particularly orthopedic and oncologic procedures. Current evidence is limited and heterogeneous. International guidelines recommend an individualized assessment of thrombotic and bleeding risk, favoring mechanical over pharmacological thromboprophylaxis, which should be reserved for selected patients under adequate factor replacement and without inhibitors. In this context, we aimed to retrospectively evaluate the safety of pharmacological thromboprophylaxis with low molecular-weight heparin (LMWH) in patients with hemophilia undergoing major surgery.

Materials and Methods. Medical records of 105 patients with moderate/severe hemophilia A or B followed at our center were retrospectively reviewed. Among these, 12 patients undergoing 18 major surgical procedures received postoperative LMWH thromboprophylaxis. Data were verified through comparison with the rare diseases registry.

Results. All included patients had severe hemophilia A and received perioperative factor replacement therapy. Trough factor levels during the first three postoperative days were ≥14%, and ≥11% thereafter. Patient characteristics, type of surgery, and trough levels are reported in *Table 1*. A single bleeding event occurred in a patient undergoing intestinal reanastomosis for previous rectal adenocarcinoma, who presented on postoperative day 4 with hematemesis and rectal bleeding, requiring LMWH discontinuation and transfusion support. No other major or minor bleeding events were observed. One patient developed a clinically evident VTE on postoperative day 8 despite LMWH thromboprophylaxis, in the presence of multiple risk factors (high-risk inherited thrombophilia and smoking). No additional clinically evident thromboembolic events were observed.

Conclusions. In a setting of limited and conflicting evidence, all patients underwent individualized assessment of thrombotic and bleeding risk. They received adequate factor replacement therapy and were monitored through factor levels. In this context, LMWH thromboprophylaxis appeared safe in the vast majority of cases. These findings support the feasibility of a personalized approach to pharmacological thromboprophylaxis in patients with hemophilia undergoing major surgery, although prospective studies are warranted to confirm its safety.

Pt	Age at surgery	Preoperative prophylaxis	Additional VTE risk factors	Surgery	VTE	Bleeding	Trough fVIII POD 1-3 (%)	Trough fVIII >POD3 (%)
1.1	60	Replacement	Heterozygous factor V Leiden + homozygous prothrombin polymorphism + smoking	Laparoscopic cholecystectomy + endoscopic bile duct clearance	NO	NO	44	80
1.2	63	Replacement	Heterozygous factor V Leiden + homozygous prothrombin polymorphism + smoking	TKA	YES	NO	59	88
2	65	Replacement	Obesity	THA	NO	NO	100	50
3	50	Replacement	History of PICC-related VTE	Infected TKA removal + debridement + knee arthrodesis with external fixation	NO	NO	55	16
4.1	66	Non replacement (Emicizumab)	Rectal adenocarcinoma + smoking	Thoracoscopic lung biopsy	NO	NO	45	NA
4.2	60	Replacement	Rectal adenocarcinoma + smoking	Rectal resection for adenocarcinoma with ileostomy	NO	NO	47	20
4.3	61	Replacement	Rectal adenocarcinoma + smoking	Surgical revision for anastomotic leak after rectal resection	NO	NO	24	17
4.4	61	Replacement	Rectal adenocarcinoma + smoking	Intestinal reanastomosis	NO	YES	35	21
5.1	54	Replacement	Klinefelter syndrome	TKA	NO	NO	49	95
5.2	50	Replacement	Klinefelter syndrome	TKA	NO	NO	106	50
6	36	Replacement	NO	TKA	NO	NO	152	160
7	62	Replacement	NO	TKA revision for periprosthetic fracture	NO	NO	58	40
8	41	Replacement	NO	TKA	NO	NO	63	11
9	67	Non replacement (Emicizumab)	NO	TKA	NO	NO	39	49
10.1	54	Replacement	NO	Patellar tendon repair	NO	NO	14	14
10.2	51	Replacement	NO	THA	NO	NO	84	104
11	28	Replacement	NO	Ischial tuberosity exostosis resection (osteoma)	NO	NO	60	45
12	67	Replacement	NO	THA	NO	NO	63	40

Abbreviations: Pt, patient; VTE, venous thromboembolism; POD: postoperative day; TKA, Total knee arthroplasty; THA, Total hip arthroplasty; NA, not available.

Abstracts printing tool powered by pagepress.org

XIX CONVEGNO TRIENNALE
VERONA
15, 16, 17 e 18 OTTOBRE 2026
Camera di Commercio di Verona
AICE Associazione Italiana Centri Emofilia

XIX Convegno Triennale sugli Aspetti Clinici e Sociali dell'Emofilia ABSTRACT N. CO-25

2.01 Hemophilia - clinical and treatment issues

MILD HEMOPHILIA A AND JOINT HEALTH IN REAL LIFE: IS THAT AN EMERGING ISSUE? A SINGLE CENTER EXPERIENCE

F. Valeri[1], G. Murante[1], C. Dainese[1], M. Capetta[1], S. Bergonzi[1], R. Pastorino[1], F. Bocchi[1], B. Bruno[2], A. Borchiellini[1]

[1]Regional Centre for Haemorrhagic and Thrombotic Disease, Hematology Division, AOU Città della Salute e della Scienza, Torino, Italy; [2]Division of Hematology, AOU Città della Salute e della Scienza, Department of Molecular Biotechnology and Health sciences, University of Turin, Italy

Background. mHA, defined by FVIII between 0.05 and 0.40 IU/mL, is characterized by sporadic bleeds that rarely lead to arthropathy. Definition of mHA includes different bleeding phenotypes with manifestations that can vary between patients. The aim of this study is to investigate joint status in our cohort of mHA patients, to detect any sign of arthropathy and to explore any relationship between joint health and FVIII, body mass index (BMI) and age. Furthermore, we perform a quality of life (QoL) assessment to detect any impairment health related.

Methods. Patients with mHA between 18 and 65 years old referred in our center in 2025 were included. Elbows, knees and ankles were evaluated by HJHS (Hemophilia Joint Health Score) and by HEAD US score (Hemophilia Early Arthropathy Detection with Ultrasound). Data regarding FVIII, BMI and pain (according to NRS scale) were also collected. Variables were analyzed globally and splitted according to age (< 49 yo and > 50 yo) and FVIII levels (form 0.05UI/ml to 0.20IU/ml and from 0.21IU/ml to 35IU/ml). EQ-5D-3L, SF36 and IPAQ questionnaires were administered to explore QoL and physical activity.

Results. Of the 96 mHA patients treated at our center, 42 patients were enrolled in the study. We found low joint health scores; median HEAD US= 2(IQR 0-5), median HJHS=2(IQR 0-5). However, only 15 (36%) patients had no joint damage (HEAD US=0), 27 (64%) had at least one joint with a HEAD-US ≥ 1. No differences were found in HEAD US and HJHS according to FVIII, but we found that for elderly patients and for whom with higher BMI there is a statistically significant increase in HEAD-US. 20 patients fulfilled all QoL questionnaires: 14/20 (70%) showed no impairment in QoL, 6/20 (30%) expressed discomfort related to musculoskeletal criticalities. In the IPAQ evaluation, 15/20 (75%) were classified as quite/very active and 5/20 (25%) inactive. We observed a correlation trend between high HJHS and worse QoL perception. No correlation between QoL and FVIII, HEAD US, age or BMI were found.

Conclusions. Our data suggest that mHA show better joint status compared to severe or moderate HA patients, without differences according to FVIII deficiency. We found a significant correlation between HEAD US and age and BMI, identifying these two parameters as risk factors for early arthropathy development. mHA patients showed good QoL, with only critical issue pain and/or musculoskeletal impairment, suggesting that the disease burden is related to articular health rather than the disease itself. In conclusion, US joints alterations, even without clinical sign of arthropathy, should be routinely investigated in mHA patients in order to prevent/detect reversible damage, especially in adulthood and in overweight patients and can affect QoL.

	all	FVIII			age			BMI		
		5%-20%	21-35%	p	< 49 yo	> 50 yo	p	< 25	> 25	p
Age	49 (33-60)	50 (33-62)	49 (34-58)		33 (29-46)	60 (57-63)		42 (30-50)	60 (56-64)	
FVIII	15(10-20)	12 (10-15)	26 (21-30)		15 (12-20)	14 (10-21)		15 (12-20)	14 (9-22)	
HEAD US	2 (0-5)	2 (0-5)	0 (0-4)	0.14	0 (0-2)	4 (1-7)	**<0.001**	0 (0-3)	4 (1-8)	**<0.005**
HJHS	2 (0-5)	2 (0-5)	1 (0-2)	0.15	1 (0-2)	2 (0-5)	0.09	2 (0-2)	2 (0-5)	0.16
NRS	0 (0-2)	0 (0-2)	0 (0-0)	0.28	0 (0-1)	0 (0-3)	0.29	0 (0-0)	0 (0-5)	0.10
BMI	25 (23-27)	24 (22-27)	25 (24-26)	0.35	24 (21-25)	27 (24-29)	**<0.001**	24 (21-25)	28 (27-30)	**<0.001**

Abstracts printing tool powered by pagepress.org

XIX CONVEGNO TRIENNALE
VERONA
15, 16, 17 e 18 OTTOBRE 2026
Camera di Commercio di Verona
AICE Associazione Italiana Centri Emofilia

CLINICAL, LABORATORY AND METABOLIC CHARACTERISTICS OF ADULT PATIENTS WITH HEMOPHILIA A

J. Di Paolo, M. Di Loreto, R. Malizia, M. Luongo, P. Massaro, M. Di Mascio, S. Verna

Immunohematology Service, Asl 02 Abruzzo, Chieti, Italy

Background and Aims. Hemophilia A is an inherited bleeding disorder caused by factor VIII (FVIII) deficiency and characterized by recurrent bleeding episodes and progressive joint damage. Improved life expectancy resulting from prophylactic treatment has increased the clinical relevance of long-term comorbidities, including metabolic and cardiovascular disorders. This study aimed to evaluate the clinical, laboratory, and metabolic characteristics of patients with hemophilia A compared with healthy controls.

Materials and Methods. 26 male patients with hemophilia A and 66 healthy male blood donors were enrolled. Mean age was 45 years in patients and 44 years in controls. Patients were classified as having mild, moderate, or severe hemophilia according to FVIII activity levels. Clinical records were reviewed to assess age at diagnosis, hemophilic arthropathy, physical activity, dietary habits, infectious history, and metabolic comorbidities. Laboratory evaluation included metabolic, nutritional, inflammatory, and biochemical parameters, together with HBV, HCV, and HIV serology.

Results. 9 patients (35%) had mild hemophilia, 5 (19%) moderate hemophilia, and 12 (46%) severe hemophilia. Severe disease was diagnosed earlier than mild disease. Eleven patients (42%) had a history of HBV and/or HCV infection, most commonly HCV (64%). Hemophilic arthropathy was among the most frequent complications, predominantly affecting knees, ankles, elbows, and hips. Reduced physical activity was frequently observed, often related to fear of bleeding; only 10 patients reported regular sports participation, mainly younger individuals. Several patients also reported unbalanced dietary habits. Metabolic comorbidities were present in 77% of patients. Dyslipidemia was observed in 35%, isolated hypertension in 12%, diabetes mellitus in 15%, combined dyslipidemia and hypertension in 12%, and combined diabetes and hypertension in 4%; only 23% of patients had no metabolic comorbidities. Compared with controls, patients showed significantly higher glucose and triglyceride levels, particularly those older than 40 years. Ferritin levels were significantly increased, likely reflecting chronic joint damage and recurrent microbleeding, whereas CRP levels did not differ significantly between groups.

Conclusions. In addition to bleeding-related and musculoskeletal complications, patients with hemophilia A exhibit a high prevalence of metabolic abnormalities and cardiovascular risk factors. Reduced physical activity and unhealthy lifestyle habits may contribute to this burden. These findings highlight the importance of a multidisciplinary approach that integrates bleeding prevention with metabolic and cardiovascular risk assessment, lifestyle counseling, and promotion of safe physical activity.

XIX CONVEGNO TRIENNALE
VERONA
15, 16, 17 e 18 OTTOBRE 2026
Camera di Commercio di Verona
AICE Associazione Italiana Centri Emofilia

XIX Convegno Triennale sugli Aspetti Clinici e Sociali dell'Emofilia ABSTRACT N. CO-27

2.01 Hemophilia - clinical and treatment issues

INNOVATIVE USE OF EPTACOG BETA TO TREAT ACUTE ELBOW HEMARTHROSIS IN A PEDIATRIC PATIENT WITH HEMOPHILIA B AND A HISTORY OF INHIBITORS, UNDERGOING SECONDARY PROPHYLAXIS WITH CONCIZUMAB

L. Laterza[1], P. Giordano[2], G. Lassandro[2]

[1]University of Bari "Aldo Moro", Interdisciplinary Department of Medicine, Bari, Italy; [2]Pediatric Haemophilia Center-AOUC Pol. Giovanni XXXIII, University of Bari "Aldo Moro", Bari, Italy

Background. People with severe hemophilia B (PWBH) require intravenous anti-hemorrhagic prophylaxis with coagulation factor IX (FIX) to prevent acute bleeding and chronic arthropathy. The development of inhibitory antibodies against FIX occurs in 3–5% of PWBH, compromising patient management, particularly in the pediatric population. Although immune tolerance induction (ITI) is the standard of care for inhibitor eradication, outcomes are variable and the occurrence of adverse reactions can compromise treatment success. In these scenarios, bypassing agents, such as recombinant activated factor VII (rFVIIa), is crucial for managing acute bleeding episodes rather than for prophylaxis. Alongside Eptacog alfa, the historical rFVIIa approved as a bypassing agent, Eptacog beta is a novel rFVIIa, potentially less thrombogenic, approved by EMA for PWHB aged over 12 years. Eptacog beta differs from eptacog alfa in its N-glycosylation profile, which can result in greater efficacy. We describe the first use of Eptacog beta to treat bleeding in a PWHB with INH and anti-TFPI prophylaxis.

Case Presentation. We report the case of an 11-year and 4-month-old male patient affected by severe hemophilia B (FIX <1%), with documented high-titer inhibitors and a prior history of an anaphylactoid reaction to a few exposure doses of rFIX. The patient's clinical history was characterized by almost ten years of on demand treatment with Eptacog alfa (ABR=4, target joint: right elbow). In October 2025, to control bleeding episodes he started secondary prophylaxis with Concizumab (a subcutaneous anti-TFPI antibody); no bleeding events were reported in the following three months. In January 2026, due to a new right elbow hemarthrosis, intravenous Eptacog-beta (Cevenfacta) was administered, off-label due to age, following parental informed consent, at a dosage of 75 μg/kg, according to the following regimen: three doses every 3 hours, followed by two doses every 4 hours and a final dose 6 hours later. Treatment with Eptacog-beta induced a rapid hemostatic response, leading to the full resolution of pain and functional impairment. The infusion was well tolerated by the patient; no adverse or hypersensitivity reactions, thrombotic events or development of anti-drug antibodies were reported during hospitalization or throughout the subsequent 90-day follow-up period.

Conclusions. This report represents the first documented evidence in literature of Eptacog beta use in a pediatric patient aged < 12 years undergoing Concizumab prophylaxis. Despite current EMA restrictions in the pediatric population, the favorable safety profile and good tolerability observed suggest that Eptacog beta may represent a valid therapeutic option for managing acute bleeding episodes in clinically complex patients

XIX CONVEGNO TRIENNALE
VERONA
15, 16, 17 e 18 OTTOBRE 2026
Camera di Commercio di Verona
AICE Associazione Italiana Centri Emofilia

XIX Convegno Triennale sugli Aspetti Clinici e Sociali dell'Emofilia ABSTRACT N. CO-28

2.01 Hemophilia - clinical and treatment issues

SYNERGISTIC EFFECT OF RECOMBINANT FACTOR INFUSION ON THROMBIN GENERATION IN HEMOPHILIA PATIENTS UNDER EMICIZUMAB OR CONCIZUMAB PROPHYLAXIS

F. Bocchi[1|2], R. Pastorino[1|2], G. Murante[1|2|3], S. Bergonzi[1|2|3], M. Capetta[1|2|3], F. Valeri[2|3], C. Dainese[2|3], A. Valpreda[4], B. Bruno[1|3], A. Borchiellini[2|3]

[1]Department of Molecular Biotechnology and Health Sciences, University of Turin, Italy; [2]Regional Centre for Thrombotic and Hemorrhagic Diseases, AOU Città della salute e della Scienza di Torino, Italy; [3]Division of Hematology, AOU Città della Salute e della Scienza, University of Turin, Italy; [4]Central Lab Baldi and Riberi, AOU Città della salute e della Scienza di Torino, Italy

Background and Aims. Hemophilia is caused by deficiency of factor VIII (FVIII) or IX (FIX). Current prophylactic strategies include non-replacement therapies such as emicizumab (emz) and concizumab (cncz), both capable of enhancing thrombin generation (TG) parameters. Nevertheless, breakthrough bleeding and surgical procedures remain challenging clinical settings, often requiring concomitant administration of recombinant clotting factors. This study aimed to evaluate the impact of recombinant factor infusion on TG profiles in patients receiving emz or cncz prophylaxis.

Materials and Methods. Twenty-three patients (pts) were screened: 21 receiving emz and 2 cncz within the Novo Nordisk study NCT04082429. Only 4 pts required recombinant factor replacement for surgery or breakthrough bleeding and were included in the analysis. The emz group comprised 3 pts with hemophilia A (1 moderate-severe, 2 severe), treated for major surgery (n=2) or bleeding (n=1). The cncz group included 1 pt with severe hemophilia B evaluated during three separate bleeding episodes requiring FIX infusion. Blood samples were collected within 12 hours after recombinant factor infusion. TG was performed in platelet-poor plasma using the ST Genesia® system (Stago, Asnières-sur-Seine, France) with STG BleedScreen reagent. Baseline TGA values were obtained from previously stored follow-up samples collected during prophylaxis with the non-replacement therapy alone.

Results. Following factor infusion, TG changes were heterogeneous in the emz group (Table 1). Pts 2 and 3 showed the expected procoagulant response, whereas Pt 1 displayed a paradoxical reduction in TG parameters together with Start-Tail prolongation. Despite achieving a post-infusion FVIII plasma level of 29%, Pt 1 showed lower thrombin generation potential compared with baseline. In the cncz-treated pt, all three bleeding episodes showed a consistent pattern characterized by increased Peak Height associated with reduced ETP and StartTail values.

Conclusions. Distinct TG kinetic profiles emerged between the two non-replacement therapies. Cncz was associated with an early thrombin burst followed by rapid degradation, whereas emz produced a more gradual TG curve, consistent with its mechanism of action. The paradoxical reduction in TG observed in Pt 1 despite adequate FVIII levels may reflect clinical factors such as increased perioperative clotting factor consumption and concomitant heparin administration, both potentially limiting TG. These findings support the role of TG as a comprehensive global assay for individualized management of prophylaxis, bleeding, and surgery in hemophilia. Future application of TGA in platelet-rich plasma may further improve physiological assessment by incorporating cellular interactions occurring in vivo.

	Emicizumab			Concizumab		
	Patient 1	Patient 2	Patient 3	Patient 4 - bleeding 1	Patient 4 - bleeding 2	Patient 4 - bleeding 3
Peak Height (nM)	-37.7	+29.9	+67.8	+11.3	+23.9	+12.2
ETP (nM.min)	-25.9	+5.7	+11.1	-8.4	-2.5	-1
Start Tail (min)	+27.1	-12.4	-27.3	-16.1	-15.2	-10.4
Total dose of recombinant factor	30 IU/Kg	50 IU/Kg	30 IU/Kg	30 IU/Kg	30 IU/Kg	30 IU/Kg
Factor level after infusion (chromogenic assay)	29.2%	38.7%	19.3%	12.2%	9%	6.6%

Table 1

A RARE BLEEDING PRESENTATION IN MODERATE HEMOPHILIA A: PARAVESICAL HEMATOMA WITH PENOSCROTAL EXTENSION MIMICKING A UROLOGICAL EMERGENCY

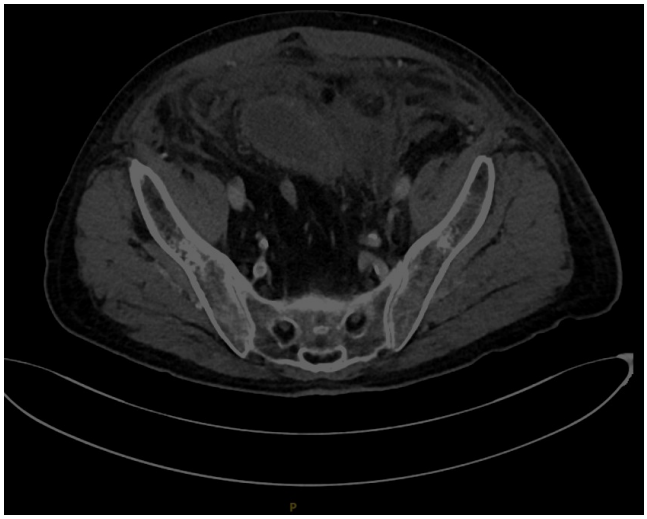
B. Stocco, C. Simion, E. Zanon, E. Dalla Porta, P. Simioni

Hemophilia Center, University Hospital of Padua, Italy

Background. Bleeding episodes in hemophilia typically involve joints and muscles, whereas deep pelvic hematomas are uncommon and may present with nonspecific symptoms, leading to diagnostic uncertainty. Paravesical hematomas are particularly rare and can mimic acute surgical or urological conditions. We report an unusual case of paravesical hematoma with penoscrotal extension in a patient with moderate hemophilia A.

Case Report. An 81-year-old man with moderate hemophilia A (factor [F]VIII 3.6%), treated on demand with plasma-derived FVIII concentrate, presented with progressive lower abdominal pain, dysuria, nausea, bilious vomiting, and acute penile and scrotal swelling with ecchymosis. One month earlier, he had undergone abdominal wall reconstruction for incisional hernia. Laboratory investigations showed leukocytosis, elevated C-reactive protein, and mild anemia (hemoglobin 11.2 g/dL). Ultrasound revealed a heterogeneous left paravesical collection measuring 8.8 × 5.6 × 3.8 cm without Doppler vascularization. Contrast-enhanced computed tomography confirmed a recent non-active paravesical hematoma measuring 10.3 × 9.5 × 5.3 cm, compressing and displacing the urinary bladder, with extension along the spermatic cord and into the penoscrotal region (Image 1). The patient was managed conservatively with factor VIII replacement therapy (37000 UI overall, for a period of ten days, starting from 70 UI/kg/day) and close clinical and radiological monitoring. No active bleeding was identified, and neither transfusion support nor surgical or radiological intervention was required. Hemoglobin reached a nadir of 9.1 g/dL during hospitalization before progressively increasing to 12.5 g/dL at discharge. Follow-up ultrasound demonstrated hematoma reduction to 7.3 × 5.9 × 3.5 cm with progressive organization of the collection. Clinical symptoms gradually resolved. Post-discharge magnetic resonance imaging showed slight reduction and resorption, confirming progressive spontaneous resolution.

Conclusions. This case expands the spectrum of atypical bleeding sites in hemophilia A and highlights paravesical hematoma as a rare cause of abdominal pain, urinary symptoms, and penoscrotal swelling. Clinicians should maintain a high index of suspicion for deep pelvic bleeding when these manifestations occur, even in patients with moderate disease. Early recognition and appropriate replacement therapy may result in favorable outcomes without the need for surgical or radiological intervention.



XIX CONVEGNO TRIENNALE
VERONA
15, 16, 17 e 18 OTTOBRE 2026
Camera di Commercio di Verona
AICE Associazione Italiana Centri Emofilia

XIX Convegno Triennale sugli Aspetti Clinici e Sociali dell'Emofilia ABSTRACT N. CO-30

2.01 Hemophilia - clinical and treatment issues

AL AMYLOIDOSIS IN A PATIENT WITH SEVERE HEMOPHILIA A AND INHIBITORS WHO HAD A MONOZYGOTIC TWIN: SAME GENES, DIFFERENT OUTCOMES

M. Biglietto[1|2], S. Sorella[1], S. Ligia[1], C. Andriola[1], R. Mormile[1], E. Baldacci[1], A. Chistolini[1], C. Santoro[1]

[1]Hematology, Department of Translational and Precision Medicine, Sapienza University of Rome, Italy; [2]Department of Molecular Biology, Sapienza University of Rome, Italy

Background. Severe hemophilia A with inhibitors has been associated, in the "pre-emicizumab era", with high bleeding risk and complex management. AL amyloidosis is a rare plasma cell dyscrasia characterized by monoclonal light chain deposition with systemic involvement. We report a case of AL amyloidosis in a patient with severe hemophilia A and high-titer inhibitors, who had a monozygotic twin.

Case Report. The patient and his monozygotic twin were referred to our center in 1973 at the age of 10 for severe hemophilia A; the proband had developed high-titer inhibitor after repeated exposure to pdFVIII and blood products and was subsequently treated with bypassing agents. Molecular analysis identified the F8 splice-site mutation c.1537+1G>A. In 1991 he tested positive for HCV, with spontaneous viral clearance. In 1995, a first immune tolerance induction (ITI) attempt with the Malmö protocol failed. The following years were complicated by multiple bleeding episodes, but the patient repeatedly refused a second ITI course. After two iliopsoas hematomas in 2010 and 2014, he agreed to a second ITI course with pdFVIII/vWF concentrate (100 IU/kg/day), started in July 2014. A transient inhibitor increase occurred, peaking at 1715 BU after two weeks. In August 2014 he experienced severe diffuse abdominal bleeding requiring large amounts of rFVIIa. Subsequently, no further bleeding events occurred and the inhibitor progressively declined to <1 BU in October 2016; pdFVIII/vWF was then tapered to 40 IU/kg/day by March 2017. During the 2014 hospitalization, laboratory tests revealed IgD-λ monoclonal gammopathy, with κ/λ ratio 0.04 and urinary λ Bence-Jones proteinuria of 195 mg/24 h. The patient declined further evaluation. In August 2016 he developed heart failure with reduced ejection fraction and concentric left ventricular hypertrophy. Periumbilical fat biopsy confirmed AL amyloidosis, and treatment with bortezomib, cyclophosphamide, and dexamethasone was started. In April 2017, a few days after treatment initiation, the patient died from sudden cardiac death. The monozygotic twin never developed inhibitors and presented only a stable lambda monoclonal gammopathy without organ involvement; he later developed cholangiocarcinoma.

Conclusions. We describe the rare coexistence of severe hemophilia A with inhibitors and AL amyloidosis in a monozygotic twin whose brother never developed inhibitors, suggesting that genetic background alone is insufficient to explain inhibitor development. Our question has remained if previous cyclophosphamide exposure and immune stimulation during ITI may have contributed to clonal progression. Environmental factors may therefore have influenced these divergent clinical histories: same genes, different outcomes.

Abstracts printing tool powered by pagepress.org

WHEN NECK PAIN HIDES A SPINAL BLEED: ANTERIOR CERVICAL EPIDURAL HEMATOMA IN A CHILD WITH HEMOPHILIA B

E. Dalla Porta, C. Simion, E. Zanon, B. Stocco, L. Spiezia, P. Simioni

Hemophilia Center, University Hospital of Padua, Italy

Cervical anterior spinal epidural hematoma is an exceptionally rare bleeding manifestation in pediatric hemophilia, with only isolated cases reported in the literature. Prompt recognition is crucial to prevent irreversible neurological sequelae. We report a child with moderate hemophilia B who developed a cervical anterior epidural hematoma successfully managed with conservative treatment.

Case Report. A 9-year-old boy with moderate hemophilia B (factor IX activity 2–5.6%), diagnosed during infancy and receiving regular factor IX replacement therapy, presented with left shoulder pain following a prolonged car journey. Within 24 hours, cervical and dorsal pain developed without neurological deficits. Magnetic resonance imaging (MRI) revealed an anterior cervical epidural hematoma extending from C3 to C7, with a maximum thickness of 5 mm and a craniocaudal extension of approximately 55 mm, causing mild spinal cord compression (Image 1). Laboratory evaluation excluded the presence of factor IX inhibitors. Given the absence of neurological impairment and the limited degree of canal compromise, neurosurgical intervention was not indicated. Recombinant factor IX replacement therapy with nonacog-alfa was intensified to 1000 IU (approximately 35 IU/kg) every other day for two weeks, under close clinical and radiological monitoring. Follow-up MRI demonstrated marked regression of the hematoma, which became confined to the anterior epidural space between C4 and C6, with reduction of both thickness (1.5 mm) and longitudinal extension (28 mm). The patient became completely asymptomatic and experienced no further bleeding complications during follow-up.

Conclusions. Cervical epidural hematoma represents an uncommon and potentially life-threatening bleeding manifestation in children with hemophilia. This case highlights the importance of maintaining a high index of suspicion when persistent cervical, dorsal, or radicular pain occurs, even in the absence of neurological deficits. Early MRI assessment was crucial for diagnosis and therapeutic decision-making. Conservative management with prompt factor IX replacement therapy allowed complete clinical recovery and substantial radiological improvement, avoiding neurosurgical intervention. The unusual cervical anterior localization and favorable outcome underline the importance of rapid recognition and multidisciplinary management of atypical bleeding presentations in hemophilia.

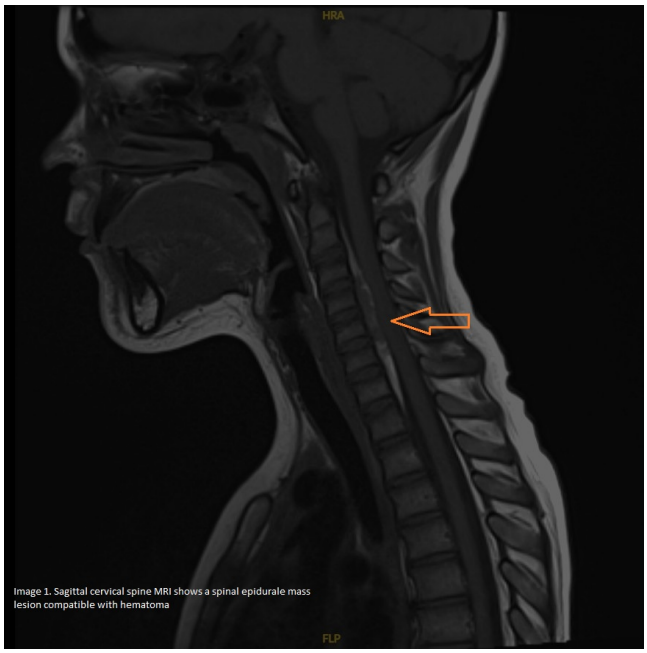


Image 1. Sagittal cervical spine MRI shows a spinal epidurale mass lesion compatible with hematoma

TRAUMA MANAGEMENT IN SEVERE HEMOPHILIA A: A CASE REPORT

J. Di Paolo, R. Malizia, M. Luongo, P. Massaro, M. Di Mascio, S. Verna

Immunohematology Service, Asl 02 Abruzzo, Chieti, Italy

Background. Hemophilia A is an X-linked hereditary bleeding disorder caused by mutations in the factor VIII (FVIII) gene, resulting in deficiency or absence of FVIII, a key component of the intrinsic coagulation pathway. The prevalence of hemophilia A is estimated at approximately 1 in 5,000 male live births. According to residual FVIII activity, hemophilia A is classified as severe (<1%), moderate (1–5%), or mild (>5% to <40%). The bleeding phenotype generally correlates with disease severity. Trauma in patients with hemophilia represents a time-dependent hemostatic emergency, characterized by a high risk of major bleeding even in the presence of apparently moderate injuries. The World Federation of Hemophilia (WFH) guidelines recommend immediate administration of replacement therapy before completion of the diagnostic workup, particularly in cases of major trauma or suspected musculoskeletal or intracranial involvement. Management is especially challenging in patients with a history of inhibitors.

Case Report. We describe the case of a patient with severe hemophilia A (FVIII <1%) with a previous history of high-responder inhibitors, a target joint involving the right knee, and a current inhibitor titer of 2 BU, admitted to the Emergency Department following a road traffic accident. The patient sustained right shoulder trauma with subluxation and multiple lacerations secondary to windshield glass injury. Given the high bleeding risk, replacement therapy with octocog alfa 8000 IU (calculated according to body weight, neutralizing dose, and incremental dose strategy), was promptly initiated, together with serial clinical, laboratory, and radiological monitoring. Imaging studies confirmed right shoulder subluxation without evidence of major bleeding or intracranial complications. Replacement treatment was continued for three consecutive days. The clinical course was favorable, with no bleeding progression or need for surgical intervention.

Conclusions. This case highlights the importance of early hemostatic treatment and a multidisciplinary approach in the management of trauma in patients with hemophilia, even in the presence of injuries initially considered moderate. A history of inhibitors represents an additional management challenge and requires close clinical and laboratory monitoring. Prompt intervention, in accordance with international recommendations, may help prevent severe hemorrhagic complications and improve clinical outcomes.

XIX CONVEGNO TRIENNALE
VERONA
15, 16, 17 e 18 OTTOBRE 2026
Camera di Commercio di Verona
AICE Associazione Italiana Centri Emofilia

XIX Convegno Triennale sugli Aspetti Clinici e Sociali dell'Emofilia ABSTRACT N. CO-33

2.01 Hemophilia – clinical and treatment issues

REAL-WORLD EXPERIENCE WITH MARSTACIMAB PROPHYLAXIS IN SEVERE HEMOPHILIA A WITHOUT INHIBITORS AND ADVANCED HEMOPHILIC ARTHROPATHY

A. Casson[1], I. Ricca[1], A. Barchieri[1], G. Guido[1], M. Tucciarone[1], P. Ocello[1], C. Francisco[2], P. Abrate[2], G. Delios[1]

[1]Centro Malattie Trombotiche ed Emorragiche - SC Servizio Trasfusionale ASL TO4, Ivrea, Torino, Italy; [2]SC Farmacia Ospedaliera ASL TO4, Ivrea, Torino, Italy

Background. Marstacimab is a novel subcutaneous anti-TFPI monoclonal antibody approved as non-replacement prophylaxis for hemophilia without inhibitors. Real-world data are still limited, particularly in patients with severe hemophilia A and advanced arthropathy.

Case Report. A 47-year-old man with severe hemophilia A (FVIII <1%), no history of inhibitors and advanced hemophilic arthropathy was followed at our Centre. His history included resolved HCV infection, bilateral knee and ankle prostheses, previous bleeding duodenal ulcer, prior pulmonary hemorrhagic parenchymal suffusion. Treatment history included on-demand cryoprecipitate and plasma-derived FVIII, then recombinant FVIII prophylaxis, followed by emicizumab from January 2021 to February 2024. Because of persistent joint disease with effusion and synovitis, prophylaxis was then switched to extended half-life recombinant FVIII (Efmoroctocog alfa 3000 IU twice weekly). In October 2025, treatment was changed to Marstacimab, with a 300 mg loading dose followed by 150 mg subcutaneously once weekly; thrombophilia screening performed before treatment initiation was reported as normal. During follow-up, reduced bleeding tendency and good hemostatic coverage were documented. In February 2026 the patient reported paresthesias, headache, diarrhea and lower-limb pain: clinical evaluation and labaoratory assessment were negative for thrombotic complications, and weekly Marstacimab was continued. At April 2026 follow-up, the patient reported subjective well-being on weekly Marstacimab prophylaxis.

Conclusions. In this adult with severe hemophilia A without inhibitors, advanced arthropathy and multiple comorbidities, Marstacimab prophylaxis proved feasible in routine practice and was associated with favorable short-term clinical perception of bleeding control. Careful surveillance remains warranted, and further real-world evidence is needed to define safety and effectiveness in complex patients.

XIX CONVEGNO TRIENNALE
VERONA
15, 16, 17 e 18 OTTOBRE 2026
Camera di Commercio di Verona
AICE Associazione Italiana Centri Emofilia

XIX Convegno Triennale sugli Aspetti Clinici e Sociali dell'Emofilia ABSTRACT N. CO-34

2.01 Hemophilia - clinical and treatment issues

SIMPLIFIED PERIOPERATIVE MANAGEMENT WITH N8-GP (TUROCTOCOG ALFA PEGOL) IN MAJOR ABDOMINAL SURGERY IN MILD HEMOPHILIA A WITH SEVERE BLEEDING PHENOTYPE: A CASE REPORT

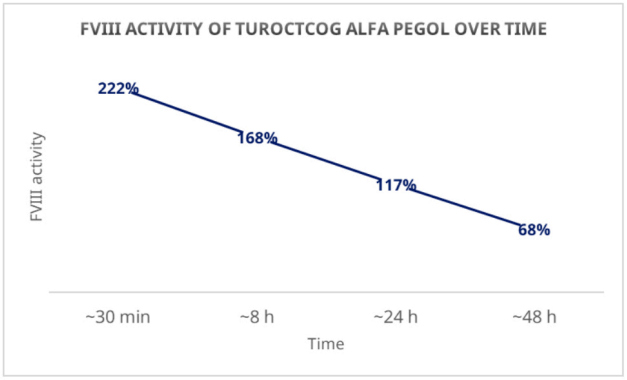
J. Di Paolo, R. Malizia, M. Luongo, P. Massaro, M. Di Mascio, S. Verna

Immunohematology Service, Asl 02 Abruzzo, Chieti, Italy

Background. Mild haemophilia A (HA; residual FVIII activity 5-40 IU/dL) is characterized by heterogeneous bleeding manifestations that are not always predicted by baseline FVIII levels. Perioperative management should be individualized according to bleeding history, surgical complexity, factor-level monitoring and, pharmacokinetic response. Current WFH guidance recommends near-normal FVIII activity (80-100%) before major surgery, followed by sustained postoperative coverage and close monitoring. Extended half-life FVIII concentrates, including N8-GP (turoctocog alfa pegol), may reduce infusion frequency while maintaining haemostatic protection, as supported by pathfinder surgical data.

Case Report. We describe the case of a 52-year-old man with mild HA (baseline FVIII approximately 6%) and a severe bleeding phenotype, receiving weekly prophylaxis with N8-GP 5000 IU (~60 IU/kg), who underwent elective laparoscopic cholecystectomy on 19 May 2026. The last prophylactic infusion had been administered 5 days before surgery. Perioperative management consisted of a single preoperative intravenous bolus of turoctocog alfa pegol 5000 IU, serial FVIII activity monitoring using a chromogenic bovine assay, and clinical/laboratory follow-up. FVIII activity reached 222% 30 minutes after infusion and remained above 50% for at least 48 hours (168% at 8h, 117% at 24h, 68% at 48h; Figure 1). One outpatient booster dose was administered after discharge before resumption of the usual prophylactic schedule. No perioperative or postoperative bleeding events occurred, and no adverse events were reported. Haemoglobin and platelet count remained stable until discharge (Hb 15.5 g/dL; platelets 166,000/uL). Haemostatic efficacy was rated as excellent.

Conclusions. This case shows that major abdominal surgery in a patient with mild HA but severe bleeding phenotype can be managed using an individualized, low-frequency perioperative regimen with turoctocog alfa pegol. A single preoperative bolus provided effective haemostatic coverage for approximately 48 hours, allowing early discharge and reduced treatment burden, with potential advantages in terms of healthcare resource utilization. Although conclusions are limited by the single-case design and require confirmation in larger real-world cohorts, these findings support a phenotype-driven and pharmacokinetic-informed approach to surgical management in haemophilia, particularly when baseline FVIII activity does not fully reflect bleeding risk.



XIX CONVEGNO TRIENNALE
VERONA
15, 16, 17 e 18 OTTOBRE 2026
Camera di Commercio di Verona
AICE Associazione Italiana Centri Emofilia

XIX Convegno Triennale sugli Aspetti Clinici e Sociali dell'Emofilia ABSTRACT N. CO-35

2.01 Hemophilia - clinical and treatment issues

TRANSITION FROM A PAEDIATRIC REFERRAL CENTER TO AN ADULT CENTER IN INHERITED BLEEDING DISORDERS: A REAL-WORLD COHORT STUDY

I. Ricca[1], A. Casson[1], T. Martini[2], B. Borsellino[2], A. Barchieri[1], G. Guido[1], P. Ocello[1], M. Tucciarone[1], R. Albiani[2], B. Pollio[2], G. Delios[1]

[1]Centro Malattie Trombotiche ed Emorragiche - SC Servizio Trasfusionale ASL TO4, Ivrea, Italy; [2]Centro Esperto Malattie Emorragiche Congenite in Età Pediatrica e della Donna in Gravidanza - SSD Medicina Trasfusionale Materno-Infantile e Traumatologica, Città della Salute e della Scienza di Torino, Italy

Background and Aims. Transition from paediatric to adult care represents a pivotal phase in the management of inherited bleeding disorders, with potential implications for treatment adherence, continuity of care, and bleeding control. This study aimed to evaluate the clinical impact of transition from a regional paediatric referral center to an adult center, focusing on adherence and annualized bleeding rate (ABR) before and after transfer.

Materials and Methods. A retrospective observational cohort study was conducted in patients transferred from the Expert Center for Congenital Bleeding Disorders (MEC), Pediatric Unit, of Turin to the Thrombotic and Hemorrhagic Disorders Center, Transfusion Service, ASLTO4, up to May 2026. Demographic and clinical variables included type of bleeding disorder, age, adherence before and after transition, ABR before and after transfer, and treatment changes following transition. The transition pathway was based on structured collaboration between paediatric and adult teams to ensure continuity of care throughout the transfer process.

Results. Twenty-two patients were included, with a mean age of 30 years (range 17-58). The cohort comprised 17 patients with haemophilia A, 3 with haemophilia B, and 2 with von Willebrand disease type 3. Adherence improved from 19/22 patients (86.4%) before transition to 20/22 (90.9%) after transition. Mean ABR decreased from 0,64 ± 0,90 before transfer to 0.23 ± 0.75 after transfer. Treatment was modified in 9/22 patients (40.9%) following transfer, mainly because innovative therapeutic options had become available. No loss to follow-up was documented.

Conclusions. In this real-world cohort, transition from a paediatric to an adult center was associated with preserved or improved adherence and reduced bleeding burden. These findings suggest that a structured, network-based transition model can maintain clinical stability and support continuity of care in inherited bleeding disorders.

XIX CONVEGNO TRIENNALE
VERONA
15, 16, 17 e 18 OTTOBRE 2026
Camera di Commercio di Verona
AICE Associazione Italiana Centri Emofilia

XIX Convegno Triennale sugli Aspetti Clinici e Sociali dell'Emofilia

ABSTRACT N. CO-36

2.02 Laboratory issues

PLATELETS MATTER: THROMBIN GENERATION IN PLATELET-RICH-PLASMA VERSUS PLATELET-POOR-PLASMA UNDER NON-REPLACEMENT THERAPIES IN HEMOPHILIA

F. Bocchi[1|2], R. Pastorino[1|2], G. Murante[1|2|3], S. Bergonzi[1|2|3], M. Capetta[1|2|3], F. Valeri[2|3], C. Dainese[2|3], A. Valpreda[4], B. Bruno[1|3], A. Borchiellini[2|3]

[1]Department of Molecular Biotechnology and Health Sciences, University of Turin, Italy; [2]Regional Centre for Thrombotic and Hemorrhagic Diseases, AOU Città della salute e della Scienza di Torino, Italy; [3]Division of Hematology, AOU Città della Salute e della Scienza, University of Turin, Italy; [4]Central Lab Baldi and Riberi, AOU Città della salute e della Scienza di Torino, Italy

Background and Aims. Non-replacement therapies have transformed the management of Hemophilia A (HA) and B (HB). Emicizumab (Emz) is a recombinant bispecific monoclonal antibody that mimics activated FVIII (FVIIIa), restoring FX activation and thrombin generation. Concizumab (Concz) is an anti–tissue factor pathway inhibitor (TFPI) monoclonal antibody that enhances thrombin generation by inhibiting the TFPI anticoagulant pathway, compensating for FVIII and FIX deficiencies. Although their mechanisms are well established, their interaction with cellular coagulation components, particularly platelets, remains poorly characterized. Platelets provide a procoagulant phospholipid surface and amplify thrombin generation, but their contribution in patients receiving non-replacement therapies is not fully understood. This study evaluated the role of platelets in patients treated with Emz or Concz by comparing thrombin generation assay (TGA) parameters in platelet-rich plasma (PRP) and platelet-poor plasma (PPP).

Materials and Methods. Among 21 patients on Emz prophylaxis and 2 on Concz prophylaxis (in Novo Nordisk study NCT04082429) followed at our Centre, blood samples were obtained from 15 patients with severe HA, with or without inhibitors, receiving stable Emz prophylaxis, and from 2 patients receiving Concz (one severe HA and one severe HB). Thrombin generation was assessed in PRP and PPP using the ST Genesia® system (Stago, Asnières-sur-Seine, France). Frozen PPP samples were analyzed with the standard protocol, whereas PRP samples were tested within 2 hours of collection using an in-house validated protocol. Evaluated parameters included Lag Time, Peak Height, Time to Peak, Endogenous Thrombin Potential (ETP), Velocity Index, and Start Tail. PRP and PPP results were compared to assess platelet contribution to thrombin generation.

Results. Six samples were excluded due to instrument malfunction. Comparison between PRP and PPP in the 11 evaluable patients is reported in Table 1. In all patients, PRP showed increased Lag Time, Time to Peak, ETP, and Start Tail, together with reduced Velocity Index, while Peak Height showed no consistent trend. No relevant differences in thrombin generation profiles were observed between patients treated with Concz and those receiving Emz.

Conclusions. Consistent differences between PPP- and PRP-based TGA were observed across all patients. PRP curves showed delayed thrombin generation onset and prolonged time to peak, associated with higher total thrombin generation and increased endogenous thrombin potential. These findings suggest that PRP-based TGA may provide a more comprehensive assessment of the hemostatic profile in patients receiving non-replacement therapies by capturing platelet-dependent coagulation mechanisms.

Increase or decrease between PPP and PRP			
Parameter	Emicizumab (Hemophilia A)	Concizumab (Hemophilia A)	Concizumab (Hemophilia B)
Lag Time	+151,80%	+133,19%	+109,06%
Peak Height	+19,53%	-0,62%	-46,81%
Time to Peak	+126,33%	+82,30%	+137,88%
ETP	+51,00%	+27,97%	+43,67%
Velocity Index	-33,49%	-62,73%	-82,04%
Start Tail	+33,47%	+43,94%	+157,67%

Abstracts printing tool powered by pagepress.org

XIX CONVEGNO TRIENNALE
VERONA
15, 16, 17 e 18 OTTOBRE 2026
Camera di Commercio di Verona
AICE Associazione Italiana Centri Emofilia

XIX Convegno Triennale sugli Aspetti Clinici e Sociali dell'Emofilia

ABSTRACT N. CO-37

2.02 Laboratory issues

STEW-EFA STUDY: MULTICENTER EVALUATION OF ONE-STAGE AND CHROMOGENIC ASSAYS FOR EFANESOCTOCOG ALFA MEASUREMENT ON STAGO AND WERFEN PLATFORMS

A.C. Molinari[1], M. Marchetti[2], A. Catalano[3], L. Contino[4], R. De Cristofaro[5], A.B. Federici[6], T. Martini[7], I. Quaglia[8], R. Rossi[9], R. Santoro[10], A. Tripodi[11], A. Valpreda[12]

[1]Regional Reference Centre for Hemorrhagic Diseases, Department of Hemato-Oncology, IRCCS Istituto Giannina Gaslini, Genova, Italy; [2]Department of Immunohematology and Transfusion Medicine, ASST Papa Giovanni XXIII, Bergamo, Italy; [3]Società per la Promozione dell'educazione Medica (S.P.E.Me), Italy; [4]Hemostasis and Thrombosis Unit, AOU SS Antonio e Biagio e C Arrigo, Alessandria, Italy; [5]Dipartimento di Medicina e Chirurgia Traslazionale, Facoltà di Medicina e Chirurgia "Agostino Gemelli," Università Cattolica S. Cuore, Roma, Italy - Servizio Malattie Emorragiche e Trombotiche, Fondazione Policlinico Universitario "A. Gemelli" Istituto di Ricerca e Cura a Carattere Scientifico, Roma, Italy; [6]School of Medicine and Surgery, University of Milan-Bicocca, Milano, Italy; [7]Hemophilia Centre, Immune-Hematology and Transfusion Medicine, University Hospital "Città della Salute e della Scienza", Torino, Italy; [8]Center for Thrombosis and Hemorrhagic Diseases, IRCCS Humanitas Research Hospital Rozzano, Milan, Italy; [9]Laboratory of Clinical Chemistry and Hematology, University Hospital of Parma, Italy; [10]Hemophilia, Hemostasis, and Thrombosis Unit, Azienda Ospedaliero Universitaria Dulbecco, Catanzaro, Italy; [11]IRCCS Ca' Granda Maggiore Hospital Foundation and Angelo Bianchi Bonomi Hemophilia and Thrombosis Center, Milano, Italy; [12]Central Laboratory Baldi and Riberi, AOU Città della Salute e della Scienza, Turin, Italy, reference laboratory of the Regional Center for Hemostasis and Thrombosis.

Background. Efanesoctocog alfa is an ultra–extended half-life recombinant FVIII enabling once-weekly prophylaxis in hemophilia A. Structural modifications of the molecule may affect FVIII level measurements across different laboratory assays. Previous studies demonstrated relevant variability among activated partial thromboplastin time (aPTT) reagents, with potential under- or overestimation of FVIII activity. Reliable monitoring is essential at low trough levels and in patients previously treated with emicizumab, whose prolonged plasma persistence may interfere with coagulation assays. Limited data are currently available regarding the analytical performance of Stago and Werfen platforms, especially in these settings.

Aims. The STEW-EFA study aims to evaluate the accuracy and reproducibility of efanesoctocog alfa (EFA) measurement using one-stage clotting assays (OSA) and chromogenic substrate assays (CSA) on Stago and Werfen platforms. Secondary objectives include assessment of product-specific calibration strategies and evaluation of assay performance in samples containing both EFA and emicizumab.

Methods. STEW-EFA is a prospective multicenter analytical laboratory study promoted by the AICE Laboratory Quality Working Group. Sixteen Italian hemophilia laboratories will participate, 8 using the Stago platform and 8 using Werfen. FVIII-deficient plasma samples spiked with efanesoctocog alfa at nominal concentrations of 100, 50, 20, 10, and 5 IU/dL will be centrally prepared and distributed by ECAT. Additional samples containing combinations of emicizumab (20 or 50 µg/mL) and efanesoctocog alfa (50 or 100 IU/dL) will be analyzed using CSA. OSA testing will be performed using PTT-A® on Stago analyzers and SynthAFax® on Werfen analyzers. Chromogenic testing will employ TriniCHROM FVIII:C and Coamatic FVIII reagents, respectively. Each laboratory will test samples using both standard commercial calibration and product-specific, generated from serial dilutions of efanesoctocog alfa–spiked plasma (100 IU/dL). All measurements will be performed in triplicate duplicate over three independent analytical sessions using fresh reagents each day. Primary endpoints include assay accuracy, expressed as percentage recovery versus nominal concentration, and intra-/inter-laboratory reproducibility assessed by coefficient of variation (CV%). Secondary endpoints include comparison between standard and product-specific calibration approaches, comparison between analytical platforms, and evaluation of CSA performance in the presence of emicizumab.

Expected Results and Conclusions. The study is expected to provide real-world multicenter data on the analytical performance of Stago and Werfen assays for EFA monitoring. Product-specific calibration may improve assay accuracy, particularly at clinically relevant trough levels. STEW-EFA may contribute to harmonization of laboratory monitoring strategies for efanesoctocog alfa, including complex scenarios involving residual emicizumab interference, and could support future recommendations for coagulation laboratories managing patients with hemophilia A.

Abstracts printing tool powered by pagepress.org

XIX CONVEGNO TRIENNALE
VERONA
15, 16, 17 e 18 OTTOBRE 2026
Camera di Commercio di Verona
AICE Associazione Italiana Centri Emofilia

XIX Convegno Triennale sugli Aspetti Clinici e Sociali dell'Emofilia

ABSTRACT N. CO-38

2.02 Laboratory issues

CALIBRATION OF HUMAN COAGULATION FACTOR VIII IN NOVEL QUALITY CONTROL MATERIALS: A COLLABORATIVE STUDY

G. Gullifa[1], A. Carocci[1], C. Albertini[1|2], L. Luchetti[1], M.T. Pasquino[1], M. Simeoni[1], L. Mandarino[1], C. Adriano[1|3], R. Risoluti[3], S. Massimi[1]

[1]Centro Nazionale per il Controllo e la Valutazione dei Farmaci, Istituto Superiore di Sanità, Roma, Italy; [2]Centro Nazionale Sangue, Istituto Superiore di Sanità, Roma, Italy; [3]Sapienza Università di Roma, Italy

Background and Aims. Participation in Proficiency Testing Schemes (PTS) enables laboratories to continuously monitor their analytical performance, demonstrate their technical competence and the validity of their quality system, identify any issues and implement appropriate corrective actions. It is considered essential for laboratories involved in haemophilia A diagnosis to prove accuracy and precision of the final outcomes and ensure patients' safety. In this study, two candidate preparations of pooled fresh frozen human plasma were characterized and calibrated to provide Quality Control Materials (QCMs) for assessing Human Coagulation Factor VIII (FVIII) assays, with the aim of proposing a proficiency study for haemophilia centres. Selection of appropriate QCMs is one of the critical factors that must be carefully evaluated when organizing an interlaboratory comparison.

Materials and Methods. Fresh frozen plasma units were involved in the production of QMCs. All starting materials were characterized for serological and molecular markers of viral infection, haemagglutinins, and factor VIII. The final preparations were calibrated in a collaborative study, organized by the National Centre for the Control and Evaluation of Medicines of the Istituto Superiore di Sanità (ISS). This study involved 21 laboratories, which performed one-stage clotting assays (OSCAs) and chromogenic substrate assays (CSAs) to estimate FVIII activity. Prior to sending samples to haemophilia centres, homogeneity and stability of the obtained materials were studied.

Results. The collaborative study enabled the assignment of FVIII potency to the two candidate preparations and the evaluation of consistency between chromogenic and one-stage clotting assay results. The results of homogeneity and stability experiments showed that preparations did not undergo any significant changes when stored at - 20°C and used within 24 hours of thawing.

Conclusions. The final materials could be used to establish a proficiency testing scheme for assessing the performance and reliability of coagulation laboratories in FVIII testing.

Abstracts printing tool powered by pagepress.org

XIX CONVEGNO TRIENNALE
VERONA
15, 16, 17 e 18 OTTOBRE 2026
Camera di Commercio di Verona
AICE Associazione Italiana Centri Emofilia

XIX Convegno Triennale sugli Aspetti Clinici e Sociali dell'Emofilia

ABSTRACT N. CO-39

2.02 Laboratory issues

MYELOID CELL FUNCTION AND CYTOKINE PROFILES IN PEDIATRIC HEMOPHILIA A: INSIGHTS FROM FACTOR VIII AND EMICIZUMAB PROPHYLAXIS

T. Martini[1], A. Cottonaro[2], S. Akula[2], B. Pollio[1], I. Ricca[3], J. Agnelli Giacchello[4], P. Sciancalepore[4], R. Santi[4], A. Follenzi[2|4], S. Merlin[2]

[1]Haemophilia Centre, Immune-Haematology and Transfusion Medicine, University Hospital "Città della Salute e della Scienza", Torino, Italy; [2]Department of Health Sciences, Università del Piemonte Orientale, Novara, Italy; [3]Transfusion Medicine, Ivrea Hospital, Ivrea, Italy; [4]Azienda Ospedaliera SS. Antonio e Biagio e Cesare Arrigo, Alessandria, Italy

Background and Aims. Haemophilia A (HA) is an X-linked bleeding disorder caused by factor VIII (FVIII) deficiency, treated with FVIII infusions or, more recently, Emicizumab subcutaneously. Although Emicizumab is safe and effective, FVIII is still required for severe bleeding, trauma, or surgery, and few studies have compared these prophylactic options in paediatric patients. This study explores the immunological and haematological profiles of paediatric HA patients receiving FVIII or Emicizumab, using haemophilia B patients and healthy controls.

Materials and Methods. The immunological and cytokine profiles of pediatric patients with hemophilia A (stratified by treatment), hemophilia B, and healthy controls were characterized by flow cytometry and multiplex plasma assays. In parallel, macrophages were generated in vitro from patient monocytes to assess their immune response following FVIII stimulation. Cytokine levels and gene expression profiles of these cultured cells were finally quantified by ELISA and RT-qPCR assays, respectively.

Results. Clinical parameters and immune cell populations showed no major differences aside from age-related variations. However, HA patients displayed higher HLA-DR expression on CD14+ cells than healthy controls, and Emicizumab-treated patients showed increased HLA-DR expression on CD11c+ cells compared with FVIII-treated patients. Plasma cytokines including IL-12p40, TNF-α, CCL-22, IL-18, and CCL-4 were elevated in HA, suggesting a dysregulated myeloid compartment in HA. Patient-derived macrophages exhibited a stronger pro-inflammatory (M1-like) polarization after in vitro FVIII stimulation, with increased TNF-α and reduced TGF-β gene expression. Stratification by prophylaxis showed that macrophages from FVIII-treated patients maintained the M1 phenotype, whereas those from Emicizumab-treated patients showed no clear shift and tended toward an immune-regulatory profile (figure 1).

Conclusions. These findings highlight distinct myeloid and cytokine signatures associated with different prophylaxis, emphasizing the need for optimized therapeutic strategies.

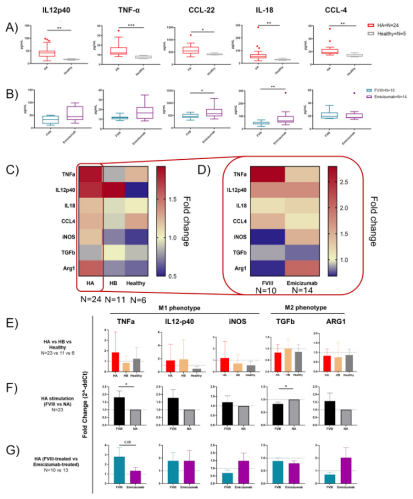


Figure 1. **(A-B)** Broad spectrum of monocyte/macrophages-related cytokines in haemophilic patient plasma. **(A)** Graphs showing comparison of IL12p40, TNF-a, CCL-22, IL-18 and CCL-4 quantification in plasma of HA patients and healthy donors. **(B)** Stratification of HA patients according to their undergoing treatment, either rFVIII or Emicizumab. All data are represented as a Tukey plot where the out-of-range samples are represented as a dot. Mann–Whitney test has been used for comparing the two groups (*$p < 0.05$; **$p < 0.01$; ***$p < 0.001$; ****$p < 0.0001$). **C-G)** Gene expression analysis of patient-derived macrophages stimulated with FVIII in vitro, to understand if they shift toward an M1 or M2 phenotype. **(C-D)** Heatmaps showing gene expression profiles of HA (N = 23), HB (N = 11) and healthy (N = 6) macrophages **(C)**, and subsequent stratification of HA patients according to their undergoing treatment, either rFVIII or Emicizumab **(D)**. Values for each gene are calculated as fold-change of FVIII-treated over non-treated samples and they are represented as double-gradient heatmap as group's mean value. Comparison of TNF-a, IL12p40, iNOS, TGFb and ARG1 mRNAs expression between HA, HB and healthy macrophages **(E)**, HA macrophages stimulated with FVIII and their untreated controls **(F)**, and stratification of HA patients according to their undergoing treatment, either rFVIII or Emicizumab **(G)**. Data are represented as Tukey plots (out-of-range samples are represented as a dot) and Mann–Whitney test has been used for comparing the two groups) **(A-B)**. Histogram plots with bars representing the means of the individual groups ± SD. One-way ANOVA or two-way ANOVA have been used for comparing the three groups, while unpaired t-test was used when two groups were compared **(C-G)** (*$p < 0.05$; **$p < 0.01$; ***$p < 0.001$; ****$p < 0.0001$).

Abstracts printing tool powered by pagepress.org

XIX CONVEGNO TRIENNALE
VERONA
15, 16, 17 e 18 OTTOBRE 2026
Camera di Commercio di Verona
AICE Associazione Italiana Centri Emofilia

XIX Convegno Triennale sugli Aspetti Clinici e Sociali dell'Emofilia
ABSTRACT N. CO-40
2.02 Laboratory issues

ONE-STAGE ASSAYS *VS.* CHROMOGENIC ASSAYS IN RPFVIII: STILL A DISCREPANCY?

L. Banov, G. Gazzelli, Y. Azzanelli, C. Vernarecci, F. Marotta, F. Giacopelli, F. Tappino, A.C. Molinari

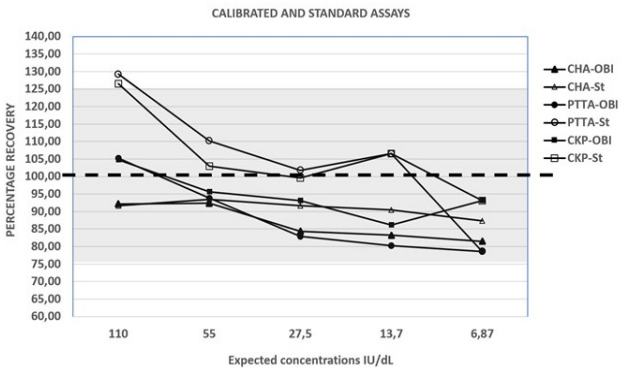
IRCCS Istituto Giannina Gaslini, Genova, Italy

Background and Aims. Acquired Hemophilia A (AHA) management requires accurate monitoring of susoctocog alfa (rpFVIII, Obizur®). Chromogenic assays (CHA) have been reported to underestimate rpFVIII activity compared with one-stage assays (OSA). In addition, discrepancies between spiked and in vivo studies have been described, further complicating interpretation. Data on the performance of Stago reagents in this setting remain limited. Clinicians relying on Stago platforms may face uncertainty in result interpretation and dose optimization. This study aims to evaluate the performance of Stago OSA and CHA reagents for susoctocog alpha measurement.

Methods. The susoctocog alfa calibrator, provided by Takeda, served as the primary standard.v It was analyzed both undiluted and at four serial dilutions (1:2, 1:4, 1:10, 1:20) in FVIII-deficient plasma (Stago). Based on the certified potency of the calibrator, the expected FVIII activity levels were defined as 110, 55, 27.5, 13.75, and 6.87 IU/dL. For standard clotting assays, Unicalibrator® (Stago) was utilized as the reference plasma to establish the standard curves All measurements were performed on the STA R Max3® (Stago) automated coagulation analyzer using three different methodological approaches: two OSA (CK-Prest®, and PTT-A®) and a CHA (TriniCHROM®). All reagents and deficient plasmas were stored and handled in strict accordance with the manufacturer's instructions Each dilution was analyzed in five replicates to ensure statistical robustness and assess intra-assay precision. The same dilution series was analyzed against a dedicated calibration curve established using the susoctocog alfa (Obizur) calibrator itself. We first compared the performance of the OSA against the CHA based solely on measurements derived from the calibrated curve. Subsequently, we compared the activity levels measured using the standard curve with those obtained using the calibrated curve. Results were expressed as percentage recovery relative to the expected theoretical activity.

Results. All analytical methods and reagents tested demonstrated high repeatability across all concentrations and experimental conditions. When the assays were calibrated specifically using the Obizur (susoctocog alfa) calibrator, all reagents showed high concordance with each other and closely matched the certified expected values. In contrast, when using a standard calibration curve: the two OSA (kaolin-based and silica-based) consistently yielded activity levels that were slightly higher than those produced by the CHA but falling almost entirely within the clinically acceptable range of ±25% of the expected theoretical activity.

Conclusions. OSA and CHA Stago reagents provide high precision and accuracy for the measurement of rpFVIII. However, as this study was conducted using spiked samples, these findings must be confirmed in a clinical setting. Further studies on plasma samples from rpFVIII treated AHA patients are necessary to validate these analytical performances in the presence of real-world biological variables and inhibitors



Filled symbols: Assays calibrated with the Obizur®-specific calibrator.
Empty symbols: Assays performed using a standard calibration curve (Unicalibrator ®).
CKP: CK Prest® (kaolin-based one-stage assay); PTTA: PTT-A® (silica-based one-stage assay); CHA: TriniChrom® (chromogenic assay)
The dashed line indicates 100% recovery, while the shaded area represents the ±25% clinical acceptability range

Abstracts printing tool powered by pagepress.org

XIX CONVEGNO TRIENNALE
VERONA
15, 16, 17 e 18 OTTOBRE 2026
Camera di Commercio di Verona
AICE Associazione Italiana Centri Emofilia

XIX Convegno Triennale sugli Aspetti Clinici e Sociali dell'Emofilia

ABSTRACT N. CO-41

2.02 Laboratory issues

CO-MPARISON OF COAGULATION AND CHROMOGENIC METHODS IN PHARMACOKINETICS WITH EXTENDED HALF-LIFE FACTOR VIII

R. Pastorino[1|2], F. Bocchi[1|2], G. Murante[1|2|3], S. Bergonzi[1|2|3], M. Capetta[1|2|3], F. Valeri[2|3], C. Dainese[2|3], A. Valpreda[4], B. Bruno[1|3], A. Borchiellini[2|3]

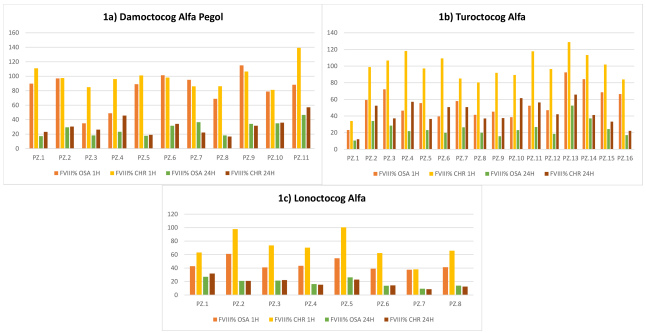
[1]Department of Molecular Biotechnology and Health Sciences, University of Turin, Italy; [2]Regional Centre for Thrombotic and Hemorrhagic Diseases, AOU Città della salute e della Scienza di Torino, Italy; [3]Division of Hematology, AOU Città della Salute e della Scienza, University of Turin, Italy; [4]Central Lab Baldi and Riberi, AOU Città della salute e della Scienza di Torino, Italy

Background and Aims. Personalized prophylaxis is still considered the standard of care for severe Hemophilia A. Replacement prophylaxis can now rely on extended half-life factor VIII concentrates (FVIII-EHL), very effective but difficult to monitor. For some of them, differences in Factor VIII levels are found using different dosage methods and it is still unclear which is optimal assay. For each pharmacokinetic, performed as an essential step in the patient's therapeutic pathway, we investigated: a) whether, for some concentrates, the differences between methods highlighted a more suitable to monitoring recovery in vivo; b) if our data matched the manufacturer's recommendation for monitoring.

Materials and Methods. A total of 56 pharmacokinetics were performed. For each timepoint, plasma FVIII levels were assessed on an ACL TOP 750 (Werfen Company - Barcelona, Spain) using the following methods: 1. One-stage clotting assay (OSA) with SynthasIL reagent. 2. Chromogenic substrate assays (CSA) with Coamatic FactorVIII

Results. A sufficient number to compare results between methods was reached only for the pharmacokinetics with 3 concentrates: 2 FVIII-EHL (Turoctocog Alfa and Damoctocog Alfa Pegol, both B domain deleted) and a single-chain FVIII (Lonoctocog Alfa). Turoctocog Alfa (16 kinetics) and Lonoctocog Alfa (8 kinetics), in line with literature data, highlighted higher FVIII levels when tested with CSA. However for Lonoctocog Alfa levels found with CSA they are not double compared to those with OSA (as indicated in the technical data sheet) and moreover the differences at 24 hours seem to disappear. Instead, Efmoroctocog Alfa (despite only 4 kinetics have been evaluated) at some timepoints did not show significant differences between OSA and CSA. For all these concentrates the same behavior (differences or equivalences) was observed for all patients. But for the kinetics with Damoctocog Alfa Pegol (11 kinetics), OSA and CSA highlighted differences but with heterogeneous behavior between patients. The numerically significant kinetics are reported in the histograms of the figure 1.

Conclusions. To offer the best personalized replacement prophylaxis, it is essential to know whether in vivo factor levels can be monitored interchangeably with CSA and OSA (and which reagent for aPTT) or necessarily with one of these. The availability of a product-specific laboratory standard could eliminate the differences and becomes crucial when a concentrate presents heterogeneity in behavior among patients and the most appropriate method is unpredictable.



XIX CONVEGNO TRIENNALE
VERONA
15, 16, 17 e 18 OTTOBRE 2026
Camera di Commercio di Verona
AICE Associazione Italiana Centri Emofilia

XIX Convegno Triennale sugli Aspetti Clinici e Sociali dell'Emofilia

ABSTRACT N. CO-42

2.02 Laboratory issues

LONGITUDINAL THROMBIN GENERATION PROFILING IN A PATIENT WITH SEVERE HEMOPHILIA A DURING ANTITHROMBIN-LOWERING THERAPY, CANCER, AND MAJOR SURGERY

C. Simion[1|2], C. Bulato[1], E. Campello[1|2], E. Zanon[1|2], B. Serena[1], S. Toffanin[1], P. Simioni[1|2]

[1]First Chair of Internal Medicine and Thrombotic and Haemorrhagic Diseases Unit, Department of Medicine, Padova University Hospital, Italy; [2]Hemophilia Center, Padova University Hospital, Italy

Background and Aims. Thrombin generation (TG) is one of the few functional assays available to assess global hemostatic balance in patients with hemophilia receiving non-replacement therapies. However, longitudinal TG data over extended periods and during major biological stressors, such as cancer and surgery, remain limited. We aimed to describe five-year longitudinal changes in plasma TG in a patient with severe hemophilia A receiving the antithrombin-lowering siRNA therapy fitusiran, including the impact of cancer diagnosis and major surgery.

Materials and Methods. Serial TG measurements were performed in platelet-poor plasma from 2020 to 2025 using the calibrated automated thrombogram (CAT). TG was assessed at low (1 pM) and intermediate (5 pM) tissue factor (TF) concentrations at predefined clinical timepoints: pre-treatment, stable therapy, peri-cancer diagnosis, and post-surgical resection. Lag time, endogenous thrombin potential (ETP), peak thrombin, velocity index, and tail formation were analyzed. Antithrombin levels were measured in parallel. Pooled normal plasma was included as a reference. Written informed consent was obtained according to local ethical standards.

Results. At 1 pM TF, a trend toward shorter lag time and higher peak thrombin was observed during the pre-tumor phase compared with stable therapy, while ETP remained non-measurable due to persistent thrombin activity. No relevant changes were observed around colorectal cancer diagnosis. Following colorectal cancer resection in March 2024, thrombin generation at 1 pM TF became fully measurable at the first post-surgical assessment, with ETP increasing from unmeasurable to 895 nM·min and late-phase tail formation (StartTail 55 min), despite only moderate peak thrombin (45 nM) (Figure 1). Antithrombin levels ranged between approximately 15–30% during stable follow-up before surgery and decreased to about 10-26% after surgery. At 5 pM TF, TG remained consistently high throughout the entire observation period, confirming preserved thrombin-generating capacity.

Conclusions. In this long-term longitudinal case, colorectal cancer diagnosis was not associated with major changes in low-trigger TG, consistent with a localized disease stage. In contrast, surgical resection induced a distinct qualitative shift in TG dynamics, with the emergence of sustained thrombin activity despite moderate peak values. These findings suggest that, in pharmacologically rebalanced hemophilia, major biological stressors may primarily affect thrombin persistence rather than overall thrombin generation.

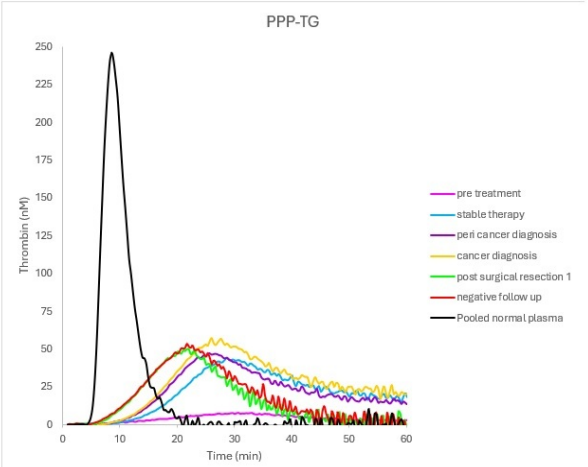


Figure 1. Platelet-poor plasma thrombin generation (PPP-TG) assessed at low tissue factor concentration (1 pM TF) at different longitudinal time points in a patient with severe hemophilia A under antithrombin-lowering non-replacement therapy. Curves represent pre-treatment, stable antithrombin-lowering therapy, peri-cancer diagnosis, cancer diagnosis, post-surgical resection, and negative follow-up phases. Pooled normal plasma is shown for reference. Low-TF conditions allow visualization of qualitative differences in thrombin generation dynamics, particularly in the decay phase and curve closure over time.

Abstracts printing tool powered by pagepress.org

XIX CONVEGNO TRIENNALE
VERONA
15, 16, 17 e 18 OTTOBRE 2026
Camera di Commercio di Verona
AICE Associazione Italiana Centri Emofilia

XIX Convegno Triennale sugli Aspetti Clinici e Sociali dell'Emofilia

ABSTRACT N. CO-43

2.02 Laboratory issues

VALIDATION OF THROMBIN GENERATION MEASUREMENT IN PLATELET-RICH-PLASMA: EVOLUTION IN THE ST GENESIA® SYSTEM

F. Bocchi[1|2], R. Pastorino[1|2], G. Murante[1|2|3], S. Bergonzi[1|2|3], M. Capetta[1|2|3], F. Valeri[2|3], C. Dainese[2|3], A. Valpreda[4], B. Bruno[1|3], A. Borchiellini[2|3]

[1]Department of Molecular Biotechnology and Health Sciences, University of Turin, Italy; [2]Regional Centre for Thrombotic and Hemorrhagic Diseases, AOU Città della salute e della Scienza di Torino, Italy; [3]Division of Hematology, AOU Città della Salute e della Scienza, University of Turin, Italy; [4]Central Lab Baldi and Riberi, AOU Città della salute e della Scienza di Torino, Italy

Background and Aims. Thrombin generation assay (TGA) is a promising tool for monitoring novel non-replacement therapies in haemophilia. The ST Genesia® system (Stago, Asnières-sur-Seine, France) is validated for thrombin generation (TG) measurement in platelet-poor plasma (PPP), but no standardized method is currently available for platelet-rich plasma (PRP). PRP testing could improve the assessment of platelet–drug interactions and provide a more comprehensive evaluation of haemostatic function. This study aimed to validate the technical reliability of TG measurement in PRP using the ST Genesia® system by assessing intra- and inter-run reproducibility, PRP sample stability, normalization by reference plasma, absence of platelet-related methodological interference, and overall method robustness.

Materials and Methods. The procedure employed CAT PRP-Reagent (Stago), containing relipidated Tissue Factor for reaction initiation, a homemade PPP reference plasma (RefPlasma) prepared from a pool of at least 20 healthy donors for normalization, analytical variability monitoring and internal calibration, and PRP samples under investigation. RefPlasma validation included calculation of intra-run (≥10 replicates) and inter-run (≥3 days) coefficients of variation (CV%), together with routine coagulation testing (PT, aPTT, fibrinogen, antithrombin). PRP stability was evaluated by measuring TG at baseline (T0), 1 hour (T1), and 3 hours (T2) after collection.

Results. RefPlasma validation showed acceptable intra-run and inter-run CV%, with most values below 10% (Table 1). Routine coagulation parameters were within normal reference ranges. PRP stability testing demonstrated a progressive decline in Peak Height, ETP, and Velocity Index from T0 to T2, associated with increased Lag Time, Time to Peak, and Start Tail.

Conclusions. The RefPlasma showed satisfactory reproducibility both within single runs and across different days, supporting its suitability for normalization and quality control. The progressive reduction of TG parameters over time indicates that PRP samples should ideally be analysed within 3 hours of collection to minimize pre-analytical degradation. This aspect deserves further investigation, particularly regarding the feasibility of centralized testing for samples from external centres. Overall, this procedure represents a validated approach for TGA in PRP and may provide a more physiologically relevant assessment of drug–coagulation interactions and global haemostatic function.

Parameter	CV% INTRA-RUN	CV% INTER-RUN
Lag Time	2.63%	11.74%
Peak Height	2.37%	3.43%
Time to Peak	2.89%	8.07%
ETP	2.65%	2.37%
Vel.Index	6.02%	8.69%
Start Tail	2.91%	5.81%

Abstracts printing tool powered by pagepress.org

XIX CONVEGNO TRIENNALE
VERONA
15, 16, 17 e 18 OTTOBRE 2026
Camera di Commercio di Verona
AICE Associazione Italiana Centri Emofilia

XIX Convegno Triennale sugli Aspetti Clinici e Sociali dell'Emofilia

ABSTRACT N. CO-44

2.02 Laboratory issues

EVALUATION OF THE DEVIATION BETWEEN PRESCRIBED AND RECOMMENDED EMICIZUMAB DOSING IN PATIENTS WITH CONGENITAL HEMOPHILIA A

A.C. Giuffrida[1], S. Abeysinghe Gunawardhana[1], S. Amato[2], F. Casoli[2], C. Recchi[2], M. Saggioro[2], E. Bonetti[3], M. Bodini[1], G. Poli[2]

[1]Centro Emofilia, UOC Medicina Trasfusionale, AOUI Verona, Italy; [2]UOC Laboratorio Analisi, AOUI Verona, Italy; [3]UOC Oncoematologia Pediatrica, AOUI Verona, Italy

Background. Emicizumab, the first non-replacement therapy approved for the treatment of HA, has significantly improved patient management. However, the label-recommended dosing schedule is highly rigid and, if strictly applied, may lead to unavoidable drug wastage and increased healthcare costs. We analyzed the experience of a single center to assess whether patients received the exact dosage specified in the prescribing information and, in case of deviation, to evaluate the potential impact on clinical outcomes through the analysis of plasma levels of emicizumab.

Patients and Methods. We conducted a retrospective observational study of patients receiving emicizumab prophylaxis at the Hospital of Verona, Italy. Laboratory data, including activated partial thromboplastin time (aPTT), factor VIII (FVIII) activity, plasma emicizumab concentrations, and the occurrence of spontaneous bleeding episodes, were collected between May 2023 and September 2025.

Results. The emicizumab prophylaxis regimens adopted were 1.5 mg/kg once weekly (QW), 3 mg/kg every two weeks (Q2W), and 6 mg/kg once monthly (Q4W). A total of 24 plasma samples were analyzed. Only one patient received the exact label-recommended dose; all other patients were treated with slightly lower doses (mean deviation: 8.13%; range: 3-16.6%). The aPTT ratio ranged from 0.62 to 0.9 (mean of 0.74). Plasma emicizumab concentrations ranged from 16.5 µg/mL to 90.3 µg/mL (mean: 48 µg/mL). Mean plasma emicizumab concentrations per patient ranged from 25.80 µg/mL to 86.43 µg/mL. According to the dosing schedule, mean plasma emicizumab concentrations were 40.56 µg/mL for the 1.5 mg/kg QW regimen, 65.02 µg/mL for the 3 mg/kg Q2W regimen, and 31.51 µg/mL for the 6 mg/kg Q4W regimen. No spontaneous bleeding episodes were observed in any patient. Based on our calculations, strict adherence to the label-recommended dose would have resulted in the disposal of approximately 5 to 18 mg of emicizumab per administration per patient. On an annual basis, this would correspond to a total of 2,922.72 mg of discarded drug, equivalent to approximately 20 vials of 150 mg/mL formulation.

Conclusions. Despite the limited number of patients and samples analyzed, our findings show that most patients received a slightly lower dose of emicizumab than the label-recommended without compromising treatment efficacy or safety. Plasma emicizumab concentrations were generally within the therapeutic range, and no spontaneous bleeding events were reported. These small deviations from the recommended dosing regimen allowed for substantial reduction in drug wastage while maintaining effective prophylaxis.

Abstracts printing tool powered by pagepress.org

XIX CONVEGNO TRIENNALE
VERONA
15, 16, 17 e 18 OTTOBRE 2026
Camera di Commercio di Verona
AICE Associazione Italiana Centri Emofilia

XIX Convegno Triennale sugli Aspetti Clinici e Sociali dell'Emofilia

ABSTRACT N. CO-45

2.02 Laboratory issues

BRIDGING THE CLINICAL CHASM: GENETIC ANALYSIS AS A CONFIRMATORY TOOL IN MISMATCHED GLANZMANN THROMBASTHENIA

R. Pastorino[1|3], F. Bocchi[1|3], A. Valpreda[4], G. Murante[1|2|3], S. Bergonzi[1|2|3], M. Capetta[1|2|3], F. Valeri[1|2], C. Dainese[1|2], M. Gilestro[5], D. Peruccio[6], E. De Candia[7], P. Concolino[8], B. Bruno[2|3], A. Borchiellini[1|2]

[1]Regional Centre for Hemorrhagic and Thrombotic Diseases, AOU Città della Salute e della Scienza, Italy; [2]Division of Hematology, AOU Città della Salute e della Scienza and University of Turin, Italy; [3]Department of Molecular Biotechnology and Health Sciences, University of Turin, Italy; [4]Central Laboratory Baldi and Riberi, AOU Città della Salute e della Scienza di Torino, Italy; [5]AOU Citta' della Salute e della Scienza, PO Molinette, Anatomy and Pathological Histology 1 U, Department of Laboratory Medicine - Flow Cytometry Laboratory, Torino, Italy; [6]AOU Citta' della Salute e della Scienza di Torino, Maternal-Infant and Trauma Transfusion Medicine, Regina Margherita Hospital, Department of Laboratory Medicine, Torino, Italy; [7]Haemostasis and Thrombosis Unit, Fondazione Policlinico Universitario A.Gemelli, IRCCS, Department of Translational Medicine, Università Cattolica del Sacro Cuore, Roma, Italy; [8]Fondazione Policlinico Universitario A. Gemelli, IRCCS, Department of Laboratory and Hematological Sciences, Unit of Clinical Chemistry, Biochemistry and Molecular Biology, UOSD of Molecular and Genomic Diagnostics, Roma, Italy

Background and Aims. Glanzmann thrombasthenia (GT) is a rare inherited recessive platelet function disorder caused by quantitative or qualitative defects of the glycoprotein IIb/IIIa (GPIIbIIIa), encoded by the ITGA2B/ITGB3 genes (chromosome 17), resulting in impaired platelet aggregation. Several pathogenic variants have been described, mainly in ITGA2B gene because of its larger size compared with ITGB3; however the associated clinical phenotypes are indistinguishable. We report the case of a 55-year-old woman referred to our centre for recently developed haemorrhagic diathesis: epistaxis, prolonged wound or gum bleeding and easy bruising, but negative bleeding history even in trigger conditions (surgery, pregnancy, delivery), no comorbidities at diagnosis and no family history. This atypical clinical presentation, including late-onset bleeding, raised suspicion for an acquired form. In this way genetic test helped. The aim of this study is to show the usefulness of genetic analysis as a confirmatory step in the diagnostic work-up, particularly when a mismatch exists between laboratory results and medical history.

Materials and Methods. Platelet function was assessed by Platelet Function Analyser (PFA-100), Total Thrombus- Formation Analysis System (T-TAS®01) and aggregometry. Absence of GPIIb/IIIa and presence of platelet autoantibodies/alloantibodies were tested by flow cytometry (Beckman Coulter Epics, High Wycombe, UK). Platelet antibody specificity was determined by Enzyme- Linked Immunosorbent Assay (ELISA). Owing to the discrepancy between the medical history and laboratory findings suggestive of congenital GT, molecular genetic analysis was performed.

Results. PFA-100 and T-TAS were elongated. Aggregometry showed a profile consistent with GT. Flow cytometric analysis showed a GPIIb/IIIa expression profile comparable to that observed in a patient with a confirmed diagnosis of GT. No antibodies or associated disease were detected. Genetic testing identified two heterozygous mutations c.1947-1_1947ins in ITGA2B gene, never reported in ClinVar, that represents a novel mutation, and another one c.260G>A reported only once in the GnomAD database.

Conclusions. Because this disorder is rare and its diagnostic work-up complicated, its management remains challenging, particularly when discrepancies arise between laboratory findings and the patient's medical history. For this reason, it may be important to include molecular genetic analysis not as an exclusive test for specific cases, but as a fundamental tool in the diagnostic process.

Abstracts printing tool powered by pagepress.org

XIX CONVEGNO TRIENNALE
VERONA
15, 16, 17 e 18 OTTOBRE 2026
Camera di Commercio di Verona
AICE Associazione Italiana Centri Emofilia

XIX Convegno Triennale sugli Aspetti Clinici e Sociali dell'Emofilia

ABSTRACT N. CO-46

2.05 Musculoskeletal issues

MILD HEMOPHILIA A AND JOINT HEALTH IN REAL LIFE: IS THAT AN EMERGING ISSUE? A SINGLE CENTER EXPERIENCE

G. Murante[1|2|3], F. Valeri[1|2], S. Bergonzi[1|2|3], M. Capetta[1|2|3], C. Dainese[1|2], A. Valpreda[4], R. Pastorino[1|3], F. Bocchi[1|3], B. Bruno[2|3], A. Borchiellini[1|2]

[1]Regional Centre for Hemorrhagic and Thrombotic Diseases, AOU Città della Salute e della Scienza of Turin, Italy; [2]Division of Hematology, AOU Città della Salute e della Scienza, University of Turin, Italy; [3]Dep. of Molecular Biotechnology and Health Sciences, University of Turin, Italy; [4]Central Lab. Baldi and Riberi, AOU Città della Salute e della Scienza of Turin, Italy

Background and Aims. Mild hemophilia A (mHA) is characterized by sporadic bleeds that rarely lead to symptomatic arthropathy. Data on joint damage in mHA are limited. The aim of this study is to investigate joint status in our cohort of mHA patients, in order to detect any significant sign of arthropathy and to explore any relationship between joint health and FVIII levels, body mass index (BMI) and age. We perform a quality of life (QoL) assessment in order to detect any impairment health related.

Materials and Methods. Patients with mHA and between 18 and 65 years old referred in our center in 2025 were included. For each patient HJHS (Hemophilia Joint Health Score) and HEAD US (Hemophilia Early Arthropathy Detection with Ultrasound) protocol were performed. Data regarding FVIII basal value, BMI and pain (NRS scale) were also collected. Variables were analyzed for the entire cohort and splitted according to age (< 49 yo and > 50 yo) and FVIII levels (from 5% to 20% and from 21% to 35%). EQ-5D-3L, SF36 and IPAQ questionnaires were also administered.

Results. Of the 96 mHA patients, 42 hemophilia patients fulfilled inclusion criteria and were enrolled in the study. Results are reported in table 1. We globally found median HEAD US and HJHS were 2 (IQR 0-5). Only 15 (36%) patients had no joint damage (HEAD US=0), 27 (64%) had at least one joint with a HEAD-US. No differences in HEAD US and HJHS according to FVIII, nevertheless we found that for elderly patients and for whom with higher BMI there is a statistically significant increase in HEAD-US. 20 patients fulfilled all QoL questionnaires: 14/20 (70%) patients showed no impairment in QoL, 6/20 (30%) expressed discomfort related to musculoskeletal criticalities. In the IPAQ evaluation, 15/20 (75%) patients were classified as quite or very active and 5/20 (25%) inactive. Despite low sample size, we observed a correlation trend between high HJHS and worse QoL perception. No correlation between QoL and FVIII levels, HEAD US, age or BMI were found.

Conclusions. Our data suggest that mHA patients show overall better joint status compared to not mild HA patients, without any differences according to severity FVIII deficiency. No correlation between HJHS and others variables was detected. We found a significant correlation between HEAD US and age and BMI, identifying these two parameters as risk factors for early arthropathy development. mHA patients showed overall good QoL, with only critical issue represented by pain and/or musculoskeletal impairment, suggesting that the disease burden is more related to articular health. In conclusion, joints US should be routinely investigated in mHA patients to detect any early damage, that can occur especially in adulthood and in overweight patients and can affect QoL.

	all	FVIII			age			BMI		
		5%-20%	21-35%	p	< 49 yo	> 50 yo	p	< 25	> 25	p
Age	49 (33-60)	50 (33-62)	49 (34-58)		33 (29-46)	60 (57-63)		42 (30-50)	60 (56-64)	
FVIII	15(10-20)	12 (10-15)	26 (21-30)		15 (12-20)	14 (10-21)		15 (12-20)	14 (9-22)	
HEAD US	2 (0-5)	2 (0-5)	0 (0-4)	0.14	0 (0-2)	4 (1-7)	**<0.001**	0 (0-3)	4 (1-8)	**<0.005**
HJHS	2 (0-5)	2 (0-5)	1 (0-2)	0.15	1 (0-2)	2 (0-5)	0.09	2 (0-2)	2 (0-5)	0.16
NRS	0 (0-2)	0 (0-2)	0 (0-0)	0.28	0 (0-1)	0 (0-3)	0.29	0 (0-0)	0 (0-5)	0.10
BMI	25 (23-27)	24 (22-27)	25 (24-26)	0.35	24 (21-25)	27 (24-29)	**<0.001**	24 (21-25)	28 (27-30)	**<0.001**

Abstracts printing tool powered by pagepress.org

XIX CONVEGNO TRIENNALE
VERONA
15, 16, 17 e 18 OTTOBRE 2026
Camera di Commercio di Verona
AICE Associazione Italiana Centri Emofilia

XIX Convegno Triennale sugli Aspetti Clinici e Sociali dell'Emofilia ABSTRACT N. CO-47

2.05 Musculoskeletal issues

JOINT ULTRASOUND FOLLOW-UP IN PEDIATRIC PATIENTS WITH HEMOPHILIA: A 12-YEAR PROSPECTIVE SINGLE-CENTER EXPERIENCE

I. Ricca[1], B. Borsellino[2|3], T. Martini[2], C. Martinoli[4], B. Pollio[2]

[1]Transfusion Medicine, Ivrea Hospital, Ivrea, Italy; [2]Haemophilia Centre, Immune-Haematology and Transfusion Medicine, University Hospital "Città della Salute e della Scienza", Torino, Italy; [3]Department of Biomedicine and Prevention, PhD in Immunology, Molecular Medicine and Applied Biotechnology, University of Rome Tor Vergata, Roma, Italy; [4]Department of Health Science DISSAL, University of Genova, Unit of Radiology and IRCCS San Martino Hospital, Genova, Italy

Background and Aims. Periodic monitoring of joints status in patients with haemophilia (PwH) is recommended to identify and prevent the arthropathies. Ultrasound (US) is able to detect and quantify markers of disease activity and degenerative damage. The "Haemophilia Early Arthropathy Detection with Ultrasound" (HEAD-US) scoring scale is an accurate imaging method for identifying joint damage. Nevertheless, data on large cohorts of pediatric PwH, are still lacking. The aim of this study is to describe the joint status of 61 pediatric PwH assessed by US, using the HEAD-US protocol and analyse the efficacy of primary prophylaxis on the severe subset.

Materials and Methods. We prospectively analyzed 61 pediatric PwH (severe hemophilia A=29, B=7; moderate A=8, B=2; mild A=7, B=8), referred to the "Haemophilia Centre, Regina Margherita Hospital, Turin, Italy" and collected data on joints status using the HEADUS protocol, from November 2012 to November 2024. The Haemophilia Joint Health Score (HJHS) was performed in 44 patients and compared with the HEAD-US score.

Results. In total we performed 276 US exams, with a median of 4 exams per patient. Sorting our cohort into 3 age groups (early childhood: 1-5 years; school age: 6-14 years; adolescence and young adult age: 15-18 years) we found that in early childhood patients, the mean HEAD-US score was 0, in scholar age 0.56 (SD±1.17) and in adolescent and young adult patients was 1.76 (SD±2.22). Focusing the analysis on 31 patients with severe haemophilia treated with primary prophylaxis, we found that in early childhood patients mean HEAD-US score was 0, in scholar age 0.24 (SD±0.73) and in adolescent and young adult patients was 0.91 (SD ±1.38). In case of discordance between the HEAD-US and the HJHS scores (27%, HJHS=0 and HEAD-US>0), the HEAD-US score detected subclinical synovitis in 83% of cases.

Conclusions. Our data show that pediatric PwH treated with primary prophylaxis, show less joint damages compared to the same age patients, comprehending those not treated with primary prophylaxis. The HEAD-US score is a feasible and efficient clinical tool in pediatric PwH and, in our setting, it resulted even more sensitive in detecting subclinical joint damage, compared to the HJHS score.

XIX CONVEGNO TRIENNALE
VERONA
15, 16, 17 e 18 OTTOBRE 2026
Camera di Commercio di Verona
AICE Associazione Italiana Centri Emofilia

XIX Convegno Triennale sugli Aspetti Clinici e Sociali dell'Emofilia

ABSTRACT N. CO-48

2.05 Musculoskeletal issues

HEMOFISH: A NEW ANIMAL MODEL FOR STUDY THE ROLE OF FACTOR VIII IN BONE DISEASE

M. Berni[1], L. Caliogna[1], F. Tonelli[2], C. Aresi[2], G. Rizzi[1], A. Forlino[2], G. Pasta[1]

[1]Orthopedics and Traumatology Clinic, IRCCS Policlinico San Matteo Foundation, Pavia, Italy; [2]Dep. of Molecular Medicine, Biochemistry Unit, University of Pavia, Italy

Background and Aims. Haemophilia A is a rare hereditary X-linked recessive disease caused by deficient activity of blood coagulation factor VIII. Patients show a significant reduction in bone mineral density with a greater risk of developing pathological fractures or fractures due to mild trauma. Factor VIII is a plasmatic multi-domain glycoprotein involved in the coagulation cascade mainly synthesized by hepatocytes. In recent years, several studies have confirmed that the reduced levels of FVIII are involved in bone mineral density, bone reduction, osteoporosis and several molecular pathways on bone physiology and turnover. Zebrafish is an excellent animal model because approximately 70% of its genes have an ortholog in human genome. It shows a bone structure, metabolism, and turnover very similar to humans. It is an ideal model for studying bone diseases because it is useful for study bone matrix deposition, bone mineralization, osteogenesis, bone metabolism mechanisms and for creating models of bone diseases. The aim is to study how the lack of FVIII can lead to bone disease in a haemophilic zebrafish.

Materials and Methods. this project study the bone physiology and turnover in haemophilic (FVIII-) and wild-type (WT) zebrafish. After amputation of the bony caudal fin, zebrafish can regenerate it and it is possible to study how the fin and rays regenerate. Osteoclasts are multinucleated cells that contain several cytoplasmic granules rich in tartrate-resistant acid phosphatase (TRAP), a metalloprotein enzyme located in intracytoplasmic vesicles expressed during bone matrix degradation. On amputated fins it is possible to study osteoclasts activity with TRAP staining. Micro-computed tomography allows to study zebrafish skeletal morphology and structure with the analysis of the angle that the neural arch formed with the vertebral body.

Results. After 7 days from caudal fin amputation of 16 FVIII- and 16 WT zebrafish, the fin regeneration is significantly reduced in FVIII- group. New ray regeneration growth and bifurcation numberers significantly reduced in the FVIII- group, $p < 0{,}001$ and $p < 0{,}006$ respectively. A different osteoclasts activity is observed on 16 FVIII- and 16 WT zebrafish fin amputated with TRAP staining. Micro-computed tomography on 7 FVIII- and 17 WT zebrafish shows an increase about 6% in neural arch angle in FVIII- zebrafish, with a significance of $p < 0{,}05$.

Conclusions. the experimental data would seem to indicate that the lack of FVIII influences correct bone formation and turnover.

XIX CONVEGNO TRIENNALE
VERONA
15, 16, 17 e 18 OTTOBRE 2026
Camera di Commercio di Verona
AICE Associazione Italiana Centri Emofilia

XIX Convegno Triennale sugli Aspetti Clinici e Sociali dell'Emofilia ABSTRACT N. CO-49

2.05 Musculoskeletal issues

JOINT STATUS EVALUATION BY ULTRASOUND AND FUNCTIONAL ASSESSMENT IN PERSONS WITH NON SEVERE HEMOPHILIA ON PROPHYLAXIS WITH FOCUS ON THOSE WITH 5-YR FOLLOW UP

G. Quintavalle[1], M.I. Tassoni[1], B.M. Roccon[1], G.F. Rivolta[1], C. Costantino[2], R.M. Polo[3], A. Matichecchia[1], A. Tagliaferri[1], A. Coppola[1]

[1]SSD Centro Hub Emofilia e Malattie Emorragiche Congenite, Az. Ospedaliero-Universitaria di Parma, Italy; [2]SSD Riabilitazione Ambulatoriale e Ortogeriatrica, Az. Ospedaliero-Universitaria di Parma, Italy; [3]Clinica Ortopedica, Az. Ospedaliero-Universitaria di Parma, Italy

Background and Aims. Chronic arthropathy causes morbidity in persons with hemophilia (PWH). and Joint damage can be detected also in non-severe (NS) PWH, even without overt bleedings. Identification of early signs of damage is crucial and point-of-care ultrasound (US) provides a rapid quantification of osteochondral and synovial changes. This study aimed to evaluate the joint status of a cohort of NSPWH on continuous prophylaxis (CP), focusing on US and functional assessments.

Materials and Methods. We reviewed clinical records of NSPWH currently on CP for severe phenotype or joint damage, collecting data about diagnosis, phenotype, treatment, Hemophilia Early Arthropathy Detection with Ultrasound (HEAD-US) and HJHS scores. In a subgroup of PWH with at least 5-yr follow-up the correlation between HEAD-US and HJHS scores at baseline and after a 5 years was evaluated, tracking the longitudinal progression of arthropathy.

Results. NSPWH on CP were 25/215: 5 with mild hemophilia A (HA), 14 with moderate HA (1 female) and 6 with moderate (hemophilia B) HB. Median age (range) was 32 years (4-67), at CP start 25 (0-63), being higher in mild HA than in moderate PWH (38, 11-63 vs 29, 3-62 years). Median baseline FVIII/FIX activity was 2% (1-10). Three moderate HA PWH were on CP with non replacement therapy, while the others with EHL factor concentrates. Baseline median total HEAD US score was 4, range 0-40. The score was ≥1 in 19/25 PWH (76%): 2 mild HA, 10 moderate HA, 6 moderate HB PWH, with highest rate for left ankle (LA, 17/25 ≥1, 68%). All but one PWH in this group, presented osteochondral change and again LA was the most affected joint by cartilage impairment (68%). 16 PWH has at least 5 years follow-up (2 mild HA, 4 moderate HB, 10 moderate HA; median age 34 years, 9-67). Median ABR in 5 years was 0.8 (0-3.8). Median HJHS was 9 (range 0-36) for this subgroup, being ≥1 in 12/16 PWH (75%). At baseline, a significant positive correlation was observed between HEAD-US and HJHS scores (Spearman r=0.869; p<0.001). After 5 years the correlation remained significant: r=0.759; p< 0.001. At longitudinal analysis, the mean HEAD-US score showed a negligible change (Δ=-0.50; Wilcoxon W=18.0, p=0.593). The mean HJHS score showed a trend to decrease (Δ=-2.00; Wilcoxon W= 36.0, p=0.298).

Conclusions. Our study showed joint damage in elevated rates of NSPWH, by both clinical and US assessments, highlighting the need for a regular follow up of joint status also in these patients, even in absence of overt bleedings. HEAD--US and HJHS scores exhibited a strong correlation over time, confirming that US mirrors clinical and functional joint impairment in hemophilic arthropathy and underlining the role of point-of-care US in the global care of hemophilia.

Abstracts printing tool powered by pagepress.org

XIX CONVEGNO TRIENNALE
VERONA
15, 16, 17 e 18 OTTOBRE 2026
Camera di Commercio di Verona
AICE Associazione Italiana Centri Emofilia

XIX Convegno Triennale sugli Aspetti Clinici e Sociali dell'Emofilia

ABSTRACT N. CO-50

2.06 Comorbidities

LEFT ATRIAL APPENDAGE OCCLUSION IN PATIENTS WITH ATRIAL FIBRILLATION AND BLEEDING DISORDERS: A SINGLE-CENTER EXPERIENCE

B.M. Roccon[1], M.I. Tassoni[1], G. Quintavalle[1], G. Benatti[2], F. Gurgoglione[2], R. Rossi[3], C. Cattabiani[3], L. Vignali[2], A. Tagliaferri[1], A. Coppola[1]

[1]SSD Centro Hub Emofilia e Malattie Emorragiche Congenite, Azienda Ospedaliero-Universitaria di Parma, Italy; [2]SSD Cardiologia Interventistica, Azienda Ospedaliero-Universitaria di Parma, Italy; [3]Laboratorio di Coagulazione, UOC Patologia Clinica, Azienda Ospedaliero-Universitaria di Parma, Italy

Introduction. Data about the management of atrial fibrillation (AF) in patients with hemophilia and other bleeding disorders (BD) are limited. The reliability of stroke risk scores (i.e. CHA2DS2VASc), used in the general population for treatment choices, and long-term safety of anticoagulation, as well the need for concomitant hemostatic prophylaxis, remain unknown. Left atrial appendage occlusion (LAAO) has been suggested as an alternative to anticoagulation in patients with high bleeding risk, few cases being reported even in BD.

Methods. Retrospective review of patients with BD and AF who underwent LAAO at the University Hospital of Parma.

Results. Eight patients were identified, 6 males and 2 females, aged 64-80 yrs (Table). Mean CHA2DS2VASc was 4 (range 2-5). Two men had mild factor VII deficiency, both on aspirin (ASA) 100 mg/d because of history of myocardial revascularization due to diffuse coronary artery disease. Combined antiplatelet-anticoagulation treatment was considered in both patients after AF diagnosis, due to very high cardiovascular and stroke risk; the concomitant bleeding risk led to consider LAAO. Three elderly men with hemophilia A (2 severe, 1 moderate) on tertiary prophylaxis were reluctant to any long-term antithrombotic treatment. A moderate hemophilia B patient treated on demand developed AF in the setting of severe chronic heart failure. The two female patients had a type 2A von Willebrand disease (VWF:RCo 10%) and an acquired von Willebrand syndrome (AVWS, VWF:RCo 5%; concomitant detection of monoclonal gammopathy of uncertain significance). In all patients but one the Amplatzer plug was successfully implanted; heparinization was managed with specific replacement treatment, achieving factor levels ≥80% during and up to 24h after the procedure. One patient experienced mild pericardial effusion. No thromboembolic events were observed. Overall, bleeding episodes occurred In 5/8 cases. Patients with mild FVII deficiencies received double antiplatelet treatment for 3-6 months reporting mild mucocutaneous bleeding, then remained on ASA. Single antiplatelet treatment and FVIII personalized prophylaxis (FVIII trough >5-10%) were used in the 3 hemophiliacs, one withdrew clopidogrel after 2 months due to severe epistaxis and joint bleeds. No relevant bleeding occurred in the old men on anticoagulation, made possible by sustained prophylaxis with extended half-life FIX, nor in the two women with VWF abnormalities on ASA (the AVWS patient received VWF-FVIII concentrate prophylaxis for 4 months).

Conclusions. Adequate factor levels to allow safe antithrombotic treatments in BD patients remain uncertain. LAAO, when performed at experienced facilities, is a safe alternative to anticoagulation in BD with AF-related stroke risk.

Table: Patient characteristics, antithrombotic treatments and associated hemostatic prophylaxis after LAAO

	#1	#2	#3	#4	#5	#6	#7	#8
Gender, age (yrs)	M, 70	M, 73	M, 74	M, 79	F, 80	M, 64	M, 76	F, 77
Bleeding disorder Factor level (%)	Mild FVII deficiency (24%)	Mild FVII deficiency (18%)	Severe HA	Severe HA	AVWS VWF:RCo 5% FVIII 40%	Moderate HA FVIII 2.5%	Moderate HB FIX 1.2%	VWD 2 A VWF:RCo 10%. FVIII 33%
Treatment regimen	On demand	On demand	Tertiary prophylaxis (SHL rFVIII)	Tertiary prophylaxis (SHL pdFVIII)	On demand	Tertiary prophylaxis (EHL rFVIII)	On demand	On demand
Cardiovascular risk factors	Metabolic syndr., ischemic heart disease	Hypertension, ischemic heart disease	Hypertension	Hypertension, previous TIA, obesity	Hypertension	Hypertension, obesity, diabetes mellitus	Hypertension, chronic heart failure	Hypertension
CHA_2DS_2VASc	4	4	2	5	4	2	2	4
Treatment prior to LAAO	ASA + rivaroxaban*	Enoxaparin 80 IU/Kg b.i.d.	None (patient reluctance)	None	None	Enoxaparin 100 IU/Kg		Enoxaparin 80 IU/Kg b.i.d.
Antithrombotic treatment after LAAO	Clopidogel + ASA (3 mo), then ASA	Clopidogel + ASA (3 mo), then ASA	Clopidogrel	Clopidogrel	ASA 100 mg	Clopidogrel, then ASA 100 mg	Dabigatran 110 mg b.i.d (18 mo), then ASA 100 mg	ASA 100 mg
Hemostatic prophylaxis	NO	NO	SHL rFVIII trough FVIII >5%	SHL pdFVIII trough FVIII >10%	FVIII-VWF (4mo)	EHL rFVIII trough FVIII >5%	EHL rFIX trough FIX >20% then FIX>5%	NO
Follow-up, mo.	125	80	98	13	87	39	36	6
Bleeding complications	Mild muco-cutaneous bleeding*	Mild muco-cutaneous bleeding*	Epistaxis, joint bleeds, clopidogrel withdrawn	Mild muco-cutaneous bleeding	Sporadic gum bleeding	NO	NO	NO

*Withdrawal due to worsening of renal function. *On double antiplatelet treatment.

Abstracts printing tool powered by pagepress.org

XIX CONVEGNO TRIENNALE
VERONA
15, 16, 17 e 18 OTTOBRE 2026
Camera di Commercio di Verona
AICE Associazione Italiana Centri Emofilia

XIX Convegno Triennale sugli Aspetti Clinici e Sociali dell'Emofilia
ABSTRACT N. CO-51

2.06 Comorbidities

HEMOSTATIC AND CARDIOVASCULAR PROFILES IN HEMOPHILIA PATIENTS WITH AND WITHOUT ATHEROSCLEROSIS

A. Napolitano, E. Zanon, L. Spiezia, G. Camporese, P. Scarinzi, F. Ahmad, G. Saggiorato, C. Bulato, S. Toffanin, S. Gavasso, F. Sartorello, C. Simion, E. Campello, P. Simioni

Hemophilia Center, University Hospital of Padua, Italy

Background and Aims. Although hemophilia is characterized by a hypocoagulable state, patients remain susceptible to atherosclerosis due to traditional cardiovascular risk factors. The relationship between atherosclerosis, global hemostasis, and platelet function in hemophilia remains poorly defined. This study compared clinical characteristics, laboratory findings, thromboelastometric parameters (ROTEM), and platelet function profiles in patients with hemophilia A and B with and without atherosclerosis, and explored potential hemostatic differences associated with vascular disease.

Materials and Methods. This cross-sectional study enrolled 105 adult patients with hemophilia A and B from the Hemophilia Centers of Padua and Castelfranco Veneto, Italy. Seventy-seven patients had no evidence of atherosclerosis and 28 had documented disease. Atherosclerosis was defined by carotid stenosis ≥50%, aortic plaque, or ABI ≤0.9. Clinical data, routine laboratory tests, ROTEM, and Multiplate assays were collected. Group comparisons were performed using the t-test, Mann–Whitney U test, or χ^2 test.

Results. Patients with atherosclerosis were older (63 ± 12.4 vs. 55.5 ± 10.9 years; p = 0.007) and had a higher prevalence of hypertension (60.7% vs. 33.7%; p = 0.013), dyslipidemia (75% vs. 35%; p < 0.001), antihypertensive therapy (53.6% vs. 28.6%; p = 0.018), lipid-lowering therapy (46.4% vs. 16.9%; p = 0.002), and previous cardiovascular or cerebrovascular events (28.6% vs. 6.5%; p = 0.002). No differences were observed in hemophilia type or severity, obesity, diabetes, alcohol use, or inhibitors. Most laboratory parameters, including hemoglobin, platelet count, renal function, lipid profile, Lp(a), hs-CRP, and HbA1c, were comparable. NT-proBNP was significantly higher but remained within the normal range. ROTEM showed shortened INTEM CT (254.9 ± 47.8 vs. 294.3 ± 140.1 sec; p = 0.04) and increased FIBTEM MCF (14 ± 3.7 vs. 12.2 ± 3.6 mm; p = 0.031), suggesting subtle procoagulant changes. EXTEM parameters and Multiplate ADP/ASPI assays did not differ significantly. Kaplan–Meier analysis showed no difference in survival between groups (p = 0.93) (Figure 1).

Conclusions. Despite inherited hypocoagulability, patients with hemophilia and atherosclerosis exhibit classical cardiovascular risk factors. ROTEM detected subtle procoagulant changes, including faster clot initiation and increased fibrin-based clot firmness. These findings highlight the importance of assessing both cardiovascular risk and global hemostasis in hemophilia and support ROTEM as a sensitive tool for identifying early coagulation alterations associated with atherosclerosis.

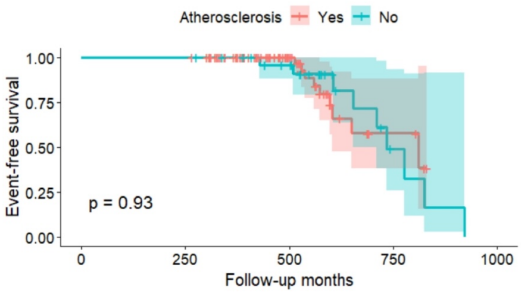


Figure 1. Survival curves in patients with and without atherosclerosis in patients with hemophilia A and B

XIX CONVEGNO TRIENNALE
VERONA
15, 16, 17 e 18 OTTOBRE 2026
Camera di Commercio di Verona
AICE Associazione Italiana Centri Emofilia

XIX Convegno Triennale sugli Aspetti Clinici e Sociali dell'Emofilia

ABSTRACT N. CO-52

2.06 Comorbidities

CARDIOVASCULAR EVENTS AND SUBCLINICAL ATHEROSCLEROSIS IN HEMOPHILIA A AND B PATIENTS: A MULTICENTER COHORT STUDY

A. Napolitano, E. Zanon, L. Spiezia, G. Camporese, P. Scarinzi, F. Ahmad, G. Saggiorato, C. Bulato, S. Toffanin, S. Gavasso, F. Sartorello, C. Simion, E. Campello, P. Simioni

Hemophilia Center, University Hospital of Padua, Italy

Background and Aims. Advances in hemophilia care have increased life expectancy, exposing patients to age-related cardiovascular risk. Although hemophilia has traditionally been considered protective against thrombosis, cardiovascular events are increasingly reported. This study evaluated the prevalence and predictors of cardiovascular events in patients with hemophilia A and B and their association with clinical and subclinical atherosclerosis.

Materials and Methods. We conducted a multicenter ambispective cohort study including 163 patients aged >40 years with hemophilia A (n=139) or B (n=24) followed at the Hemophilia Centers of Padua and Castelfranco Veneto, Italy. Patients were classified according to the occurrence of cardiovascular or thrombotic events (myocardial infarction, stroke/TIA, venous thrombosis). Demographic, clinical, laboratory, and treatment data were collected. Hemostatic function was assessed by ROTEM and Multiplate assays. Vascular evaluation included carotid ultrasound, abdominal aorta diameter measurement, and ankle-brachial index (ABI). Associations with outcomes were analyzed using univariate and multivariable logistic regression.

Results. Twenty-seven patients (16.6%) experienced at least one event. Events were more frequent in mild than severe hemophilia (70.4% vs 40.4%; p=0.0199), with no difference between hemophilia A and B (p=0.545). Patients with events were older (67.8±12.2 vs 55.7±10.7 years; p=0.001) and had a higher prevalence of hypertension (66.6% vs 38.2%; p=0.01), dyslipidemia (59.3% vs 38.2%; p=0.04), and cancer (37% vs 13.2%; p=0.004). Multivariable analysis identified HIV infection (OR 6.51, 95% CI 1.38–30.77), hypertension (OR 3.17, 95% CI 1.31–7.68), and dyslipidemia (OR 2.38, 95% CI 1.02–5.56) as independent predictors of events. Patients with events showed greater carotid plaque thickness (p=0.006), larger abdominal aorta diameter (p=0.03), and a higher prevalence of abnormal ABI (<1; p=0.001). Laboratory findings included lower hemoglobin (p=0.0076) and platelet counts (p=0.0037), higher creatinine (p=0.0182), NT-proBNP (p=0.02), and troponin I levels (p=0.004). ROTEM analysis demonstrated shorter INTEM clotting time (p=0.0037), while Multiplate testing showed lower ASPI AUC (p=0.03) and TRAP AUC (p=0.002). Kaplan–Meier analysis revealed no significant difference in event-free survival between mild and severe hemophilia (p=0.94) (Figure 1).

Conclusions. Cardiovascular and thrombotic events occurred in a minority of patients with hemophilia but were associated with older age, mild disease, HIV infection, and traditional cardiovascular risk factors. Their association with markers of subclinical atherosclerosis highlights the importance of comprehensive cardiovascular assessment in this population.

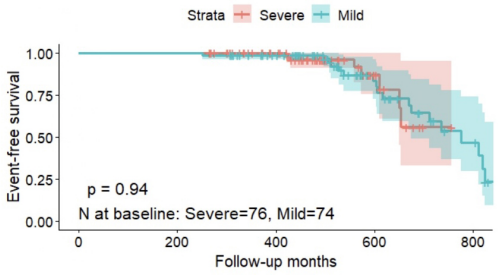


Figure 1. Kaplan–Meier curve for cardiovascular events in severe and moderate hemophilia A and B

XIX CONVEGNO TRIENNALE
VERONA
15, 16, 17 e 18 OTTOBRE 2026
Camera di Commercio di Verona
AICE Associazione Italiana Centri Emofilia

XIX Convegno Triennale sugli Aspetti Clinici e Sociali dell'Emofilia

ABSTRACT N. CO-53

2.06 Comorbidities

LIVER FIBROSIS, STEATOSIS AND SUBCLINICAL ATHEROSCLEROSIS IN PATIENTS WITH HEMOPHILIA: A CROSS-SECTIONAL STUDY

C. Simion[1|2], B. Stocco[1|2], I. Condonato[1|2], E. Dalla Porta[1|2], A. Napolitano[1|2], E. Zanon[1|2], L. Fabris[1], L. Spiezia[1|2], P. Simioni[1|2]

[1]First Chair of Internal Medicine and Thrombotic and Haemorrhagic Diseases Unit, Department of Medicine, Padova University Hospital, Italy; [2]Hemophilia Center, Padova University Hospital, Italy

Background and Aims. Metabolic dysfunction–associated steatotic liver disease (MASLD) is an emerging cardiovascular risk factor. As patients with hemophilia (PWH) age and develop metabolic comorbidities, cardiovascular disease is becoming increasingly relevant despite their inherited bleeding tendency. In addition, liver disease is common in PWH owing to the combined impact of metabolic dysfunction and previous viral infections. Whether liver fibrosis and steatosis contribute to cardiovascular risk in this population remains unclear. This study investigated their association with subclinical atherosclerosis.

Materials and Methods. We report an interim analysis of a cross-sectional study evaluating liver health in (PWH). Liver fibrosis was assessed and graded from F0 to F4, while liver steatosis was evaluated and graded from S0 to S3. Subclinical atherosclerosis was assessed and recorded as present or absent. Clinical data included age, hemophilia type and severity, viral history (HCV, HBV, HIV), liver enzymes, platelet count, FIB-4, and traditional cardiovascular risk factors. Fibrosis and steatosis were analyzed as both ordinal variables and clinically relevant categories. Associations with atherosclerosis were assessed using non-parametric tests and contingency-table analyses.

Results. A total of 49 patients with hemophilia were included (median age 55 years). Baseline characteristics of the study population are summarized in Table 1. Subclinical atherosclerosis was detected in 8/45 patients (16.3%). Liver fibrosis was generally mild, with significant fibrosis (F2–F4) observed in 6/49 patients (12.2%). Steatosis was present in 21/41 patients (51.2%), with moderate-to-severe steatosis (S2–S3) in 11/41 (26.8%). No significant association was found between fibrosis stage and the presence of atherosclerosis (p=0,524). Similarly, steatosis was not associated with atherosclerosis (p=0,389). Traditional cardiovascular risk factors were common, with hypertension in 42.8%, dyslipidemia in 32.6%, and active or previous smoking in 71.4% of patients. Atherosclerosis was more frequently observed in patients with a higher burden of cardiovascular risk factors (p=0,043). Number of cardiovascular risk factors showed a trend toward association with atherosclerosis (OR 2.22, 95% CI 0.94–5.22; p=0.068).

Conclusions. In this cohort of patients with hemophilia, liver fibrosis and steatosis were not associated with subclinical atherosclerosis. Cardiovascular risk appears to be mainly driven by traditional risk factors rather than liver-related parameters. These findings highlight the complex and heterogeneous nature of liver disease in this population and warrant further investigation in larger cohorts.

	Overall population (n.49)	Without atherosclerosis (n. 37)	With atherosclerosis (n.8)
Age, years [IQR]	55 [48-63]	54 [48-64]	57 [48-61]
Type of Hemophilia, n (%)			
HA	45 (91.8)	34 (94.4)	6 (75)
HB	4 (8.2)	2 (5.6)	2 (25)
Severe	30 (61.2)	22 (61.1)	6 (75)
BMI, kg/m^2 [IQR]	24.9 [23.3-27.8]	25.5 [24.0-28.3]	23.6 [21.8-26.2]
Number of cardiovascular risk factors, n (%)			
0	7 (14.3)	4 (11.1)	-
1	15 (30.6)	12 (33.3)	1 (12.5)
2	14 (28.6)	11 (30.6)	3 (37.5)
3	11 (22.4)	8 (22.2)	3 (37.5)
4	2 (4.1)	1 (2.8)	1 (12.5)
Cardiovascular risk factors, n (%)			
Obesity	5 (10.2)	5 (13.9)	-
Arterial hypertension	21 (42.8)	15 (41.7)	5 (62.5)
Dyslipidemia	16 (32.6)	11 (30.6)	5 (62.5)
Active or previous smoke	35 (71.4)	11 (30.6)	7 (87.5)
Diabetes	3 (6.1)	1 (2.8)	2 (25.0)
Other comorbidities, n (%)			
Active cancer	3 (6.1)	2 (5.6)	1 (12.5)
Rheumatological diseases	4 (8.2)	3 (8.3)	1 (12.5)
Venous thromboembolism	2 (4.1)	1 (2.8)	1 (12.5)
Mild thrombophilia	5 (10.2)	5 (13.9)	0
HCV, n (%)			
Active	2 (4.1)	1 (2.8)	1 (12.5)
Eradicated	30 (61.2)	24 (66.7)	4 (50.0)
FIB-4 score, [IQR]	1.43 [0.97-1.97]	1.48 [1.00-1.97]	1.42 [0.82-1.76]
Liver stiffness (LSM), KPa[IQR]	5.2 [4.3-6.4]	5.1 [4.3-6.3]	5.3 [4.5-6.3]
Severity of stiffness, n (%)			
F0	19 (38.8)	14 (38.9)	3 (37.5)
F1	24 (49.0)	17 (47.2)	4 (50.0)
F2	4 (8.2)	3 (8.3)	1 (12.5)
F3	1 (2.0)	1 (2.8)	-
F4	1 (2.0)	1 (2.8)	-
Steatosis (CAP), dB/m [IQR]	247 [204-284]	249 [217-293]	263 [190-297]
Severity of steatosis, n (%)			
S0	22 (51.2)	15 (41.7)	2 (33.3)
S1	10 (23.3)	8 (22.2)	2 (33.3)
S2	-	-	-
S3	11 (25.6)	9 (25.0)	2 (33.3)

Table 1. Clinical, hepatic and cardiovascular characteristics of the study population stratified by subclinical atherosclerosis; data are presented as median [interquartile range] or number (%); cardiovascular risk factors include obesity, arterial hypertension, dyslipidemia, diabetes and active or previous smoking; liver fibrosis was assessed by liver stiffness measurement (F0–F4) and steatosis by controlled attenuation parameter (S0–S3); abbreviations: IQR, interquartile range; HA, hemophilia A; HB, hemophilia B; BMI, body mass index; HCV, hepatitis C virus; FIB-4, fibrosis-4 index; LSM, liver stiffness measurement; CAP, controlled attenuation parameter.

Abstracts printing tool powered by pagepress.org

XIX CONVEGNO TRIENNALE
VERONA
15, 16, 17 e 18 OTTOBRE 2026
Camera di Commercio di Verona
AICE Associazione Italiana Centri Emofilia

XIX Convegno Triennale sugli Aspetti Clinici e Sociali dell'Emofilia

ABSTRACT N. CO-54

2.06 Comorbidities

DECREASED BONE MINERAL DENSITY IN HEMOPHILIA IS NOT CORRELATED WITH INCREASED RISK OF FRACTURES

M.R. Fasulo[1], F. Carrone[2], G. Mazziotti[3|4], A. Colombo[1], C. Lodigiani[1], M.E. Mancuso[1|4]

[1]Center for Thrombosis and Hemorrhagic Diseases, IRCCS Humanitas Research Hospital, Rozzano, Milano, Italy; [2]Endocrinology and Diabetology Unit, Humanitas Mater Domini, Castellanza, Varese, Italy; [3]Endocrinology, Diabetology and Medical Andrology Unit, Metabolic Bone Diseases and Osteoporosis Section, IRCCS Humanitas Research Hospital, Rozzano, Milano, Italy; [4]Department of Biomedical Sciences, Humanitas University, Pieve Emanuele, Milano, Italy

Background and Aims. A decrease in bone mineral density (BMD) is observed in people with hemophilia (PwH) due to several risk factors including arthropathy causing limited mobility as well as chronic viral infections (i.e., HCV and HIV). The aim of this study was to evaluate BMD and bone microarchitecture (as per trabecular bone score, TBS) in an unselected cohort of PwH, assessing the prevalence of osteoporosis and osteopenia and the fracture risk.

Materials and Methods. Data on BMD and TBS measured by Dual Energy X-ray Absorptiometry (DEXA), fractures and deformities at spine X-ray, body mass index (BMI), lifestyle habits, co-morbidities and serum biomarkers were collected from medical records of PwH aged ≥12 years. Osteoporosis and osteopenia were defined according to WHO criteria.

Results. Seventy-seven hemophilic men aged 14-76 years (median 44) were included. Their characteristics are reported in Table 1. Median total femoral BMD was 0.9 g/cm2 (range 0.7 - 1.4), with median T score -0.8 (range -2.5 - 2.4) and median Z score -0.6 (range -2.2 - 2.5). Median femoral neck BMD was 0.7 g/cm2 (range 0.5 - 1.3), with median T score -1.5 (range -3.0 - 3.0) and median Z score -0.7 (range -2.8 - 3.0). Median spine BMD was 1.0 g/cm2 (range 0.7 - 1.3), with median T score -0.7 (range -3.8 - 1.5) and median Z score -0.2 (range -3.6 - 1.9). Median TBS at spine level was 1.38; 13 patients (17%) had a partially degraded microarchitecture and 4 (5%) a degraded microarchitecture. Fifty-five patients (71%) had osteoporosis or osteopenia. The prevalence of osteoporosis in the spine and the femoral neck was 11% and 18%, respectively, and osteopenia in the spine and the femoral neck was seen in 44% and 73% of the patients, respectively. By pairing BMD and TBS, the risk of fracture was low in 16 patients (21%), intermediate in 41 (53%) and high in 9 (12%). A fracture or a deformity in at least 1 vertebra was found in 7 out of 46 patients (15%) who underwent spine X-ray. Among those 7, all had severe hemophilia A and 5 had previous HCV infection. With regard to biomarkers involved in mineral metabolism and bone health, the following results were found: median calcium levels 2.39 mmol/L (IQR 2.33 - 2.45), median phosphate levels 1.03 mmol/L (IQR 0.94 - 1.13), median vitamin D (25-OH) levels 24 ng/mL (IQR 17 - 31), median parathormone levels 51.1 pg/mL (IQR 42.7 - 64.0), median telopeptide levels 369.7 pg/L (IQR 226.3 - 667.0) and median alkaline phosphatase bone isoenzyme levels 15.5 mcg/L (IQR 11.7 - 22.8).

Conclusions. This study confirms that PwH have a high prevalence of osteoporosis and/or osteopenia, but highlights that only 12% have a significantly increased risk for fractures.

Table 1. Characteristics of patients enrolled in the study.

	Total = 77 patients
Patients with Hemophilia A, N (%)	63 (81%)
Patients with severe hemophilia, N (%)	59 (77%)
Patients with inhibitor history*, N (%)	20 (26%)
Patients on primary prophylaxis, N (%)	4 (5%)
BMI, Median (range)	24.8 (17.0 - 35.2)
Smokers**, N (%)	32 (42%)
Patients with sedentary habit, N (%)	33 (43%)
Patients with previous HCV infection, N (%)	45 (58%)
Patients with HIV infection, N (%)	14 (18%)
Patients with chronic hemophilic arthropathy, N (%)	56 (73%)
Patients who underwent previous orthopedic surgery, N (%)	35 (45%)

* Includes patients with previous and current inhibitors.
** Includes smokers and previous smokers.

DEVELOPMENT OF ENGINEERED LONG-ACTING BYPASSING FX VIA ALBUMIN FUSION FOR HEMOPHILIA WITH INHIBITORS

A. Martucci[1], R. Tarantino[1], K.H. Aaen[2], M. Pinotti[1], J.T. Andersen[2], A. Branchini[1]

[1]Department of Life Sciences and Biotechnology, University of Ferrara, Ferrara, Italy; [2]Institute of Clinical Medicine, Department of Pharmacology, University of Oslo, Norway

Background and Aims. The management of bleeding in patients with Hemophilia and inhibitors requires effective bypassing agents to restore hemostasis. We engineered a novel Factor X variant with bypassing activity (FXBP), featuring an activation peptide modified to be cleaved and activated by FXIa, triggering the thrombin production independently from the intrinsic tenase complex. To extend its plasma half-life, we fused FXBP with an albumin variant (QMP) characterized by enhanced affinity for neonatal Fc receptor (FcRn). This study evaluates and compares two albumin fusion strategies to balance prolonged circulation with optimal procoagulant efficacy.

Materials and Methods. The engineered FXBP variant was generated under two configurations: a direct C-terminal fusion and a conditional release construct via a cleavable linker. Both chimeras were expressed in Expi293 cells and purified via affinity chromatography and size-exclusion chromatography. Human FcRn binding affinity and kinetic constants were evaluated at different pH conditions via ELISA and Surface Plasmon Resonance (SPR). The functional profile of fusion proteins was evaluated i) in PT assays in FX-deficient plasma to assess extrinsic pathway function, ii) in aPTT assays in Hemophilia A and Hemophilia B plasma for bypassing activity, and iii) by FXIa-mediated activation.

Results. Both fusions demonstrated robust expression, purity, and efficacy. The in vitro assay with FXIa successfully validated specific proteolytic cleavage and conditional activation of FXBP. ELISA and SPR confirmed that both the direct fusion (FXBP-QMP direct) and the cleavable construct (FXBP-Linker-QMP) retained high pH-dependent affinity for human FcRn at pH 5.5, exhibiting an outstanding KD of 2.77 nM. PT assays showed that the albumin fusion strategy only slightly impaired native extrinsic FX activation compared to plasma-derived FX. Crucially, aPTT assays demonstrated bypassing activity for both constructs, which shortened clotting times in both Hemophilia A and B plasma compared to their wild-type counterparts. In particular, FXB variants showed higher bypassing activity in Hemophilia B plasma.

Conclusions. Fusing the engineered bypassing FX variant with QMP represents a highly successful strategy to optimize pharmacokinetics while preserving procoagulant function. The high-affinity FcRn binding kinetics strongly predict a prolonged plasma half-life through the receptor-mediated recycling pathway. Moreover, bypassing efficacy in hemophilic plasma confirms the therapeutic potential of these chimeras.

XIX CONVEGNO TRIENNALE
VERONA
15, 16, 17 e 18 OTTOBRE 2026
Camera di Commercio di Verona
AICE Associazione Italiana Centri Emofilia

XIX Convegno Triennale sugli Aspetti Clinici e Sociali dell'Emofilia ABSTRACT N. CO-56

2.07 Novel therapeutic products and approaches (including gene therapy)

EVALUATING AN AI MODEL'S HEMATOLOGY CONSULTATION PERFORMANCE FOR HOSPITALIZED PATIENTS WITH BLEEDING DISORDERS

G. Sottilotta[1], F. Misiti[2], G. Praticò[1], D. Megalizzi[1], F. Luise[3]

[1]UOSD Microcitemie - Emostasi e Trombosi. Grande Ospedale Metropolitano di Reggio Calabria, Italy; [2]Associazione Emofilici di Reggio Calabria, Italy; [3]Laboratorio Analisi. Grande Ospedale Metropolitano di Reggio Calabria, Italy

Introduction. Artificial intelligence (AI) is increasingly proposed as a decision-support tool in clinical medicine. Decisions in hemostasis and thrombosis often require nuanced interpretation of bleeding history,laboratory results, and procedural risk. This study evaluated whether a general-purpose AI could provide consultation-level guidance comparable to an expert hematologist for inpatients across diverse hospital services.

Objectives. The objective was to assess the concordance between AI-generated hematology recommendations and those issued by real-life hematology consultants for inpatient questions concerning diagnostic workup, prophylaxis, or on-demand therapy for bleeding and coagulation disorders.

Materials and Methods. We retrospectively selected 18 prior consultations deemed suitable for head-to-head comparison. The cases involved 18 patients (12 male, 6 female) aged 5 to 82 years (mean 47.4). For each case, the original clinical question and context were provided to the AI, which then generated a de novo response. Concordance between the AI and the consultant's recommendation was scored from 0 to 100 against the clinician's answer. A score of 90–100 indicated virtually overlapping recommendations;75–89 indicated very close concordance with minor or prudential differences;60–74 indicated partial concordance with a similar rationale but different therapy;40–59 indicated a clinically important difference; and below 40 indicated a substantially incorrect framing of the problem. The AI also produced a self-rating after comparing its own output to the clinician's response.

Results. across the 18 consultations,the mean AI self--assessed score versus the clinician standard was 78.4. This indicates overall very close concordance, with predominantly minor or caution-driven deviations. Performance was consistent across surgical and medical services.There was frequent alignment on perioperative hemostatic strategies, factor replacement thresholds, and laboratory triage, such as targeted factor assays, von Willebrand evaluation, and mixing studies when appropriate. Discrepancies most often reflected therapeutic conservatism, such as higher suggested replacement targets or extended monitoring, or differences in drug selection within a class rather than opposing clinical logic. In some cases, partial concordance arose from similar diagnostic reasoning but divergence in dosing intensity or duration. No cases were rated as grossly misframed relative to the human consultant. Patient characteristics and AI concordance are provided in table 1.

Conclusions. In this real-world consultation set spanning multiple specialties and age groups,an AI model's recommendations for bleeding and coagulation questions were, on average, very close to expert hematology guidance

Table1. Patient Characteristics and AI Concordance Results

Total Patients (n)	18
Sex	12 Male (66.7%), 6 Female (33.3%)
Age Range	5 – 82 years
Mean Age	47.4 years
Consultation Services (Origin)	Neurosurgery (6), Otorhinolaryngology (5), Gynecology (3), Urology (2), Internal Medicine (1), Orthopedics (1)
AI Concordance Score	Mean Score: 78.4 (Range: 45-98)
Bleeding Disorder / Factor Deficiency	**Number of patients**
Factor VII Deficiency	4
Combined Factor VII & Factor V Deficiency	3
Combined Factor VII & Factor XIII Deficiency	5
Combined Factor X & XI Deficiency	1
von Willebrand Disease	1
Factor XII Deficiency	1
Hypofibrinogenemia	1
Isolated Prolonged Prothrombin Time (PT)	1
Isolated Prolonged Partial Thromboplastin Time (aPTT)	1

Abstracts printing tool powered by pagepress.org

XIX CONVEGNO TRIENNALE
VERONA
15, 16, 17 e 18 OTTOBRE 2026
Camera di Commercio di Verona
AICE Associazione Italiana Centri Emofilia

XIX Convegno Triennale sugli Aspetti Clinici e Sociali dell'Emofilia ABSTRACT N. CO-57

2.07 Novel therapeutic products and approaches (including gene therapy)

NXT007 PROPHYLAXIS IN PEOPLE WITH HEMOPHILIA A WITH OR WITHOUT FACTOR VIII INHIBITORS: COMBINED ANALYSIS OF TWO PHASE I/II MULTIPLE-ASCENDING-DOSE STUDIES

M.E. Mancuso[1|2], M. Shima[3], J.M. Staber[4], Y.C. Chen[5], F.J. López-Jaime[6], M.C. Shen[7], G. Ventriglia[8], M. Takeyama[9], C. Schmitt[8], Y.S. Park[10], A. Kiialainen[8], N. Mizuno[11], M. Niggli[8], T. Miyake[11], D. Matino[12], T. Saito[11], V. Jiménez-Yuste[13], R. Kobayashi[11], D. Hart[14], K. Nogami[15]

[1]Department of Biomedical Sciences, Humanitas University, Pieve Emanuele, Milano, Italy; [2]Center for Thrombosis and Hemorrhagic Diseases, IRCCS Humanitas Research Hospital, Rozzano, Milano, Italy; [3]Thrombosis and Hemostasis Research Center, Nara Medical University, Kashihara, Nara, Japan; [4]Stead Family Department of Pediatrics, Carver College of Medicine, University of Iowa, Iowa City, USA; [5]Hemophilia Care and Research Center, Tri-Service General Hospital, National Defense Medical University, Taipei, Taiwan; [6]Servicio de Hematología, Hospital Universitario Regional de Málaga / Instituto de Investigación Biomédica de Málaga (IBIMA), Málaga, Spain; [7]Department of Internal Medicine, Changhua Christian Hospital, Changhua, Taiwan; [8]F. Hoffmann-La Roche Ltd, Basel, Switzerland; [9]Division of Hemophilia, National Hospital Organization, Osaka National Hospital, Osaka, Japan; [10]Department of Pediatrics, Kyung Hee University Hospital at Gangdong, Seoul, South Korea; [11]Chugai Pharmaceutical Co., Ltd, Tokyo, Japan; [12]McMaster University, Hamilton, Ontario, Canada; [13]La Paz University Hospital-IdiPAZ, Autónoma University, Madrid, Spain; [14]Roche Products Ltd, Welwyn Garden City, UK; [15]Department of Pediatrics, Nara Medical University, Kashihara, Nara, Japan

Background. NXT007, a next-generation bispecific antibody based on emicizumab that mimics activated factor (F)VIII function in people with hemophilia A (HA), was investigated in two Phase I/II, open-label, non-randomized, multicenter, multiple-ascending-dose (MAD) studies: one in Asia (NXTAGE Part B; jRCT2080224835), one Global (NCT05987449).

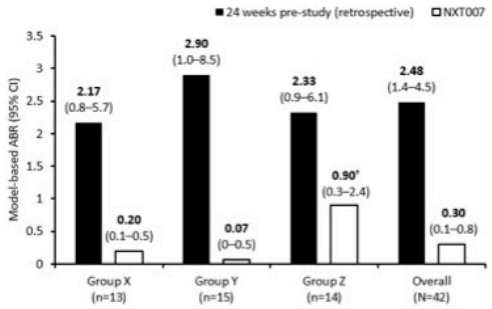
Aims. Report outcomes in three pooled NXT007 dose cohorts from two MAD studies (F. Hoffmann-La Roche Ltd/Chugai Pharmaceutical Co., Ltd) with equivalent dosing.

Methods. Eligible participants were emicizumab-naïve and aged 12–64 years (Global study: ≤59 years). Subcutaneous NXT007 maintenance doses in NXTAGE cohorts B2, B3 and B4 are identical to Global cohorts 1, 2 and 3 (0.28, 0.70, and 1.08 mg/kg, respectively, every 4 weeks; predicted to achieve non-hemophilic FVIII activity), and are pooled into Groups X, Y, and Z. Loading doses were weekly in NXTAGE Group X and Y (X: six doses; Y: four doses) and as two doses at 2-week intervals in the Global study and NXTAGE Group Z. Informed consent and ethics approval were obtained. Outcomes included safety, pharmacokinetics, pharmacodynamics, immunogenicity, and model-based annualized bleeding rates (ABRs).

Results. Overall, 42 participants received NXT007 (Group X: n=13; Group Y: n=15; Group Z: n=14). Forty (95.2%) had severe HA; one (2.4%; Global study) had FVIII inhibitors. Median (range) age was 36 (12–56) years. At cut-off (NXTAGE: 06-Nov-24; Global: 21-Apr-25), median (range) observation periods in Groups X, Y, and Z were 80.0 (61.1–113.3), 44.1 (42.1–72.4), and 21.6 (5.4–34.4) weeks, respectively. NXT007 had favorable safety outcomes across doses. D-dimer remained within normal range and prothrombin fragment 1+2 elevated slightly; neither increased dose-dependently. ABR (95% confidence interval) for treated bleeds in the maintenance period was 0.3 (0.1–0.8; Figure); 36/42 (85.7%) participants had zero treated bleeds. NXT007 plasma concentrations increased dose-dependently, with no ethnic differences. Thrombin generation peak height increased from baseline with all doses. Overall, 34/42 (81.0%) participants developed anti-drug antibodies (ADAs); one (2.4%; Group Y, NXTAGE) had ADAs impacting pharmacokinetics; none impacted safety or cross-reacted with emicizumab.

Conclusions. NXT007 had favorable safety outcomes, with low treated ABRs. One participant had ADAs impacting pharmacokinetics. These data support progression to Phase III trials.

Figure. Treated bleeding rates*



	Group X (n=13)	Group Y (n=15)	Group Z (n=14)	Overall (N=42)
Median (range) NXT007 maintenance observation duration	76.0 weeks (57.1–107.3)	40.1 weeks (38.1–68.4)	17.6 weeks (1.4–30.4)	40.1 weeks (1.4–107.3)
Participants with zero treated bleeds, n (%)	9/13 (69.2)	14/15 (93.3)	13/14 (92.9)	36/42 (85.7)

*ABRs are derived from a negative binomial regression model, and represent bleeds reported during the NXT007 maintenance dose period.

†Four treated bleeds, observed in one notable outlier in the Global study who experienced arterial bleeds secondary to direct trauma to a vessel in a replaced knee.

ABR, annualized bleeding rate; CI, confidence interval

XIX CONVEGNO TRIENNALE
VERONA
15, 16, 17 e 18 OTTOBRE 2026
Camera di Commercio di Verona
AICE Associazione Italiana Centri Emofilia

2.07 Novel therapeutic products and approaches (including gene therapy)

SUCCESSFUL TREATMENT WITH EFANESOCTOCOG ALFA OF INTRACRANIAL HAEMORRHAGE IN A NEWBORN AFFECTED BY SEVERE HEMOPHILIA A

T. Martini[1], B. Borsellino[1|2], B. Pollio[1]

[1]Haemophilia Centre, Immune-Haematology and Transfusion Medicine, University Hospital "Città della Salute e della Scienza", Torino, Italy; [2]Department of Biomedicine and Prevention, PhD in Immunology, Molecular Medicine and Applied Biotechnology, University of Rome Tor Vergata, Roma, Italy

Background. Intracranial haemorrhage (ICH) in the neonatal period is a non-rare and potentially life-threatening complication of haemophilia A. Use of ultra extended half-life factor VIII concentrate (UHL-FVIII) Efanesoctocog Alfa can be crucial in this setting, but until now there is no published experience in this clinical scenario.

Case Report. A term male neonate was born after a dystocic vaginal delivery with vacuum extraction. Initial postnatal adaptation required CPAP support, followed by clinical improvement. On day 3 of life, because of pallor and subcyanotic appearance suggestive of anaemia, cranial ultrasound raised suspicion of intraventricular bleeding and the patient was transferred to the neonatal intensive care unit. Coagulation testing performed that evening revealed an isolated prolonged aPTT ratio of 3.21 (HemosIL SynthaSil ® Werfen) and severely reduced factor VIII activity of 0.2% (HemosIL SynthaSil ® Werfen), consistent with diagnosis of severe haemophilia A. No family history of haemophilia was reported along the maternal lineage, and the mother had no known bleeding phenotype. Brain CT then demonstrated a substantial haemorrhage in the fourth ventricle, with additional mild blood deposition in the occipital horns and along the tentorium and retrocerebellar region, without intraparenchymal bleeding. Efanesoctocog Alfa was administered on day 4 of life (50 IU/kg). On day 6, approximately 40 hours after the first infusion, factor VIII activity was 74.7% (HemosIL Synthafax ® Werfen), supporting a largely sustained haemostatic coverage. A second infusion at the same dose was administered on day 7 of life. In the meantime, MRI reassessment showed a mild reduction of the intraventricular haemorrhage, with no neurosurgical indication. On day 8, follow-up cranial ultrasound confirmed mild bilateral ventricular dilatation without signs of hypertension and no new bleeding sites. Because of difficult peripheral venous access, a midline peripherally-inserted venous catheter was placed on day 10, when a third infusion of Efanesoctocog Alfa was administered. Emicizumab prophylaxis is planned to be started once the haemorrhage is clearly resolving, with the aim of subsequently discontinuing Efanesoctocog Alfa after the second loading dose.

Conclusions. To our knowledge, this is the first case of Efanesoctocog Alfa use in a severe haemophilia A newborn with ICH. Our case suggests that Efanesoctocog Alfa represents an innovative and effective strategy, offering prolonged haemostatic coverage with a reduced number of infusions in an exceptionally fragile clinical setting.

XIX CONVEGNO TRIENNALE
VERONA
15, 16, 17 e 18 OTTOBRE 2026
Camera di Commercio di Verona
AICE Associazione Italiana Centri Emofilia

XIX Convegno Triennale sugli Aspetti Clinici e Sociali dell'Emofilia ABSTRACT N. CO-59

2.07 Novel therapeutic products and approaches (including gene therapy)

CO-NCIZUMAB IN A YOUNG CHILD WITH SEVERE HEMOPHILIA B WITH INHIBITOR: EFFECTIVE BLEED CONTROL AND SAFE HOME MANAGEMENT

T. Martini[1], B. Borsellino[1|2], B. Pollio[1]

[1]Haemophilia Centre, Immune-Haematology and Transfusion Medicine, University Hospital "Città della Salute e della Scienza", Torino, Italy; [2]Department of Biomedicine and Prevention, PhD in Immunology, Molecular Medicine and Applied Biotechnology, University of Rome Tor Vergata, Roma, Italy

Background. Inhibitors remain one of the major therapeutic hurdles in severe hemophilia B (HB). They develop in ~1–6% of patients—most often in those with severe genotypes—typically after 10–20 factor IX (FIX) exposure days and frequently within the first 75 infusions. By neutralizing FIX activity, they make replacement therapy ineffective and are associated with higher annualized bleeding rates (ABR), serious intracranial/visceral hemorrhage, progressive arthropathy, substantial healthcare costs, and increased mortality. Unlike hemophilia A, HB inhibitors can also be accompanied by IgE-mediated infusion reactions, including anaphylaxis, and by immune-complex–mediated nephrotic syndrome.

Case Report. A male child (born October 2022) with severe HB carrying a large F9 deletion (c.724-5_731del) was diagnosed at birth after a subgaleal hematoma. His mother is a carrier, and two cousins have HB with inhibitors. In the first 18 months of life, managed with on demand therapy, the child suffered a large cheek hematoma; prophylaxis with albutrepenonacog alfa (Idelvion®) 75 IU/Kg every 14 days was started in May 2024. In 9 months, 3 hemarthrosis happened. After the 24th infusion (February 2025), he developed a low-titer inhibitor (1 BU/mL) together with a diffuse urticarial eruption treated with IV corticosteroids and antihistamines. Given the risk of anaphylaxis and nephrotic syndrome, FIX was discontinued. During the following 5 months the child, treated with on demand bypassing agent (recombinant activated factor VII, rFVIIa), had 4 severe hemarthrosis (ankle, knee). Compassionate-use concizumab (anti-TFPI monoclonal antibody) was started on August 2025 with a loading dose of 1 mg/kg/day SC followed by a maintenance dose of 0.2 mg/kg/day. Breakthrough events were minimal: a labial laceration treated with tranexamic acid alone, and a right ankle mild traumatic hemarthrosis treated with rFVIIa. Based on therapeutic drug monitoring, the dose was increased in October 2025 to 0.25 mg/kg. At follow-up in March 2026, joint ultrasound showed only grade 1 tibiotarsal synovitis. Parents-reported patient quality-of-life improved markedly, and they quickly learned how to administer concizumab and felt confident performing the injections at home soon after treatment initiation.

Conclusions. By blocking TFPI, concizumab provides factor-independent hemostatic protection and isn't affected by FIX inhibitors. This case is consistent with phase 3 trial Explorer7 results about concizumab clinical value in pediatric HB with inhibitors, showing effective bleed prevention, reduced morbidity, and the practical benefit of safe, caregiver-led home administration.

XIX CONVEGNO TRIENNALE
VERONA
15, 16, 17 e 18 OTTOBRE 2026
Camera di Commercio di Verona
AICE Associazione Italiana Centri Emofilia

XIX Convegno Triennale sugli Aspetti Clinici e Sociali dell'Emofilia ABSTRACT N. CO-60

2.07 Novel therapeutic products and approaches (including gene therapy)

A TURNING POINT IN THE MANAGEMENT OF HEMOPHILIA B WITH INHIBITORS: OUTCOMES OF CONCIZUMAB PROPHYLAXIS IN TWO CHILDREN FROM EXPLORER10

G. Quintavalle[1], A. Matichecchia[1], M.I. Tassoni[1], B.M. Roccon[1], F. Riccardi[1], R.P. Serra[2], A. Tiri[2], P. Bertolini[2], A. Tagliaferri[1], A. Coppola[1]

[1]Regional Hub Center for Hemophilia and Congenital Bleeding Disorders, University Hospital of Parma, Italy; [2]Pediatric Hematology-Oncology Unit, University Hospital of Parma, Italy

Introduction. Although less frequent than in hemophilia A (HA), inhibitors pose a severe challenge to the management of hemophilia B (HB). Beyond neutralizing factor IX (FIX) concentrates, anti-FIX antibodies are often associated with allergic reactions, including anaphylaxis, upon FIX exposure. Thus, prophylaxis and eradication by immune tolerance induction are unfeasible in most cases, exposing patients to the risk of severe bleeding and joint morbidity. Concizumab, a high-affinity anti-TFPI monoclonal antibody, has been recently authorized for prophylaxis in patients with HA and B with inhibitors aged >12 years, based on the results of the explorer trials. The pediatric trial explorer10 is ongoing.

Objectives and Methods. Outcomes of concizumab prophylaxis were evaluated in two children enrolled in explorer10 (follow-up 37 months). Annual bleeding rates (total, ABR; joint, AJBR), recombinant FVIIa (rFVIIa) use, hospital admissions and joint status were compared to those in the three years prior to the trial. The study sponsor, Novo Nordisk, authorized data presentation.

Results. Both children (11 and 9 yr-old at study entry) had sporadic severe HB, due to high inhibitor risk F9 variants (multiexon deletion and nonsense, respectively). At inhibitor detection (16 BU/mL and 0.8 BU/mL) both presented with suspected allergic reactions (11 and 12 exposure days to nonacog alfa and eftrenonancog alfa, respectively). Before study entry, the older child had a lower ABR than the younger one, but most were joint bleeds resulting in three target joints (TJ). In both children rFVIIa prophylaxis failed, due to bleeding recurrence and venous access issues. After starting concizumab prophylaxis the older child did not experience any treated or joint bleed, resolving his TJ and eliminating rFVIIa use. The younger patient minimized bleeding rates, experiencing zero joint bleed. However, three bleeds (including a severe tonsillar hemorrhage) required admission and rFVIIa (overall decreased by >85%). Improved functional and ultrasound joint scores were observed (Table 1). The reduced 'disease burden' progressively improved the overall well-being of these children and their families. Both children increased physical activity and engaged in sports. Concizumab was well tolerated; two possibly treatment-related adverse events (hand cyanosis and focal liver steatosis) occurred in the younger patient.

Conclusions. Starting concizumab prophylaxis in explorer 10 was a turning point in the management of these two children with HB and inhibitor. Effective protection from bleeding, particularly into joints, was observed, along with relevant reduction of the disease and treatment burden and favorable effects on quality of life. Long-term efficacy and safety data are needed.

Table 1: Patients' bleeding rates, rFVIIa use, hospital admissions and joint scores before study entry and during explorer10.

Variable	Patient #1			Patient #2		
	pre	on C	differ. %	pre	on C	differ. %
ABR*	6.7	0	-100	21.3	1.3	-94
AJBR*	4.0	0	-100	4.0	0	-100
rFVIIa, mg*	467	0	-100	657	63	-90.5
Admissions, days (n)*	6 (22)	0 (0)	-100	35 (6.7)	5 (0.7)	-86
HJHS 2.1^	4	2	-50	2	2	0
HEAD-US^	3	1	-66	2	1	-50

C, concizumab; differ., difference; HEAD-US, Hemophilia Early Arthropathy Detection with Ultrasound Score; HJHS, Hemophilia Joint Health Score. *Mean of annual data over the 3 years before study entry (pre) and during explorer10 participation (on C). ^Last available assessment before study entry (pre) and during explorer10 participation (on C).

Abstracts printing tool powered by pagepress.org

XIX CONVEGNO TRIENNALE
VERONA
15, 16, 17 e 18 OTTOBRE 2026
Camera di Commercio di Verona
AICE Associazione Italiana Centri Emofilia

XIX Convegno Triennale sugli Aspetti Clinici e Sociali dell'Emofilia ABSTRACT N. CO-61

2.07 Novel therapeutic products and approaches (including gene therapy)

REAL-WORLD IMPLEMENTATION OF GENE THERAPY FOR HEMOPHILIA: A SHARED PATHWAY AMONG HEALTHCARE AUTHORITY, SPECIALIST CENTERS AND PATIENT ORGANIZATIONS IN THE EMILIA-ROMAGNA REGION

A. Coppola[1], L. Valdrè[2], C. Biasoli[3], E. Ferri Grazzi[4], E. Rozzi[5], M. Volta[5], R. Giroldini[6], A. Tagliaferri[1]

[1]SSD Centro Hub Emofilia e Malattie Emorragiche Congenite, Azienda Ospedaliero-Universitaria di Parma, Italy; [2]SSD Malattie Emorragiche Congenite, IRCCS Azienda Ospedaliero-Universitaria di Bologna, Italy; [3]SSI Presa in Carico delle Malattie Emorragiche e Tromboemboliche, AUSL Romagna, Ospedale Bufalini, Cesena, Italy; [4]FEDRED, Federazione delle Associazioni Emofilici della Regione Emilia Romagna, Italy; [5]Servizio Assistenza Ospedaliera, Malattie Rare, Direzione Generale Cura della Persona, Salute e Welfare, Regione Emilia Romagna, Italy; [6]Area Governo del Farmaco e Dispositivi Medici, Direzione Generale Cura della Persona, Salute e Welfare, Regione Emilia Romagna, Italy

Introduction. Gene therapy (GT) was licensed in Italy for hemophilia A (HA) in early 2024 (then withdrawn from the market by the manufacturer in May 2026) and in September 2025 for hemophilia B (HB). Implementing such a complex and resource-demanding treatment into clinical practice requires highly multidisciplinary and coordinated expertise across different steps, including patient engagement, eligibility assessment, informed decision-making, dosing and follow-up, aiming to enable patients to achieve maximum GT efficacy and safety. Within the National Health System, access to GT is regulated at the regional level. In the Emilia-Romagna region (RER) a hub (Parma)-and-spoke (Bologna, Cesena) network of specialist centers was established to organize, deliver and monitor homogeneous comprehensive care for persons with congenital bleeding disorders.

Objectives and Methods. An ad hoc working group (WG), composed of the directors of the hemophilia centers and of representatives of RER healthcare authority (rare disease and pharmaceutical governance areas) and patient organizations was tasked with defining the pathway for implementing GT delivery and follow-up. A literature review, the analysis of center facilities and potential candidate assessment were performed and discussed in virtual meetings every 1-2 months (May 2024-Mar 2025), followed by periodic updates.

Results. The WG identified providing unbiased, complete yet patient-friendly information and criteria for liver health assessment as priorities. A detailed information sheet covering GT available efficacy and safety data, as well the potential benefits and risks, was developed to guide the decision-making pathway, with the crucial contribution of the patient representative. By involving expert hepatologists from the three centers, clinical (anamnesis, physical examination), laboratory (hematochemical, virological and immunological) and instrumental (liver ultrasound, elastography) data for assessing and monitoring liver health were clearly defined. Two official documents of the RER healthcare authority were issued. The WG also highligted the need for dedicated psychologists addressing patient motivation, expectations and resilience. After analyzing center facilities and expertise, patient selection, treatment and follow-up were authorized at all three centers, aiming at preserving patients' convenience and established relationships. Overall, nine HA candidates were identified, seven completed the eligibility steps and five received GT. The same approach is currently ongoing for HB GT.

Conclusions. A tight collaboration among health authority, clinicians and patient organizations led to a formalized shared pathway for implementing GT in a regional network of hemophilia centers.

Abstracts printing tool powered by pagepress.org

XIX CONVEGNO TRIENNALE
VERONA
15, 16, 17 e 18 OTTOBRE 2026
Camera di Commercio di Verona
AICE Associazione Italiana Centri Emofilia

XIX Convegno Triennale sugli Aspetti Clinici e Sociali dell'Emofilia ABSTRACT N. CO-62

2.07 Novel therapeutic products and approaches (including gene therapy)

ACCESS TO ULTRA-LONG HALF-LIFE FACTOR VIII AS THE DEFINITIVE MOTIVATION FOR ITI IN THE ERA OF NON-REPLACEMENT THERAPIES

B. Borsellino[1], T. Martini[1], I. Ricca[2], C. Linari[3], B. Pollio[1]

[1]Paediatric Haemophilia Centre, Immune-Haematology and Transfusion Medicine, University Hospital "Città della Salute e della Scienza", Torino, Italy; [2]Transfusion Medicine, Ivrea Hospital, Ivrea, Italy; [3]Department of Laboratory Medicine, Azienda Ospedaliera Universitaria Città della Salute e della Scienza, Turin, Italy

Background. Inhibitor development remains the most challenging complication of severe haemophilia A, especially in children with null F8 variants and early exposure to factor VIII. Although emicizumab has transformed bleed prevention, eradication of inhibitors is still clinically relevant because it restores access to factor VIII replacement. This case highlights the long-term value of repeated immune tolerance induction (ITI) in a child with severe haemophilia A and recurrent inhibitor relapse, ultimately enabling transition to efanesoctocog alfa prophylaxis with sustained trough FVIII levels.

Case Report. A boy born in 2012 with severe haemophilia A (FVIII:C <1%) due to a p.Trp979Stop mutation in F8 was diagnosed in 2013 after tongue bleeding. After fewer than ten exposures to octocog alfa, he developed a high-titre inhibitor (32 BU/mL). A first ITI course with octocog alfa (200 U/kg/day), started in 2015, achieved negativisation in 2016, but repeated relapses occurred during tapering. In 2018, rescue ITI with simoctocog alfa was required; despite a reactive inhibitor peak during a febrile illness, complete eradication was obtained by September 2018. In May 2021, prophylaxis was continued with emicizumab to improve quality of life, with excellent bleed control and preserved physical activity. In 2024, however, a post-traumatic fracture of the anterior superior iliac spine required several days of simoctocog alfa, followed by recurrence of a low-titre inhibitor. A third ITI course with simoctocog alfa was therefore started in September 2024. Emicizumab was suspended in January 2025 once the inhibitor became undetectable, and FVIII replacement was continued through June 2025 without further bleeds, confirming complete inhibitor eradication. Musculoskeletal assessment showed only mild ankle synovitis without significant functional impairment. In April 2026, after sustained negative inhibitor testing, the patient switched to weekly efanesoctocog alfa prophylaxis. Seven days after infusion, FVIII activity remained 15%, a particularly meaningful result in light of his previous inhibitor history.

Conclusions. This case shows that inhibitor eradication remains a key long-term objective even in the era of emicizumab. In a child with severe haemophilia A and multiple inhibitor relapses, three successive ITI courses ultimately restored the possibility of FVIII prophylaxis and enabled access to efanesoctocog alfa, an ultra-long half-life product capable of maintaining clinically meaningful trough levels on a weekly schedule. Beyond bleed prevention, this strategy offers a major practical and motivational advantage for patients and families. ITI, when feasible, may therefore still be justified to unlock the full therapeutic potential of modern FVIII replacement.

ACQUIRED VON WILLEBRAND SYNDROME IN AN ELDERLY PATIENT WITH EARLY-STAGE B-CLL

A. Casson[1], I. Ricca[1], A. Barchieri[1], G. Guido[1], P. Ocello[1], M. Tucciarone[1], S. Prestigio[2], A. Alfano[2], G. Delios[1]

[1]Centro Malattie Trombotiche ed Emorragiche - SC Servizio Trasfusionale ASL TO4, Ivrea, Italy; [2]SC Laboratorio Analisi ASL TO4, Ivrea, Italy

Background. Acquired von Willebrand syndrome (AvWS) is a rare bleeding disorder commonly associated with lymphoproliferative, myeloproliferative, cardiovascular, or autoimmune diseases and may mimic inherited von Willebrand disease. Recognition of this condition is particularly relevant in elderly patients presenting with new-onset bleeding in the absence of a family history of congenital bleeding disorders.
Case Report. In August 2020, an 88-year-old man was admitted for extensive cutaneous bleeding and muscular hematomas. His history included B-CLL Rai stage A diagnosed in 2004 without signs of progression, benign prostatic hyperplasia, and hypertension. Baseline blood tests showed hemoglobin 12.2 g/dL, white blood cells 19.77 x10^9/L (lymphocyte predominant), platelets 219 x10^9/L, normal creatinine and LDH, PT ratio 1.0, prolonged aPTT ratio 1.21, antithrombin 89%, and D-dimer 250 ng/mL; coagulation tests in 2015 had been normal. Further hemostatic work-up revealed FVIII:C 29.5%, vWF:RCo 4.5%, vWF:Ag 17.1%, vWF:RCo/vWF:Ag ratio of 0.26; no FVIII inhibitor was detected. Family screening was negative for bleeding abnormalities. Additional evaluation (ANA, CT scan, serum protein electrophoresis, transthoracic echocardiography) excluded autoimmune, malignant or valvular causes. Because of late onset, negative family screening, previously normal coagulation tests, and underlying B-CLL, a diagnosis of AvWS was established. Acute management included tranexamic acid and recombinant activated FVII 90 mcg/kg every 4 hours with gradual discontinuation after one week, intravenous methylprednisolone followed by oral prednisone tapering, and supportive care. In September 2020, intravenous immunoglobulins every 4 weeks were started and are still ongoing. The patient has experienced no further bleeding manifestations.
Conclusions. AvWS should be considered in elderly patients with new bleeding symptoms and laboratory evidence of combined FVIII/VWF reduction, especially in the presence of lymphoproliferative disease. Prompt hemostatic control and an etiologic diagnostic work-up are essential, while IVIG may represent an effective maintenance option in selected patients.

XIX CONVEGNO TRIENNALE
VERONA
15, 16, 17 e 18 OTTOBRE 2026
Camera di Commercio di Verona
AICE Associazione Italiana Centri Emofilia

XIX Convegno Triennale sugli Aspetti Clinici e Sociali dell'Emofilia ABSTRACT N. CO-64

3.01 Von Willebrand Factor and von Willebrand Disease

REAPPRAISAL OF DESMOPRESSIN FOR MANAGEMENT OF MILD/MODERATE VON WILLEBRAND DISEASE: RESULTS OF A RETROSPECTIVE ANALYSIS IN 127 ITALIAN PATIENTS SUGGEST FURTHER ORGANIZATION OF PROSPECTIVE OBSERVATIONAL STUDIES TO PREDICT DESMOPRESSIN FAILURE WITH IMMEDIAT

A.B. Federici[1], G. Castaman[2]

[1]Ematologia e Medicina Trasfusionale, Ospedale Luigi Sacco, Polo Didattico Università di Milano, Italy; [2]Centro Emofilia e Malattie Emorragiche Regione Toscana, Ospedale Careggi, Firenze, Italy

Background. Desmopressin (DDAVP) has been always considered the treatment of choice for patients with mild/moderate von Willebrand disease (VWD), but no standardized criteria have been reported so far to predict benefits/limits of DDAVP in the management of very large cohort of VWD.

Aims. To establish correct indications of DDAVP, we have recently re-analyzed clinical data of patients who received DDAVP treatment at two Italian Centers during the last 15 years (2010-2025)

Methods. The following criteria were required to include cases into this retrospective analysis: age >12 years, bleeding score >5 by BAT, 10-40 U/dL of Platelet-Derived VWF activity (PD-VWF:ACT) and/or VWF collagen binding assay (VWF:CB), trial to determine biological response with assessment of PD-VWF:ACT, VWF:CB, FVIII:C, VWF:AG at baseline and 1-2 hours following DDAVP. Exclusion criteria were known cases with VWD3 and VWD2B, children <12 years, absence or uncompleted data of trial, no patients consent to retrieve their clinical data. DDAVP was given either by sub-cutaneous injections or intravenously during minor/major surgeries. Efficacy/safety of DDAVP were assessed by statistics after retrieving data from patients charts into EXCEL files. DDAVP failure was defined when VWF-C were required. Side effects were also registered.

Results. among 153 cases, 127(83%) met inclusion criteria as VWD1(n=78), VWD1C(n=16), VWD2A(n=15), VWD2M(n=18). Biological response was complete, partial and absent in 75%, 23% and 2%. These 127 VWD received DDAVP for bleeds (n=104), oral surgeries (n=33), deliveries (n=12), minor/major surgeries (n=25). Total injections were 652 with median, range/episode during bleeds (2,1-12), oral surgeries (1,1-10), deliveries (3,1-13), minor/major surgeries (3.6,1-16). Efficacy was excellent/good in bleeding (83%), oral surgery (100%), deliveries (87%), minor/major surgeries (82%). Failure was found in VWD1C who required VWF-C after caesarean section and in 5/25 minor/major surgeries [abdominal(n=2), hysterectomy(n=1), tonsillectomy(n=1), orthopedic(n=1)] in VWD2A and VWD1. Side effects(n=16) were mainly minor (flushing, headache, tachycardia) with 2 cases of water retention reported (>12 doses).

Conclusions. DDAVP should be always recommended as first line therapy in responsive mild/moderate VWD patients in bleeding episodes, oral surgery, deliveries and major surgeries. Prospective clinical observations, as those recently proposed by European Investigators, are required to predict DDAVP failure with immediate indication of VWF-C.

XIX CONVEGNO TRIENNALE
VERONA
15, 16, 17 e 18 OTTOBRE 2026
Camera di Commercio di Verona
AICE Associazione Italiana Centri Emofilia

XIX Convegno Triennale sugli Aspetti Clinici e Sociali dell'Emofilia ABSTRACT N. CO-65

3.01 Von Willebrand Factor and von Willebrand Disease

CO-VID-19-ASSOCIATED HYPERCOAGULABILITY IN TYPE 2B VON WILLEBRAND DISEASE: INSIGHTS FROM GLOBAL HEMOSTATIC ASSAYS

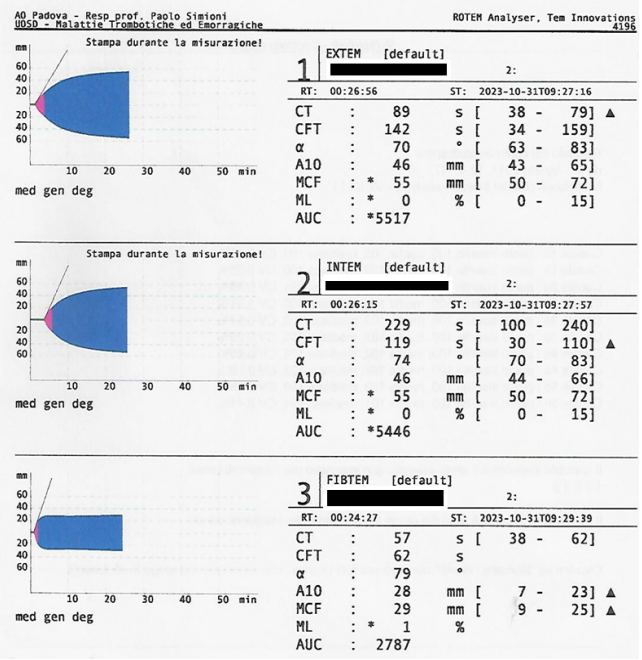
I. Condonato, C. Simion, E. Zanon, P. Simioni

Hemophilia Center, University Hospital of Padua, Italy

Background. Type 2B von Willebrand disease (VWD) is a rare inherited bleeding disorder characterized by gain-of--function variants of von Willebrand factor (VWF), resulting in enhanced platelet binding, loss of high-molecular-weight multimers, and variable thrombocytopenia. SARS-CoV-2 infection is associated with endothelial activation, thromboinflammation, and hypercoagulability, but its impact on patients with congenital bleeding disorders remains poorly characterized. We report a patient with type 2B VWD who developed severe thrombocytopenia during COVID-19 and underwent comprehensive hemostatic assessment.

Case Report. An 88-year-old man with type 2B VWD, followed at our Hemophilia Centre and treated on demand with FVIII/VWF concentrates, was admitted during SARS-CoV-2 infection because of malaise and suspected arrhythmia recurrence. Laboratory investigations revealed profound thrombocytopenia (platelet count 2×10^9/L), acute kidney injury, and positive nasopharyngeal swab for SARS-CoV-2. During hospitalization, he experienced a syncopal episode followed by dorsal ecchymosis, without evidence of major bleeding or traumatic lesions on imaging studies. The patient received platelet transfusion, FVIII/VWF replacement therapy, hydration, and antiviral treatment with nirmatrelvir/ritonavir, with progressive clinical improvement and normalization of platelet count. Hemostatic assessment showed FVIII activity 106%, VWF antigen 115%, ristocetin cofactor activity 47%, and collagen-binding activity 24%, consistent with loss of high-molecular-weight multimers typical of type 2B VWD. During platelet recovery (platelet count approximately 60×10^9/L), rotational thromboelastometry demonstrated preserved clot firmness (EXTEM MCF 55 mm, INTEM MCF 55 mm) and increased fibrin-based clot strength (FIBTEM MCF 29 mm), suggesting a hypercoagulable state (Image 1). Platelet function testing by Multiplate showed only mild impairment of aggregation limited to the ASPI test. No major hemorrhagic complications occurred during hospitalization.

Conclusions. This case highlights the complex interaction between congenital bleeding disorders and SARS-CoV-2 infection. Although COVID-19 was associated with profound thrombocytopenia, global hemostatic assessment performed during platelet recovery revealed a hypercoagulable phenotype characterized by preserved clot firmness and enhanced fibrin-based clot strength. These findings seem to confirm that SARS-CoV-2–related thromboinflammatory activation may substantially influence the overall hemostatic balance even in patients with inherited bleeding disorders. Global hemostatic assays may provide clinically relevant information beyond conventional laboratory parameters and contribute to a more comprehensive evaluation of hemostasis in complex clinical settings.



XIX CONVEGNO TRIENNALE
VERONA
15, 16, 17 e 18 OTTOBRE 2026
Camera di Commercio di Verona
AICE Associazione Italiana Centri Emofilia

XIX Convegno Triennale sugli Aspetti Clinici e Sociali dell'Emofilia

ABSTRACT N. CO-66

3.02 Rare bleeding disorders

PREGNANCY OUTCOMES AND PERIPARTUM MANAGEMENT IN WOMEN WITH CONGENITAL FIBRINOGEN DISORDERS: A SINGLE-CENTRE EXPERIENCE

T. Martini[1], B. Borsellino[1|2], B. Pollio[1]

[1]Haemophilia Centre, Immune-Haematology and Transfusion Medicine, University Hospital "Città della Salute e della Scienza", Torino, Italy; [2]Department of Biomedicine and Prevention, PhD in Immunology, Molecular Medicine and Applied Biotechnology, University of Rome Tor Vergata, Roma, Italy

Background and Aims. Congenital fibrinogen disorders (CFD) are rare inherited disorders that may cause not only bleeding but also thrombosis. Pregnancy is a high-risk setting because of increased incidence of miscarriage, vaginal bleeding, placental complications, post-partum haemorrhage (PPH) and thromboembolism. Our study aimed to describe clinical and obstetric phenotype of CFD women followed at a single centre, focusing on pregnancy outcome and peripartum management.

Materials and Methods. Medical records of women with CFD who delivered between 2013 and 2025 at Sant'Anna Hospital, Turin, were retrospectively reviewed. Collected data included patient characteristics (diagnosis, bleeding/thrombotic history, family history, recurrent miscarriage) and pregnancy characteristics (conception mode, pregnancy outcome, delivery mode, gestational age at delivery, PPH, fibrinogen activity level at delivery, use of fibrinogen concentrate, use of tranexamic acid, low-molecular-weight heparin [LMWH] prophylaxis, newborn diagnosis of CFD). Categorical variables were reported as number and percentage, and continuous variables as median and interquartile range.

Results. Eight women were included, median age 34 (table 1). Three had hypofibrinogenemia, 2 dysfibrinogenemia, 3 hypo-dysfibrinogenemia. Bleeding symptoms were reported in 2 patients (25%), history of thrombotic events in 2 (25%); one had recurrent miscarriage (12.5%). Four women (50%) had a positive family history. Twelve pregnancies were recorded: 8 (66.7%) spontaneous, 4 (33.3%) with assisted reproductive technology. All pregnancies resulted in live birth. Caesarean and vaginal delivery occurred in 6 pregnancies each, 1 delivery was instrumental (12.5%). Median gestational age at delivery was 38 weeks. Placental abnormalities (abruptio placentae in 1st trimester) and obstetric complications (preeclampsia and intrauterine growth restriction) occurred in 1 pregnancy (8.3%) each. PPH occurred in 2 pregnancies (16.7%). Median fibrinogen activity at delivery was 213 mg/dL in vaginal deliveries and 204 mg/dL in caesarean deliveries. Haemostatic prophylaxis was used in 10 pregnancies (83.3%): fibrinogen concentrate in all, tranexamic acid in 2 (20%). In 6 pregnancies LWMH prophylaxis was used. Four neonates were diagnosed with CFD, 1 had a major bleeding at birth (intracranial haemorrhage).

Conclusions. In this cohort all pregnancies outcomes were favourable, all resulting in live birth; PPH rate was the same of general obstetric population, reflecting frequent use of concentrate achieving high fibrinogen activity levels at delivery. Given the rarity of CFD, this cohort represents a meaningful real-world series and adds clinically relevant data to the limited evidence on pregnancy management in these patients.

Characteristics	Value
Pregnancies, n	12
Conception, spontaneous, n (%)	8 (66.7)
Conception, ART, n (%)	4 (33.3)
Live birth, n (%)	12 (100.0)
Placental abnormalities, n (%)	1 (8.3)
Miscarriage, n (%)	0 (0.0)
Cesarean delivery, n (%)	6 (50.0)
Vaginal delivery, n (%)	6 (50.0)
Instrumental delivery, n (%)	1 (8.3)
Gestational age at delivery, median (IQR)	38 (37-38)
Obstetric complications, n (%)	1 (8.3)
Post-partum hemorrhage, n (%)	2 (16.7)
Fibrinogen concentrate at delivery, n (%)	10 (83.3)
Fibrinogen level at delivery, vaginal deliveries, median (IQR)	213 (204-246)
Fibrinogen level at delivery, cesarean deliveries, median (IQR)	204 (179-277)
Tranexamic acid, n (%)	2 (16.7)
LMWH in pregnancy/puerperium, n (%)	6 (50.0)
Newborn bleeding, n (%)	1 (8.3)
Newborn fibrinogen congenital disorder diagnosis, n (%)	3 (25)

Table 1: pregnancy characteristics of women with congenital fibrinogen disorders. ART: assisted reproductive technology; LMWH: low molecular weight heparin

Abstracts printing tool powered by pagepress.org

XIX CONVEGNO TRIENNALE
VERONA
15, 16, 17 e 18 OTTOBRE 2026
Camera di Commercio di Verona
AICE Associazione Italiana Centri Emofilia

XIX Convegno Triennale sugli Aspetti Clinici e Sociali dell'Emofilia

ABSTRACT N. CO-67

3.02 Rare bleeding disorders

CO-NGENITAL DYSFIBRINOGENEMIA: BLEEDING PHENOTYPE, THROMBOTIC COMPLICATIONS, AND LONG-TERM MANAGEMENT IN A MULTICENTER COHORT

M. Biglietto[1|2], M. Presti[1], R.C. Santoro[3], I. Nichele[4], M. Napolitano[5], S. Pasca[6], A. Borchiellini[7], B. Pollio[8], E. Zanon[9], G. Barillari[10], A. Poz[10], S. Sorella[1], S. Ligia[1], R. Mormile[1], E. Baldacci[1], G. Castaman[11], F. Peyvandi[12|13], C. Santoro[1]

[1]Hematology, Department of Translational and Precision Medicine, Sapienza University of Rome, Italy; [2]Department of Molecular Biology, Sapienza University of Rome, Italy; [3]Hemostasis and Thrombosis Unit, Azienda Ospedaliera Pugliese-Ciaccio, Catanzaro, Italy; [4]Hematology Unit, Azienda ULSS 8 Berica - San Bortolo Hospital, Vicenza, Italy; [5]Department of Health Promotion, Mother and Child Care, Internal Medicine and Medical Specialties, University of Palermo, Italy; [6]Coagulation Diseases Center, Transfusion Medicine Department - Azienda Sanitaria Universitaria Integrata del Trentino, Trento, Italy; [7]Centro di Riferimento Regionale Malattie Emorragiche e Trombotiche dell'Adulto, Divisione di Ematologia, Università Città della Salute e della Scienza di Torino, Italy; [8]SIMT Immunohematology and Transfusion Medicine Service, Diagnostic Department, A.O. Città della Salute e della Scienza, Torino, Italy; [9]Department of Medicine, Haemophilia Centre, University Hospital of Padua, Italy; [10]Center for Hemorrhagic and Thrombotic Diseases, General and University Hospital S. Maria della Misericordia, Udine, Italy; [11]Centre for Bleeding Disorders and Coagulation, Careggi University Hospital, Firenze, Italy; [12]IRCCS Fondazione Ca' Granda Ospedale Maggiore Policlinico, Angelo Bianchi Bonomi Hemophilia and Thrombosis Center, Milano, Italy; [13]Università degli Studi di Milano, Department of Pathophysiology and Transplantation, Milano, Italy

Background and Aims. Congenital dysfibrinogenemia is a disorder caused by structural abnormalities of the fibrinogen molecule, resulting in impaired fibrinogen function. While most patients remain asymptomatic, some may present with bleeding manifestations and/or an increased risk of thrombosis. This multicenter study aims to describe the clinical phenotype of a cohort of patients with congenital dysfibrinogenemia.

Materials and Methods. Patients diagnosed with congenital dysfibrinogenemia as per ISTH communication (Casini A., 2018) between 1992 and 2025 at different hemophilia centers affiliated with the Italian Association of Hemophilia Centers (AICE) were included. Bleedings were classified as per ISTH classification (Schulman S., 2005; Kaatz S., 2015) in minor, clinically relevant non major (CRNM) and major.

Results. Patients' characteristics are summarized in Table 1. One-hundred and ten patients were included, 64 females and 46 males. Median follow-up is 4.7 years (0.1-30.1). Three patients presented with a thrombotic phenotype. ISTH-BAT score at diagnosis was suggestive of bleeding disorder in 4 patients, normal in 89 and not available in 17. During follow-up no changes in ISTH-BAT score were observed. Thirty-two patients experienced at least one CRNM bleeding in their life and two patients experienced major bleedings following sleeve gastrectomy and hip replacement surgeries. Three patients experienced one venous thrombotic event and one other an arterial one. No patient received long-term anti-hemorrhagic prophylaxis. Seventy-nine subjects underwent 173 surgeries, of whom 13 were performed with antihemorrhagic prophylaxis using either tranexamic acid, fibrinogen concentrate or fresh frozen plasma. Eight surgeries were complicated by CRNM bleedings and 2 by major bleedings. Major bleedings were managed only with red blood cell transfusions. Twenty-eight women underwent 51 pregnancies. No woman received either antithrombotic or anti-hemorrhagic prophylaxis during pregnancy. Forty-two pregnancies were carried to term. Seven miscarriages occurred and two voluntary abortions were performed. Two patients received prophylactic enoxaparin in the puerperium, and three received anti-hemorrhagic prophylaxis at delivery: one with tranexamic acid, one with fibrinogen concentrate, and one with fresh frozen plasma. No pregnancy was complicated by hemorrhagic or thrombotic complications.

Conclusions. In this cohort, dysfibrinogenemic patients showed a mild and heterogeneous clinical phenotype, with most subjects remaining asymptomatic. Pregnancy and surgical procedures underwent generally without complications, even in the absence of antihemorrhagic prophylaxis. Overall, these findings support a conservative and individualized management approach.

Table 1. Patients' characteristics

	N (%)*
Sex	
Female	64 (58.2)
Male	46 (41.8)
Ethnicity	
Caucasian	109 (99.1)
North African	1 (0.9)
ISTH classification	
Dysfibrinogenemia	107 (97.3)
Thrombotic-related dysfibrinogenemia	3 (2.7)
Duration of follow up (years) – Median (range)	4.7 (0.1-30.1)
Surgery unrelated clinically relevant non major bleedings	
Cutaneous	10 (9.1)
Epistaxis	9 (8.2)
Menometrorrhagia	8 (7.3)
Gastrointestinal	6 (5.5)
Hematuria	3 (2.7)
Muscular	2 (1.8)
Oral cavity	1 (0.9)
Thrombosis	4 (3.6)
Portal vein thrombosis	1 (0.9)
Recurrent thrombophlebitis	2 (1.8)
Ictus cerebri	1 (0.9)
Surgeries without bleeding or thrombotic complications	163 (94.2)
Tooth extractions	46 (26.6)
Tonsillectomy	18 (10.4)
Appendicectomy	17 (9.8)
Orthopedic procedures	14 (8.1)
Excision of small cutaneous lesions	9 (5.2)
Myomectomy	8 (4.6)
Inguinal hernia	7 (4)
TURP/TURB	5 (2.9)
Safenectomy	5 (2.9)
Nasal polypectomy	3 (1.7)
Colecistectomy	3 (1.7)
Disc herniation	2 (1.2)
Frenulectomy	2 (1.2)
Mammoplasty	2 (1.2)
Thyroidectomy	2 (1.2)
Varicocele	2 (1.2)
Others	18 (10.4)
Surgeries with bleeding complications	10 (5.8)
Tooth extractions[§]	4 (2.3)
Sleeve gastrectomy[°]	2 (1.2)
Frenuloplasty	2 (1.2)
Meniscus repair	1 (0.6)
Hip replacement[°]	1 (0.6)
Women that underwent at least one pregnancy	28 (47.8)
Pregnancies	51 (100)
Carried to term	42 (82.4)
Miscarriages	7 (13.7)
Voluntary abortions	2 (3.9)

* If not otherwise specified
[§]One procedure was performed with prophylactic administration of fibrinogen concentrate
[°]One sleeve gastrectomy and one hip replacement surgery were complicated by major bleedings

Abstracts printing tool powered by pagepress.org

XIX CONVEGNO TRIENNALE
VERONA
15, 16, 17 e 18 OTTOBRE 2026
Camera di Commercio di Verona
AICE Associazione Italiana Centri Emofilia

XIX Convegno Triennale sugli Aspetti Clinici e Sociali dell'Emofilia

ABSTRACT N. CO-68

3.02 Rare bleeding disorders

ACQUIRED FACTOR XIII DEFICIENCY ASSOCIATED WITH CROHN'S DISEASE: A CHALLENGING DIAGNOSTIC AND THERAPEUTIC CASE

A. Colombo[1], A. Dal Buono[2|3], I. Quaglia[1], C. Novembrino[4], M.R. Fasulo[1], C. Lodigiani[1], M.E. Mancuso[1|2]

[1]Center for Thrombosis and Hemorrhagic Diseases, IRCCS Humanitas Research Hospital, Rozzano, Milano, Italy; [2]Department of Biomedical Sciences, Humanitas University, Pieve Emanuele, Milano, Italy; [3]IBD Center, IRCCS Humanitas Research Hospital, Rozzano, Milano, Italy; [4]Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico Angelo Bianchi Bonomi, Hemophilia and Thrombosis Center and Fondazione Luigi Villa, Milano, Italy

Background. Acquired factor XIII (FXIII) deficiency is a rare bleeding disorder that may be associated with autoimmune diseases, malignancies or inflammatory conditions. Diagnosis is challenging because routine coagulation tests are normal.

Case Report. A 60-year-old man was referred for haematuria, anaemia, and multiple spontaneous muscle hematomas. His bleeding history was negative, despite several haemostatic challenges. Terminal ileitis was found 6 months earlier treated with a 10-week course of budesonide. At presentation, hemoglobin dropped from 14 to 7.5 g/dL. Routine coagulation tests (PT, aPTT) were normal. Acquired von Willebrand syndrome and platelet dysfunction were ruled out. FXIII measurement revealed severe deficiency (2-4%). Neutralizing anti-FXIII antibodies were not detectable, however exogenous FXIII given intravenously was rapidly cleared from the bloodstream. Partial and transient correction was achieved through continuous infusion of pdFXIII concentrate at 2 IU/kg/h. Given the reported association between inflammatory bowel disease (IBD) and FXIII deficiency, intestinal ultrasound and MR enterography were performed suggesting Crohn's disease. Active IBD has been associated with decreased FXIII levels through coagulation activation, accelerated FXIII turnover and consumption during tissue repair and mucosal healing. Initial treatment with intravenous corticosteroids and infliximab induction failed to significantly improve FXIII activity (4-7%), and patient experienced multiple recurrent spontaneous hematomas involving the left shoulder and arm, requiring repeated hospitalizations and continuous FXIII infusions. Intravenous immunoglobulin infusion was attempted unsuccessfully. As consequence of the muscle hematomas in the left arm, he developed permanent sensorimotor neuropathy. Two months after initiation of oral corticosteroids and infliximab maintenance therapy, MR enterography showed marked improvement of bowel inflammation, paralleled by stabilization of FXIII levels around 15% and resolution of major bleeding episodes. Infliximab was discontinued because of severe cutaneous rash and replaced with adalimumab, and FXIII levels progressively increased up to 30% despite steroid tapering, with no further haemorrhagic complications (fig.1). Due to radiological evidence of intestinal activity, biologic therapy was recently switched to guselkumab.

Conclusions. This case highlights the diagnostic and therapeutic challenges of acquired FXIII deficiency not due to the presence of anti-FXIII antibodies. Our case supports the evidence of a link between IBD and such acquired coagulopathy. Effective control of the underlying inflammatory condition was crucial for restoring FXIII levels and preventing bleeding complications.

Time since diagnosis (weeks)	FXIII activity	Corticorsteroid therapy	IBD therapy	Bleeding complications
0	4%			
3	2%			
6	7%	metilprednisolone 40 mg ev		
11	4%	prednisone 12.5 mg	Infliximab	
17	15%	prednisone 25 mg	Infliximab	Left shoulder and elbow hematomas; left subscapular and antecubital fossa hematomas; left brachial biceps and subscapularis muscle hematomas
24	12%	prednisone 37.5 mg	Infliximab	
41	29%	prednisone 18.75 mg	Adalimumab	Left subcostal and rectus abdominis muscle hematomas
62	40%	prednisone 10 mg	Guselkumab	

Abstracts printing tool powered by pagepress.org

XIX CONVEGNO TRIENNALE
VERONA
15, 16, 17 e 18 OTTOBRE 2026
Camera di Commercio di Verona
AICE Associazione Italiana Centri Emofilia

XIX Convegno Triennale sugli Aspetti Clinici e Sociali dell'Emofilia

ABSTRACT N. CO-69

3.02 Rare bleeding disorders

IN VITRO CORRECTION OF SEVERE FACTOR V DEFICIENCY USING A NOVEL PLASMA-DERIVED FV CONCENTRATE: A WHOLE BLOOD THROMBIN GENERATION STUDY

C. Bulato[1], E. Campello[1], L. Spiezia[1], B. Serena[1], S. Toffanin[1], C. Simion[1], A. Caricasole[2], M. Sotgiu[2], A. Salvatore[2], F. Pierantoni[2], T.M. Hackeng[3|4], H.M.H. Spronk[3|4], P. Simioni[1]

[1]First Chair of Internal Medicine, Thrombotic and Haemorrhagic Diseases Unit and Haemophilia Centre, Department of Medicine, Padova University Hospital, Padova, Italy; [2]Kedrion SpA, Barga Lucca, Italy; [3]Coagulation Profile B.V., Maastricht, Netherland; [4]Department of Biochemistry, Cardiovascular Research Institute Maastricht, Maastricht University, Maastricht, Netherland

Background and Aims. Severe factor V (FV) deficiency is a rare bleeding disorder currently managed with fresh frozen plasma. A novel plasma-derived FV concentrate has been developed as a targeted potential replacement therapy. We evaluated the *in vitro* ability of this concentrate to restore global hemostatic function in patients with severe FV deficiency using whole blood thrombin generation (WBTG).

Materials and Methods. Whole blood from 10 patients with severe FV deficiency was spiked *in vitro* with FV concentrate (0%, 25%, 50%, and 100%). Owing to limited sample availability, 2 patients were not tested at 25%. WBTG was assessed with 1 pM tissue factor by measuring lag time, peak thrombin, and endogenous thrombin potential (ETP). Rotational thromboelastometry (ROTEM; INTEM, EXTEM, FIBTEM) was also performed. A mixed-effects model (REML) was used for statistical analysis, followed by Dunnett's multiple comparisons test versus baseline (0%). The interquartile range (IQR) of a healthy control group was used as reference for lag time, peak thrombin, and ETP.

Results. FV supplementation decreased lag time (F(1.003, 8.361)=20.06, p=0.0018), with all concentrations showing shorter lag time than baseline (25%, p=0.0059; 50%, p=0.0032; 100%, p=0.0027). Peak thrombin increased (F(1.576, 13.13)=17.96, p=0.0003), with differences versus baseline at all concentrations (25%, p=0.0126; 50%, p=0.0026; 100%, p=0.0037). ETP increased at all concentrations, reaching significance at 50% (p=0.0006) and 100% (p=0.0009), but not at 25% (p=0.0624). At baseline, lag time was prolonged in all patients and returned within the IQR of controls already at 25% FV (Fig. 1A-B). Peak thrombin was normal or increased in half of cases (Fig. 1C), while ETP was within or above the IQR of controls in most patients (Fig. 1D); in five patients with low baseline peak thrombin values, levels at 25% FV exceeded the IQR of controls (Fig. 1C). Consistently, ROTEM showed prolonged clotting times at baseline. Both INTEM and EXTEM-clotting time normalized after FV supplementation at 25% in most patients, although a minority required 50% FV to reach normal values. Parameters reflecting clot propagation and strength were largely within the normal range at baseline and FV supplementation had no relevant effect.

Conclusions. WBTG and ROTEM suggest that delayed coagulation initiation is the predominant functional abnormality in severe FV deficiency, while thrombin and fibrin-generating capacity is variably preserved. In our study, the novel plasma-derived FV concentrate effectively corrected this defect, restoring lag and clotting times within the IQR of healthy controls already at 25% FV. These findings support the potential clinical utility of WBTG as a global assay to evaluate treatment response.

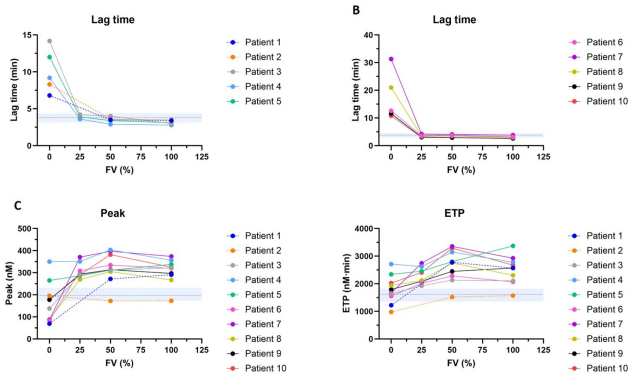


Figure 1. Effect of a novel plasma-derived factor V (FV) concentrate on whole blood thrombin generation parameters in patients with severe FV deficiency. (A–B) Lag time, (C) peak thrombin, and (D) endogenous thrombin potential (ETP) at FV concentrations of 0%, 25%, 50%, and 100% following supplementation with the FV concentrate in individual patients (n=10). Patients 1-5 are shown in panel A and patients 6-10 in panel B for lag time; panels C and D include all patients. Each line represents an individual patient. The dashed horizontal line indicates the median, and the shaded area the interquartile range, of healthy controls. Dashed lines for patients 1 and 2 indicate missing data at 25% FV.

Abstracts printing tool powered by pagepress.org

XIX CONVEGNO TRIENNALE
VERONA
15, 16, 17 e 18 OTTOBRE 2026
Camera di Commercio di Verona
AICE Associazione Italiana Centri Emofilia

XIX Convegno Triennale sugli Aspetti Clinici e Sociali dell'Emofilia

ABSTRACT N. CO-70

3.02 Rare bleeding disorders

CO-NGENITAL AFIBRINOGENEMIA: BLEEDING PHENOTYPE, THROMBOTIC COMPLICATIONS, AND LONG-TERM MANAGEMENT IN A MULTICENTER COHORT

M. Biglietto[1|2], M. Presti[1], R.C. Santoro[3], I. Nichele[4], M. Napolitano[5], S. Pasca[6], A. Borchiellini[7], B. Pollio[8], E. Zanon[9], G. Barillari[10], A. Poz[10], S. Sorella[1], S. Ligia[1], R. Mormile[1], E. Baldacci[1], G. Castaman[11], F. Peyvandi[12|13], C. Santoro[1]

[1]Hematology, Department of Translational and Precision Medicine, Sapienza University of Rome, Italy; [2]Department of Molecular Biology, Sapienza University of Rome, Italy; [3]Hemostasis and Thrombosis Unit, Azienda Ospedaliera Pugliese-Ciaccio, Catanzaro, Italy; [4]Hematology Unit, Azienda ULSS 8 Berica - San Bortolo Hospital, Vicenza, Italy; [5]Department of Health Promotion, Mother and Child Care, Internal Medicine and Medical Specialties, University of Palermo, Italy; [6]Coagulation Diseases Center, Transfusion Medicine Department - Azienda Sanitaria Universitaria Integrata del Trentino, Trento, Italy; [7]Centro di Riferimento Regionale Malattie Emorragiche e Trombotiche dell'Adulto, Divisione di Ematologia, Università Città della Salute e della Scienza di Torino, Italy; [8]SIMT Immunohematology and Transfusion Medicine Service, Diagnostic Department, A.O. Città della Salute e della Scienza, Torino, Italy; [9]Department of Medicine, Haemophilia Centre, University Hospital of Padua, Italy; [10]Center for Hemorrhagic and Thrombotic Diseases, General and University Hospital S. Maria della Misericordia, Udine, Italy; [11]Centre for Bleeding Disorders and Coagulation, Careggi University Hospital, Firenze, Italy; [12]IRCCS Fondazione Ca' Granda Ospedale Maggiore Policlinico, Angelo Bianchi Bonomi Hemophilia and Thrombosis Center, Milano, Italy; [13]Università degli Studi di Milano, Department of Pathophysiology and Transplantation, Milano, Italy

Background and Aims. Congenital afibrinogenemia is characterized by severe bleedings and high thrombotic risk. Due to its rarity, there are no evidence-based strategies for the management of these patients. This multicentric experience aims to describe the phenotype of a cohort of afibrinogenemic patients.

Materials and Methods. Patients diagnosed with congenital afibrinogenemia as per ISTH communication (Casini A., 2018) between 1970 and 2025 at different hemophilia centers affiliated with the Italian Association of Hemophilia Centers (AICE) were included. Bleedings were classified as per ISTH classification (Schulman S., 2005; Kaatz S., 2015) in minor, clinically relevant non major (CRNM) and major; surgeries were classified in major and minor based on ESA consensus (Martin D., 2020).

Results. Patients' characteristics are summarized in Table 1. Ten patients were included, 6 females and 4 males. Median follow-up is 19 years (0.1-55). Five patients presented with a bleeding phenotype and five with a bleeding and thrombotic phenotype. ISTH-BAT score at diagnosis was suggestive of a bleeding disorder in 8 patients, normal in 1 and not available in 1. During follow-up, ISTH-BAT score increased in 5/8 patients. All patients experienced at least one CRNM bleeding in their life, and half of them a major hemorrhage. Two patients experienced at least one venous thrombotic event, 2 an arterial one and 1 both: 3 events occurred during fibrinogen concentrate administration. Five patients are receiving long-term anti-hemorrhagic prophylaxis, 4 with fibrinogen concentrate and 1 with fresh frozen plasma. Median age at prophylaxis start was 15 years (0.1-39) with a median duration of prophylaxis of 17 years (5-22). The reason for prophylaxis start was cerebral hemorrhage in 2 patients, hematemesis and frequent bleeding in 2, arterial thrombosis of left lower limb that needed amputation and life-long dual antiplatelet prophylaxis in 1. During prophylaxis only one patient experienced bleeding diathesis, in particular epistaxis and muscular hematomas. Five patients underwent at least one major surgery: a post-traumatic splenectomy was complicated by massive portal vein thrombosis. No woman underwent pregnancy.

Conclusions. In our cohort of 10 patients, all experienced at least one CRNM bleeding and 5 major hemorrhages occurred. Thrombotic events occurred in half of the cohort. This confirms the dual nature of the disease, with an increased bleeding and thrombotic risk. Long-term prophylaxis was frequently required and initiated at a young age, mainly following life-threatening bleeding episodes or thrombotic complications. These findings highlight the complexity of clinical management in congenital afibrinogenemia and the need for individualized therapeutic strategies.

Table 1. Patients' characteristics

	N (%)*
Sex	
Female	6 (60)
Male	4 (40)
Ethnicity	
Caucasian	5 (50)
North African	3 (30)
Asian	2 (20)
Consanguinity	5 (50)
ISTH classification	
Afibrinogenemia	5 (50)
Afibrinogenemia with thrombotic phenotype	5 (50)
Duration of follow up (years) – Median (range)	19 (0.1-55)
Surgery-unrelated clinically relevant non major and major bleedings	
Muscular	6 (60)
Oral cavity	4 (40)
Umbilical stump	3 (30)
Gastrointestinal	3 (30)
Hemarthrosis	3 (30)
Epistaxis	3 (30)
Cerebral	3 (30)
Menometrorrhagia	2 (20)
Cutaneous	1 (10)
Intra-abdominal	1 (10)
Thrombosis	5 (50)
Cephalic vein thrombosis	1 (10)
Massive portal vein thrombosis, cephalic vein thrombophlebitis	1 (10)
Arterial left lower limb thrombosis	1 (10)
Ictus cerebri	1 (10)
Aortic thrombosis, partial inferior vena cava thrombosis	1 (10)
Long-term bleeding prophylaxis	5 (50)
Fibrinogen concentrate	4 (40)
Fresh frozen plasma	1 (10)
Age at bleeding prophylaxis start (years) – Median (range)	15 (0.1-39)
Duration of bleeding prophylaxis (years) – Median (range)	17 (5-22)
Major surgeries[§]	11 (100)
Complicated°	1 (9.1)

* If not otherwise specified
° Splenectomy post-trauma, complicated by massive portal vein thrombosis
[§] All surgeries were performed with anti-hemorrhagic prophylaxis using either fresh frozen plasma or fibrinogen concentrate

Abstracts printing tool powered by pagepress.org

ACQUIRED FACTOR XIII DEFICIENCY IN A PATIENT POST-CAR-T THERAPY FOR NON HODGKIN LYMPHOMA: A CASE REPORT

A. Strangio, M. Leotta, A. Ierardi, R.C. Santoro

Hemophilia, Hemostasis and Thrombosis Unit, Azienda Ospedaliero Universitaria Renato Dulbecco, Catanzaro, Italy

Introduction. Factor XIII-A (FXIII-A) deficiency is an ultra-rare bleeding disorder characterized by high rates of morbidity and mortality, primarily resulting from intracranial hemorrhage, umbilical cord bleeding, and miscarriage, whereas patients with severe FXIII-B deficiency present with a milder phenotype. individuals with heterozygous FXIII-A deficiency, particularly women, are more likely to experience hemorrhagic complications during hemostatic challenges. Chimeric antigen receptor (CAR)-T cell therapy is an innovative approach to immune cell therapy that works by modifying the T cells of a patient to express the CAR protein on their surface, and thus induce their recognition and destruction of cancer cells. CAR-T therapy has emerged as a promising treatment for lymphoid malignancies, including lymphomas. During treatment, coagulation abnormalities, which are prevalent complications in CAR-T cell therapy, can range in severity from simple abnormalities in coagulation parameters to serious hemorrhage or disseminated intravascular coagulation associated with life-threatening multiorgan dysfunction. However, it is not known whether coagulation alterations may be present or persist several months after treatment, especially with regard to potential acquired deficiencies.

Case Presentation. We report a 29-year-old female patient with a history of lymphoma (LNH) successfully treated with CAR-T therapy, achieving remission. Notably, her medical history revealed no prior bleeding episodes. Recently, she presented with cutaneous hemorrhages and increased menstrual bleeding, raising suspicion for an acquired coagulation disorder. A complete blood count was performed, which returned normal results, along with a comprehensive coagulation screening tests which also yielded normal results. In addition, a comprehensive screening for von Willebrand were conducted and returned normal results. However, the FXIII assay indicated a reduced FXIII level (4%). Screening of both parents showed normal FXIII levels, further complicating the clinical picture. Following fears of a relapse of the disease, in-depth evaluations were carried out which ruled out a recurrence of the lymphoma. Four weeks after the initial evaluation, laboratory tests confirmed reduced levels of FXIII, with persistent increased menstrual bleeding and mild cutaneous hemorrhages.

Discussion. The patient's condition highlights the importance of monitoring coagulation factors in patients undergoing CAR-T therapy, as acquired deficiencies can occur without prior bleeding history. The patient continues to be under close observation, and genetic testing is pending to explore potential underlying causes of her FXIII deficiency.

XIX CONVEGNO TRIENNALE
VERONA
15, 16, 17 e 18 OTTOBRE 2026
Camera di Commercio di Verona
AICE Associazione Italiana Centri Emofilia

XIX Convegno Triennale sugli Aspetti Clinici e Sociali dell'Emofilia

ABSTRACT N. CO-72

3.02 Rare bleeding disorders

HEREDITARY FACTOR X DEFICIENCY UNMASKED BY NECROTIZING HEMORRHAGIC PANCREATITIS: A CASE REPORT

M. Leotta, A. Strangio, A. Ierardi, R.C. Santoro

Hemophilia Treatment Center AOU Dulbecco, Catanzaro, Italy

Background. Factor X (FX) deficiency is one of the rarest coagulation disorders, typically manifesting as an autosomal recessive trait. While clinicians often suspect an acquired deficit in the presence of severe systemic inflammation or major necrotic events, such as necrotizing hemorrhagic pancreatitis (NHP), the possibility of an underlying genetic condition must be considered when the coagulopathy appears disproportionate to the clinical state. NHP creates a high-risk environment for both massive hemorrhage and thrombosis. This case report discusses the diagnostic journey of a patient whose critical illness led to the discovery of a familial coagulation defect, fundamentally changing the therapeutic approach.

Case Report. A 72-year-old male (born 11/11/1953) was transferred from the Gastroenterology department following severe NHP. His condition was complicated by a Resuscitative Cardiopulmonary (RCP) event, resulting in a vast peripancreatic hematoma and splenic vein thrombosis. Laboratory tests showed a PT ratio of 1.24 and an aPTT ratio of 1.53. Specific assays revealed a Factor X activity of 26%. Initially, an acquired deficiency was strongly suspected due to potential factor consumption within the hematoma or proteolytic degradation by pancreatic enzymes. However, to clarify the etiology, a familial screening was conducted. Surprisingly, both of the patient's daughters were found to have a similar Factor X deficiency, shifting the diagnosis from acquired to hereditary Factor X deficiency. To identify the causative mutation, genetic analysis via sequencing of the F10 gene is currently ongoing. Despite the hemorrhagic risk posed by the vast hematoma and the genetic deficit, the patient required anticoagulation for the splenic vein thrombosis. He was started on Fondaparinux. Currently, the patient is stabilized and awaiting a follow-up abdominal CT scan to monitor the hematoma's evolution and the efficacy of the anticoagulation in the context of this newly identified genetic risk factor.

Conclusions. This case demonstrates that while necrotizing hemorrhagic pancreatitis can exacerbate coagulopathy, an unexpectedly low Factor X level (26%) should prompt an investigation into the patient's genetic background. The discovery of the same deficit in both daughters confirms a hereditary rather than a purely acquired etiology. Genetic testing, which is currently underway to identify the specific F10 gene mutation, and family screening are essential in these rare scenarios to provide accurate diagnosis, genetic counseling, and tailored hematological management for both the patient and their relatives. Frequent radiological monitoring remains the gold standard for navigating this complex clinical equilibrium.

XIX CONVEGNO TRIENNALE
VERONA
15, 16, 17 e 18 OTTOBRE 2026
Camera di Commercio di Verona
AICE Associazione Italiana Centri Emofilia

XIX Convegno Triennale sugli Aspetti Clinici e Sociali dell'Emofilia

ABSTRACT N. CO-73

3.02 Rare bleeding disorders

WHEN BLEEDING MIMICS THROMBOSIS: DIAGNOSTIC DELAY AND THROMBOTIC COMPLICATIONS IN ACQUIRED HEMOPHILIA A

R. Tomasello[1], M. Mattana[1], S. Raso[1], F. Schirò[1], P. Polidori[2], M.I. Di Lena[3], F. La Gattuta[4], M. Napolitano[1]

[1]Ematologia e malattie rare, PO Cervello di Palermo, Italy; [2]Farmacia ospedaliera, PO Cervello di Palermo, Italy; [3]Direzione medica, PO Cervello di Palermo, Italy; [4]Radiologia interventistica, PO Villa Sofia di Palermo, Italy

Background. Acquired hemophilia A (AHA) is a rare autoimmune bleeding disorder caused by neutralizing anti-FVIII antibodies. Its recognition may be delayed when acute limb swelling mimics venous thrombosis, exposing patients to potentially harmful anticoagulation. We report a case of AHA associated with systemic lupus erythematosus, initially misinterpreted as upper-limb thrombosis and later complicated by catheter-related femoral thrombosis.

Case Report. A 62-year-old Caucasian man with recently diagnosed systemic lupus erythematosus presented to another emergency department with progressive swelling of the left arm. Suspected deep vein thrombosis led to low-molecular-weight heparin administration before transfer. Initial tests showed severe anemia (Hb 7.8 g/dL), isolated prolonged aPTT (85 s) and normal INR. At our center, CT angiography documented a large left arm/axillary/pectoral hematoma (6 x 5.3 x 11.7 cm) with active arterial contrast extravasation. Coagulation work-up showed FVIII:C 0.2%, normal VWF antigen/activity, a mixing test consistent with an inhibitor and anti-FVIII inhibitor titre of 25.92 BU/mL, confirming AHA. Antiphospholipid antibodies, viral serology and tumor markers were negative. Haemostasis was achieved with activated prothrombin complex concentrate, escalated from 3000 IU to 4000 IU three times daily because of limb progression and then reduced after clinical and hemoglobin stabilization. Emergency embolization of the bleeding site was also performed. Inhibitor eradication included methylprednisolone 1 mg/kg/day, cyclophosphamide and low-dose rituximab (100 mg weekly for four doses). During hospitalization, after femoral vascular access for embolization, the patient developed painful right leg swelling. Ultrasound and CT angiography showed right femoral deep vein thrombosis with femoral pseudoaneurysm (25 x 16 x 45 mm). Since full-dose anticoagulation was contraindicated by life-threatening bleeding, he received submaximal low-molecular-weight heparin, ultrasound-guided thrombin embolization of the pseudoaneurysm and temporary inferior vena cava filter placement. At discharge, FVIII:C was still <10%, while inhibitor titre had decreased to 1.56 BU/mL. After rituximab completion and steroid tapering, FVIII:C increased to 79% with undetectable inhibitor on March 27, 2026. Anticoagulation was switched to dabigatran and the cava filter was removed uneventfully on April 1, 2026.

Conclusions. This case illustrates the diagnostic and therapeutic challenges of acquired hemophilia A, where delayed recognition may expose patients to inappropriate anticoagulation while subsequent invasive procedures may increase thrombotic risk. Early diagnosis and multidisciplinary management remain crucial to successfully navigate the bleeding–thrombosis balance

Abstracts printing tool powered by pagepress.org

XIX CONVEGNO TRIENNALE
VERONA
15, 16, 17 e 18 OTTOBRE 2026
Camera di Commercio di Verona
AICE Associazione Italiana Centri Emofilia

XIX Convegno Triennale sugli Aspetti Clinici e Sociali dell'Emofilia ABSTRACT N. CO-74

3.03 Women and Bleeding Disorders

WHAT WOMEN ARE NOT ASKED A MODEL OF CARE FOR WOMEN AND GIRLS WITH BLEEDING DISORDERS

S. Pancetti, A.C. Ferrini, E. Magnani, P. Pedrazzi, C. Biasoli

Osp. M.Bufalini, Cesena, Italy

Background and Aims. In modern Western history, menstrual health was kept outside public discussion and managed through discretion and concealment. Although public discussion has widened, menstrual-product advertising has often portrayed menstruation as a matter of hygiene, freshness, confidence and control, with limited attention to heavy bleeding, pain, or functional impairment. For women with inherited bleeding disorders, this framing may make pathological bleeding harder to name and recognize. Heavy menstrual bleeding (HMB) and other symptoms are often dismissed as "normal", "natural" or "part of being a woman". Women with haemophilia or symptomatic carrier status, von Willebrand disease and rare coagulation factor deficiencies may remain unheard, underdiagnosed, and inadequately supported. We aimed to describe the rationale and design of "Spazio Rosa", a dedicated multidisciplinary pathway for women followed at the Bleeding and Thrombotic Disorders Clinic, Bufalini Hospital.

Materials and Methods. During routine outpatient consultations, we examined clinical and psychosocial concerns reported by women with inherited bleeding disorders. This service-development analysis focused on menstrual bleeding, medical history, daily-life limitations, reproductive concerns, and perceived gaps in care.

Results. Three needs were identified. First, the initial clinical task was to break the menstrual silence: patients needed a setting in which HMP, pain, leakage anxiety, and embarrassment could be named before they could be assessed. HMB was often normalized, minimized, or compared with the experience of "normal" women, although it may be the first clinical clue to an underlying inherited bleeding disorder. This could weaken symptom legitimacy, delay referral and diagnostic assessment. Second, the burden extended beyond blood loss, involving fatigue, anaemia, pain, restrictions in daily life, and difficulties with sexuality and reproductive planning. Third, patients often described fragmented care and feeling unheard, with limited integration among specialists.

Conclusions. HMB in women with inherited bleeding disorders should not be reduced to ordinary menstrual variation; it is often a symptom of an unmet care. The central gap is not blood loss alone, but the persistent failure to elicit, validate, and address women's bleeding-related concerns. Embarrassment, normalization of suffering and fragmented care may leave women without timely diagnosis or adequate support. "Spazio Rosa" was conceived to address these concerns through structured assessment, individualized management and integrated haemostatic, obstetric-gynaecological and psychological care.Future evaluation should assess patient-reported outcomes, unplanned healthcare use and school/work absence.

Abstracts printing tool powered by pagepress.org

XIX CONVEGNO TRIENNALE
VERONA
15, 16, 17 e 18 OTTOBRE 2026
Camera di Commercio di Verona
AICE Associazione Italiana Centri Emofilia

XIX Convegno Triennale sugli Aspetti Clinici e Sociali dell'Emofilia

ABSTRACT N. CO-75

3.03 Women and Bleeding Disorders

ASSAY DISCREPANCY IN HEMOPHILIA A CARRIERS: CLINICAL AND GENETIC INSIGHTS

M. Leotta, A. Strangio, A. Ierardi, R.C. Santoro

Hemophilia Treatment Center AOU Dulbecco, Catanzaro, Italy

Background. Hemophilia A (HA) is an X-linked coagulopathy caused by F8 gene mutations. While research often focuses on males, female carriers frequently experience hemorrhagic diathesis due to skewed X-chromosome inactivation (lyonization). A critical diagnostic challenge is "assay discrepancy," where Factor VIII activity (FVIII:C) yields conflicting results between the One-Stage Clotting Assay (OSA) and the Chromogenic Substrate Assay (CSA). This study evaluates the incidence of these variations and their impact on clinical phenotyping in female carriers.

Methods. A cross-sectional analysis was conducted on 16 confirmed F8 mutation carriers. FVIII:C was quantified via: OSA: Based on the activated partial thromboplastin time (aPTT). CSA: Assessing the kinetics of Factor Xa (FXa) generation. Inter-assay discrepancy was defined as a CSA/OSA ratio < 0.6 or > 1.6. Genotype-phenotype correlation was performed to identify mutations associated with divergent biochemical profiles.

Results. Data indicates that 50% of carriers exhibit a significant discrepancy, which was exclusively unidirectional (OSA > CSA). This systematic overestimation by the OSA may mask underlying functional deficiencies, leading to the misclassification of carriers as "hemostatically normal." In patients with "discrepancy-prone" mutations, traditional clotting assays failed to reflect clinical bleeding symptoms (ISTH-BAT scores), whereas the CSA superiorly represented the in vivo stability of the tenase complex. Specific molecular drivers identified include: Intron 10 Inversion (INV 10 and missense variants (Exons 4 and 7) consistently fall into the critical discrepancy zone (< 0.6). With ratios as low as 0.4, these mutations cause the OSA to significantly inflate FVIII levels, as seen in Patient 8 (60% OSA vs. 24% CSA). For these specific genotypes, the 0.6 threshold confirms that the OSA is unreliable and risks masking a patient's true bleeding vulnerability. Conversely, the two methods begin to converge (> 0.6) primarily in INV 22 cases (specifically Patients 11 and 12), where ratios reach 0.8–0.9. In this range, the discrepancy narrows enough that the OSA and CSA can be considered clinically consistent. Ultimately, your data identifies the 0.6 ratio as the decisive "red line": any mutation pushing the ratio below this mark, like INV 10, mandates the use of the Chromogenic Assay to ensure diagnostic safety.

Conclusions. Dependence on the One-Stage Assay (OSA) alone offers an incomplete assessment of the hemostatic profile in carriers. The observed OSA/CSA divergence represents a distinct biological phenomenon rooted in altered protein kinetics. To enhance clinical safety, specifically regarding perioperative management, the implementation of a dual-assay diagnostic strategy is essential. Such an approach ensures that therapeutic interventions are informed by a precise measurement of true physiological coagulant capacity.

Patients	Genetic_Mutation	Chromogenic Assay (CSA)	One-Stage Assay (OSA)	Ratio (CSA/OSA)
1	Exon 7 C818 A>G	11	17.7	0.6
2	INV 10 nt-18G>A	32	67	**0.4**
3	-	31.7	48	0.6
4	-	43	67	0.6
5	Exon 4 c538 C>T	14	22	0.6
6	INV 10 nt-18G>A	16	32	**0.5**
7	C6163 C>T	25	47	**0.5**
8	C1290 T>G	24	60	**0.4**
9	INV 10 nt-18G>A	33	56	**0.5**
10	INV 22	59	91	0.6
11	INV 22	18	20	0.9
12	INV 22	15	18	0.8
13	-	20	44	**0.4**
14	-	22	44	**0.5**
15	INV 22	35	55	0.6
16	INV 10 nt-18G>A	38	69	**0.5**

Abstracts printing tool powered by pagepress.org

XIX CONVEGNO TRIENNALE
VERONA
15, 16, 17 e 18 OTTOBRE 2026
Camera di Commercio di Verona
AICE Associazione Italiana Centri Emofilia

XIX Convegno Triennale sugli Aspetti Clinici e Sociali dell'Emofilia ABSTRACT N. CO-76

3.03 Women and Bleeding Disorders

MILD HEMOPHILIA A CARRIER WITH CONCOMITANT STORAGE POOL DISEASE: DIAGNOSTIC CHALLENGES IN A SYMPTOMATIC FEMALE PATIENT

A. Strangio, M. Leotta. A. Ierardi, R.C. Santoro

Hemophilia center, AOU Renato Dulbecco, Catanzaro, Italy

Background. Women who are carriers of hemophilia A may present with significant bleeding symptoms even in the presence of mildly reduced factor VIII (FVIII) levels. In these cases, additional inherited bleeding disorders should be considered, particularly when the hemorrhagic phenotype appears disproportionate to coagulation factor levels.

Case Report. A 71-year-old woman (born in 1954), obligate carrier of mild hemophilia A was evaluated for a lifelong bleeding tendency. Baseline FVIII activity was 44% by one-stage assay and 36% by chromogenic assay. Family history was significant for mild hemophilia A affecting her father, son and nephew. The patient showed a clinically relevant hemorrhagic phenotype with an ISTH-BAT score of 13, including epistaxis, bleeding from minor wounds, severe menorrhagia, excessive bleeding after dental extractions, and post-tonsillectomy hemorrhage. She also experienced major bleeding complications after cesarean section, with development of a large surgical-site hematoma associated with severe anemia requiring blood transfusions. Although FVIII levels were compatible with mild hemophilia, the severity of bleeding manifestations appeared disproportionate to the degree of factor deficiency. Platelet function analyzer (PFA) testing showed prolonged closure times with ADP and epinephrine cartridges (132 and 185 seconds, respectively), prompting further investigation with platelet lumiaggregometry. Extended platelet studies demonstrated an associated storage pool disease, consistent with a combined inherited hemostatic disorder. A desmopressin (DDAVP) challenge test (0.3 µg/kg) showed an adequate laboratory response. In 2012, the patient successfully underwent adnexectomy after prophylactic desmopressin (Emosint®), without hemorrhagic complications. In 2023, the patient underwent appendectomy at another hospital where perioperative management was not coordinated with the specialized hemophilia center and recommended prophylactic measures were not implemented. The postoperative course was complicated by a massive 24-cm subhepatic hematoma with slow radiological resolution, further confirming the patient's high hemorrhagic risk. The patient was subsequently treated with fresh frozen plasma (FFP).

Conclusions. This case highlights the diagnostic complexity of symptomatic hemophilia A carriers and the importance of investigating associated platelet function disorders when the bleeding phenotype is not fully explained by FVIII levels alone. The coexistence of mild hemophilia A and storage pool disease may markedly increase hemorrhagic risk and influence perioperative management. The case also underlines the crucial importance of communication with specialized hemophilia centers to ensure appropriate perioperative prophylaxis and prevent severe bleeding complications.

Abstracts printing tool powered by pagepress.org

XIX CONVEGNO TRIENNALE
VERONA
15, 16, 17 e 18 OTTOBRE 2026
Camera di Commercio di Verona
AICE Associazione Italiana Centri Emofilia

XIX Convegno Triennale sugli Aspetti Clinici e Sociali dell'Emofilia ABSTRACT N. CO-77

3.03 Women and Bleeding Disorders

PERINATAL MANAGEMENT IN WOMAN WITH MILD HEMOPHILIA B: A TWIN PREGNANCY CASE

T. Martini[1], B. Borsellino[1|2], B. Pollio[1]

[1]Haemophilia Centre, Immune-Haematology and Transfusion Medicine, University Hospital "Città della Salute e della Scienza", Torino, Italy; [2]Department of Biomedicine and Prevention, PhD in Immunology, Molecular Medicine and Applied Biotechnology, University of Rome Tor Vergata, Roma, Italy

Background. Women affected by haemophilia, and haemophilia carriers, may face bleeding challenges during pregnancy and delivery, particularly for haemophilia B (HB) given that factor IX levels do not increase in pregnancy. Evidence on the use of extended half-life (EHL) factor IX concentrates in this setting remains very limited.

Case Report. This case describes the perinatal management of a 29-year-old woman with mild haemophilia B (c.707G>A p.Gly236Asp factor IX gene variant; baseline factor IX 37%; International Society of Thrombosis and Haemostasis Bleeding Assessment Tool: 0) carrying monochorionic biamniotic twin male pregnancy. Family history included severe HB in maternal uncle, cousins and great-uncle; maternal grandmother and great-aunt were HB carriers. Pregnancy course was regular. Maternal factor IX levels remained stable: 15 weeks GA (gestational age) 41%, 32 weeks GA 49%. Genetic counselling offered; invasive prenatal diagnosis declined. Elective caesarean section performed at 35 weeks GA for obstetric indication. Preoperative Eftrenonacog Alfa (Alprolix®) 3000 IU (33 IU/kg) infused 30 minutes prior, achieving post-infusion factor IX 55%; tranexamic acid 10 mg/kg IV 1h pre-procedure then every 8 hours; strict no-forceps/vacuum policy. Estimated blood loss: 500 ml. Atraumatic cord blood sampling showed neonatal factor IX levels 37%. Postpartum course was unremarkable: normal lochia and wound healing, maternal factor IX 43% at 24 hours, LMWH (Low Molecular Weight Heparin) 4000 IU/day thromboprophylaxis was started at day 1 to day 8; the patient was discharged at day 4 without bleeding. No primary/secondary postpartum haemorrhage occurred; no additional factor IX infusions were required: a single EHL factor IX infusion provided effective haemostatic coverage for caesarean delivery with minimal blood loss and excellent peripartum safety. A multidisciplinary team (haematologist, obstetrician, anaesthesiologist, neonatologist, coagulation laboratory physician) defined antenatal strategy minimizing maternal bleeding risk and neonatal trauma through coordinated replacement therapy timing, antifibrinolytics, obstetric planning and postpartum surveillance.

Conclusions. Published experience on EHL factor IX use in pregnant HB women remains scarce, particularly twin gestations where maternal-foetal management complexity increases. Our case outcome supports individualized Eftrenonacog Alfa prophylaxis as effective option for delivery management in mild HB women, making feasible a tailored peripartum care that balances maternal haemostasis, neonatal assessment and thromboprophylaxis needs in high-risk coagulation disorders.

REAL-WORLD MANAGEMENT OF ACQUIRED HEMOPHILIA A: FOCUS ON RECOMBINANT PORCINE FVIII AS FIRST-LINE HEMOSTATIC TREATMENT AND LONG-TERM OUTCOMES

M. Leotta, A. Strangio, A. Ierardi, R.C. Santoro

Hemophilia, Hemostasis and Thrombosis Centre, Azienda Ospedaliero Universitaria Renato Dulbecco, Catanzaro, Italy

Background. Acquired Hemophilia A (AHA) is a rare bleeding disorder caused by the development of neutralizing autoantibodies against endogenous coagulation Factor VIII (FVIII). The clinical presentation is often characterized by sudden, severe subcutaneous and mucosal hemorrhages. Management is inherently complex: it requires the immediate restoration of hemostasis and the simultaneous eradication of the inhibitor via immunosuppressive therapy (IST). Given that AHA predominantly affects the elderly population, treatment must be carefully tailored to account for multiple comorbidities and a high baseline thrombotic risk. This study providing a deep dive into the efficacy of rpFVIII, as a first-line agent and analyzing the long-term clinical outcomes and challenges in a real-world setting.

Methods. We conducted a retrospective observational study of 11 consecutive patients (7 males, 4 females) with AHA. The median age at diagnosis was 78 years (24–88), At presentation, the median residual FVIII level was 2.0% while the median inhibitor titer was 13.5 Bethesda Units (BU), though the cohort included a significant outlier at 269 BU. The clinical complexity was high:7 patients (64%) presented a significant baseline thrombotic risk, 5 (45%) had a history of or active malignancy and 3 were receiving oral anticoagulant therapy (2 on Coumadin, 1 on DOAC) for underlying atrial fibrillation or TEV. Additionally, two cases were identified following recent COVID-19 infection, one of which was a fourth reinfection, suggesting a potential immunological trigger.

Results. Active hemostatic treatment was required for 8 patients (73%). rpFVIII was utilized as the primary first-line hemostatic agent at an initial dosage of 100 mg/kg. The median number of administrations required to achieve stable hemostasis was 5.5 (mean: 5.25; range: 1–8). Two patients required a switch to second-line therapy with rFVIIa due to the development of anti-porcine FVIII antibodies (ADA), with titers reaching 30 and 45 BU. One patient was successfully transitioned to Emicizumab prophylaxis (starting 24 days post-diagnosis). The median time to inhibitor eradication was 21 days (mean: 25.9 days; range: 6–56). Relapse occurred in only one patient (the outlier patient) following self-discontinuation of steroid therapy. Post-eradication, two deaths occurred due to unrelated causes (urological sepsis and stroke), and two patients were lost to follow-up.

Conclusions. rpFVIII proved to be an effective first-line hemostatic agent, particularly in elderly patients with complex comorbidities. However, the development of anti-ADA antibodies remains a critical factor that may necessitate a therapeutic switch. Our data confirm that a standardized IST approach achieves inhibitor eradication in a median of three weeks, though high-titer patients require strict monitoring and adherence to prevent relapses.

XIX CONVEGNO TRIENNALE
VERONA
15, 16, 17 e 18 OTTOBRE 2026
Camera di Commercio di Verona
AICE Associazione Italiana Centri Emofilia

XIX Convegno Triennale sugli Aspetti Clinici e Sociali dell'Emofilia ABSTRACT N. CO-79

3.04 Acquired coagulation disorders

ACQUIRED FACTOR XIII DEFICIENCY: AN UNDERDIAGNOSED CAUSE OF DELAYED BLEEDING AFTER PERICARDIOCENTESIS

M. Luongo[1], J. Di Paolo[1], G. D'Amico[2], P. Massaro[1], M. Di Mascio[1], R. Malizia[1], U. Benedetto[2], S. Verna[1]

[1]Immunohematology Service, Asl 02 Abruzzo, Chieti, Italy; [2] Department of Cardiac Surgery, Asl 02 Abruzzo, Chieti, Italy

Background. Acquired factor XIII (FXIII) deficiency is a rare and underdiagnosed cause of bleeding, characterized by impaired fibrin clot stabilization despite normal results on routine coagulation tests (PT, aPTT, INR). Bleeding is typically delayed and may be difficult to interpret. Pathogenic mechanisms include peri-procedural or post-traumatic consumption, reduced synthesis, and the presence of autoantibodies, particularly in autoimmune diseases such as systemic lupus erythematosus (SLE).

Case Report. We report the case of a patient with SLE, not receiving active treatment, who underwent pericardiocentesis for cardiac tamponade secondary to pericardial effusion. The clinical course was complicated by recurrent hemopericardium despite normal coagulation parameters. Early recurrence of cardiac tamponade required re-intervention, followed by a further episode four days later requiring a third procedure. Given the normal PT and aPTT values and the suspicion of a functional impairment in the final phase of coagulation, FXIII activity was assessed, along with a mixing study and serial monitoring. FXIII activity measured on postoperative day 8 was reduced (24%). The mixing study showed partial correction (55%), suggesting the absence of a clinically significant inhibitor. Serial measurements demonstrated spontaneous recovery of FXIII levels, supporting a peri-procedural consumption mechanism. However, the incomplete correction observed in the mixing study, together with the concomitant administration of high-dose corticosteroids for acute respiratory failure, does not fully exclude a transient immune-mediated component.

Conclusions. FXIII deficiency should be suspected in unexplained, delayed, or recurrent postoperative bleeding with normal routine coagulation tests, particularly in patients with autoimmune diseases. In the absence of clinical suspicion, this condition may remain undiagnosed. In surgical settings, FXIII levels typically decline between postoperative days 4 and 7 and remain reduced longer than other coagulation factors. Although no universally accepted threshold exists, levels below 30–50% are generally considered clinically relevant. Management should be guided by clinical presentation and FXIII activity. In this case, serial monitoring supported a conservative approach, avoiding unnecessary replacement therapy, although earlier recognition might have reduced the need for repeated interventions. The incorporation of FXIII assessment into perioperative protocols may improve management and reduce unnecessary invasive procedures.

Abstracts printing tool powered by pagepress.org

XIX CONVEGNO TRIENNALE
VERONA
15, 16, 17 e 18 OTTOBRE 2026
Camera di Commercio di Verona
AICE Associazione Italiana Centri Emofilia

XIX Convegno Triennale sugli Aspetti Clinici e Sociali dell'Emofilia ABSTRACT N. CO-80

3.04 Acquired coagulation disorders

EMICIZUMAB PLASMA CONCENTRATIONS AND CLINICAL OUTCOMES IN ACQUIRED HEMOPHILIA A: A REAL-WORLD SINGLE-CENTER EXPERIENCE

C. Simion[1|2], E. Zanon[1|2], C. Bulato[1], B. Stocco[1|2], F. Righetto[1], F. Sartorello[1], P. Simioni[1|2]

[1]First Chair of Internal Medicine and Thrombotic and Haemorrhagic Diseases Unit, Department of Medicine, Padova University Hospital, Italy; [2]Hemophilia Center, Padova University Hospital, Italy

Background and Aims. Acquired hemophilia A (AHA) is a rare autoimmune bleeding disorder associated with significant bleeding morbidity. The AGEHA study established a standardized emicizumab dosing regimen for AHA, but data on plasma drug concentrations achieved in routine practice and their clinical significance remain limited. We aimed to describe serial emicizumab plasma concentrations and clinical outcomes in patients with AHA receiving emicizumab.

Materials and Methods. We retrospectively analyzed all patients with AHA who received emicizumab at the Padua Hemophilia Centre between April 2024 and February 2026. Clinical characteristics, FVIII activity, inhibitor titers, immunosuppressive treatment, emicizumab dosing regimens and plasma concentrations, and clinical outcomes were collected. Emicizumab concentrations were assessed during the first month after treatment initiation.

Results. Six patients with AHA (4 males, median age 76.5 years [range 36–83]) received emicizumab during the study period. Baseline characteristics, emicizumab exposure and clinical outcomes are summarized in Table 1. Median FVIII activity and inhibitor titer at diagnosis were 5.0% and 6.9 BU/mL, respectively. Two patients received the AGEHA loading regimen, whereas four received individualized dosing schedules. Plasma concentrations increased during the first month and showed marked interindividual variability, ranging from 11.0 to 57.9 µg/mL. Complete remission was achieved in five patients, while one patient remained on corticosteroid therapy at last follow-up. One patient experienced a relapse after achieving initial remission. No spontaneous breakthrough bleeding was observed. A single patient experienced a suspected trauma-related bleeding episode approximately one month after emicizumab initiation despite a plasma concentration of 40.4 µg/mL. Because recurrent AHA could not be excluded, bypassing-agent treatment was administered. The patient subsequently developed a distal deep vein thrombosis in the setting of concomitant immobilization. No additional thrombotic events were recorded. No apparent relationship between plasma emicizumab concentrations and clinical outcomes was observed.

Conclusions. Emicizumab was associated with favorable clinical outcomes in this real-world cohort of patients with AHA, with no spontaneous breakthrough bleeding observed. Despite the use of both standard and individualized dosing regimens, plasma emicizumab concentrations showed substantial interindividual variability. Larger studies are needed to clarify the clinical significance of emicizumab exposure and the potential role of therapeutic drug monitoring in AHA.

Patient	Sex	Age (years)	AHA-associated condition	FVIII at diagnosis (%)	Inhibitor at diagnosis (BU/mL)	AGEHA loading regimen	Peak emicizumab concentration (µg/mL)	Breakthrough bleeding	Thrombotic event	Outcome
1	M	70	Idiopathic	6.7	3.4	No	48.2	No	No	Complete remission
2	F	78	Autoimmune hemolytic anemia	3.3	8.6	No	11.0	No	No	Complete remission; relapse
3	M	80	Psoriatic arthritis	8.1	4.0	No	40.4	Suspected trauma-related bleeding	Distal DVT*	Complete remission
4	M	83	Idiopathic	11.0	11.0	No	57.9	No	No	Complete remission
5	M	75	Bullous pemphigoid	1.5	5.1	Yes	44.6	No	No	Complete remission
6	F	36	Postpartum	1.0	15.0	Yes	41.8	No	No	Ongoing corticosteroid therapy

AHA: acquired hemophilia A; DVT: deep vein thrombosis; FVIII: factor VIII.
* Developed after administration of bypassing agents for a suspected recurrence and in the setting of concomitant immobilization.

Table 1. Baseline characteristics, emicizumab exposure and clinical outcomes

Abstracts printing tool powered by pagepress.org

XIX CONVEGNO TRIENNALE
VERONA
15, 16, 17 e 18 OTTOBRE 2026
Camera di Commercio di Verona
AICE Associazione Italiana Centri Emofilia

XIX Convegno Triennale sugli Aspetti Clinici e Sociali dell'Emofilia

ABSTRACT N. CO-81

3.04 Acquired coagulation disorders

DIGITAL NETWORKING FOR ACQUIRED HEMOPHILIA A: A REGION-WIDE CARE PATHWAY FROM DIAGNOSIS TO FOLLOW-UP

M. Mattana[1], M.F. Mansueto[2], S. Raso[1], S. Siragusa[2|3], R. Tomasello[1], M. Napolitano[1|3]

[1]A.O.O.R. Villa Sofia Cervello P.O. Cervello-UOC di Ematologia per le Malattie Rare del Sangue e degli Organi Ematopoietici, Palermo, Italy; [2]UOC Ematologia Policlinico P.Giaccone Palermo, Italy; [3]Dipartimento Promozione della Salute, Materno-Infantile, di Medicina Interna e Specialistica di Eccellenza(PROMISE), Università degli studi di Palermo, Italy

Background and Aims. Acquired Hemophilia A (AHA) is a rare, potentially life-threatening bleeding disorder caused by autoantibodies against factor VIII. It mainly affects older adults and is often associated with delayed diagnosis and fragmented care, particularly outside expert centers. The aim of this project was to develop a region-wide digital care pathway connecting peripheral services with the Regional Reference Hemophilia Center of the Policlinico Universitario Paolo Giaccone in Palermo, to accelerate diagnosis, support treatment decisions, and improve follow-up of patients with AHA.

Materials and Methods. A secure digital health platform was developed to link emergency departments, hematology units, laboratories, community pharmacies, and general practitioners with the reference center. The platform supports rapid teleconsultations for suspected AHA, centralized interpretation of coagulation tests, including FVIII activity and inhibitor evaluation, and shared decision-making on haemostatic and immunosuppressive treatment. During follow-up, clinicians can update symptoms, bleeding events, therapies, and laboratory results in real time, allowing specialists to remotely adjust treatment and monitor associated conditions. Access is role-based and data protection measures comply with privacy requirements.

Results. Development began on 6 December 2023 and the platform became fully operational across the region in February 2025. Four physicians from four community hospitals were onboarded, including two from emergency departments and two from hematology units. During the first six months, twelve expert consultations were requested for suspected AHA. Two confirmed AHA patients were managed end-to-end through the shared pathway, one from the emergency setting and one from a hematology unit. After discharge, general practitioners entered regular clinical and laboratory updates, reviewed by the reference center. In both cases, treatment was tailored remotely and complete remission was achieved. Structured follow-up also enabled timely surveillance and led to the diagnosis of an early-stage cancer in one patient.

Conclusions. A digitally connected care network can bring rare-disease expertise closer to patients, even when specialist knowledge is centralized. In AHA, this model may shorten time to diagnosis, align therapeutic decisions, and ensure safe monitoring after discharge, including surveillance for associated malignancy. This approach could be extended to other rare diseases, improving equity of access, continuity of care, and real-world evidence collection within the Italian National Health System.

Abstracts printing tool powered by pagepress.org

XIX CONVEGNO TRIENNALE
VERONA
15, 16, 17 e 18 OTTOBRE 2026
Camera di Commercio di Verona
AICE Associazione Italiana Centri Emofilia

ACQUIRED SEVERE FACTOR XIII DEFICIENCY AS THE INITIAL PRESENTATION OF PAEDIATRIC ACUTE PROMYELOCYTIC LEUKAEMIA

C. Vernarecci, G. Gazzelli, L. Banov, F. Marotta, F. Giacopelli, B. Tappino, B. Antonioli, A.C. Molinari

IRCCS Istituto Giannina Gaslini, Genova, Italy

Background. Acute Promyelocytic Leukemia (APL), representing 10% of AML cases, is characterized by the t(15;17) translocation. Despite cure rates exceeding 90% with ATRA and ATO, early hemorrhagic death remains a critical challenge, occurring in 10-30% of patients. APL coagulopathy is multifactorial, involving DIC and primary hyperfibrinolysis. Malignant promyelocytes trigger these pathways via tissue factor and annexin A2 expression. Furthermore, ATRA-induced ETosis—the release of extracellular chromatin traps (NETs)—exacerbates the condition by discharging potent proteases like elastase. Crucially, these enzymes degrade Factor XIII (FXIII), a transglutaminase vital for fibrin cross-linking. This acquired FXIII deficiency destabilizes hemostasis, significantly contributing to the severe bleeding diathesis. We present an APL case where severe FXIII deficiency and related bleeding preceded the onset of characteristic APL coagulopathy.

Case Report. A 12-year-old male with no prior history of bleeding disorders presented to the emergency department with a soft, 15 mm scalp hematoma in the right parietal region, triggered by minor hair pulling. He also reported recent fatigue and low-grade fever. Coagulation tests showed a PT ratio of 1.4, a PTT ratio of 1.15, and fibrinogen levels of 151 mg/dL. Given that the severity of the hemorrhage appeared disproportionate to these mild laboratory abnormalities, Factor XIII (FXIII) levels were assessed, revealing a severe deficiency (7%). No other bleeding manifestations were present. FXIII levels improved following administration of fresh frozen plasma and subsequently normalized with purified FXIII concentrate. Over the following days, the patient developed progressive pancytopenia; peripheral blood and bone marrow investigations led to the diagnosis of Acute Promyelocytic Leukemia (APL).

Conclusions. The coagulopathy associated with Acute Promyelocytic Leukemia (APL) is traditionally attributed to disseminated intravascular coagulation (DIC) and primary hyperfibrinolysis. However, acquired Factor XIII (FXIII) deficiency represents a critical, yet often under-recognized, component of this hemostatic failure. Diagnosing acquired FXIII deficiency is challenging because routine screening tests, such as PT and aPTT, remain normal in cases of isolated deficiency. Therefore, quantitative FXIII activity assays should be prioritised in APL patients presenting with severe or unexplained bleeding. Despite the severity of these mechanisms, current international guidelines—including those from ASH, ELN, EHA, and NCCN—are highly rigorous regarding APL management but do not yet include specific recommendations for FXIII monitoring. Our case highlights a unique clinical scenario where severe acquired FXIII deficiency and its subsequent hemorrhagic manifestations preceded the formal diagnosis of APL and the onset of its characteristic coagulopathy by several days. The early detection of this deficiency allowed for the prompt initiation of replacement therapy with FXIII concentrate, effectively preventing further life-threatening bleeding complications. This observation suggests that proteolytic degradation of FXIII can act as a primary and independent driver of hemorrhage in the earliest stages of the disease. In conclusion, integrating FXIII assessment into the initial diagnostic workup of suspected APL may be crucial for early stabilization and improved clinical outcomes.

XIX CONVEGNO TRIENNALE
VERONA
15, 16, 17 e 18 OTTOBRE 2026
Camera di Commercio di Verona
AICE Associazione Italiana Centri Emofilia

XIX Convegno Triennale sugli Aspetti Clinici e Sociali dell'Emofilia

ABSTRACT N. CO-83

3.04 Acquired coagulation disorders

ACQUIRED FACTOR V DEFICIENCY IN A HIGH-THROMBOTIC-RISK PATIENT: DIAGNOSTIC DILEMMA AND SUCCESSFUL MANAGEMENT

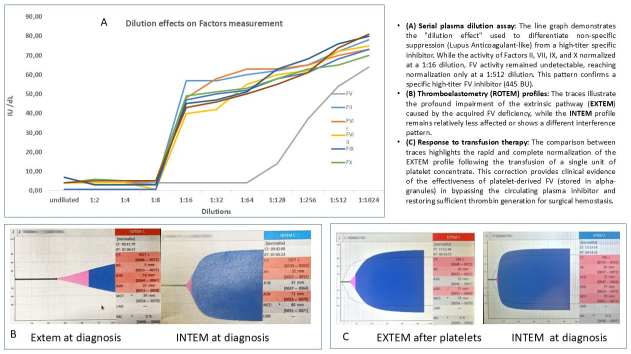
G. Gazzelli[1], L. Banov[1], Y. Azzanelli[1], C. Vernarecci[1], F. Marotta[1], F. Giacopelli[1], E. Cenni[2], V. Agostini[2], A.C. Molinari[1]

[1]IRCCS Istituto Giannina Gaslini, Italy; [2]IRCSS AOM S. Martino, Genova, Italy

Background. Acquired Factor V (FV) inhibitors are rare and typically present with unexplained prolongation of Prothrombin Time (PT) and activated Partial Thromboplastin Time (aPTT) with normal Thrombin Time (TT). Presentation varies from asymptomatic laboratory findings to life-threatening haemorrhage or, paradoxically, thrombosis.

Case Report. An 80-year-old male recently discharged following severe pneumonia presented to the emergency department with pain and a large ecchymosis on his upper arm. His medical history included hypertension, aortic stenosis, a previous myocardial infarction, and peripheral obstructive arterial disease (external iliac artery) treated with clopidogrel. Initial tests showed extreme PT/aPTT prolongation with normal platelets, TT, fibrinogen, and Factor XIII. dRVVT assays revealed a strong lupus anticoagulant (LA) effect (ratio 2.8). To distinguish a "pseudo-deficiency" from a true inhibitor, serial plasma dilutions were performed: all factors normalised at 1:16 except for Factor V, which normalised only at 1:512, confirming a specific high-titre FV inhibitor (initially 445 BU). Point-of-care viscoelastic testing (ROTEM) showed markedly pathological EXTEM. Basing on the patient's high thrombotic risk and a stable clinical phenotype, initial therapy consisted only of prednisone (1 mg/kg/day). However, after 7 days, despite a decrease in the inhibitor titre to 177 BU, the patient developed acute abdominal pain. A CT scan revealed an 8 x 6 x 10 cm rectus abdominis haematoma associated with a haemoglobin drop of 2 g/dL. Haemostatic treatment with recombinant activated factor VII (rFVIIa) at 90 µg/kg was initiated but yielded no clinical benefit or improvement in EXTEM parameters. Tragically, following rFVIIa administration, the patient suffered a cerebellar stroke. Since FV inhibitors interfere with the prothrombinase complex, often making bypassing agents ineffective, and FV stored in platelet alpha-granules is partially activated and relatively resistant to circulating inhibitors, one unit of platelet concentrate was transfused to allow for urgent embolisation of the inferior epigastric artery. This led to the normalisation of EXTEM, and the procedure was completed without further bleeding. Besides, a pulsed immunosuppressive protocol with a low cumulative dose of cyclophosphamide, rituximab and steroids (CyDRi) was started. Unfortunately, two weeks later severe sepsis led to holding the immunosuppression for fourteen days; moreover, the last scheduled dose of cyclophosphamide was not administered. The following period was uneventful, and after 45 days from the start of Cydri, the patient is well with a normal coagulation profile.

Conclusions. In cases of unexplained PT/aPTT prolongation with normal TT, FV inhibitors must be considered. When initial assays suggest a multiple factor deficiency, serial plasma dilutions are essential to unmask the specific inhibitor. Clinicians must balance haemorrhagic and thrombosis risk using bypassing agents in vasculopathic patients. Platelet transfusion represents a critical haemostatic bridge. ROTEM can demonstrate and monitor the immediate haemostatic effect of platelet transfusion, providing real-time guidance for high-risk invasive procedures.



XIX CONVEGNO TRIENNALE
VERONA
15, 16, 17 e 18 OTTOBRE 2026
Camera di Commercio di Verona
AICE Associazione Italiana Centri Emofilia

XIX Convegno Triennale sugli Aspetti Clinici e Sociali dell'Emofilia ABSTRACT N. CO-84

3.04 Acquired coagulation disorders

PARAPROTEIN-DRIVEN ACQUIRED VON WILLEBRAND SYNDROME IN A PATIENT WITH MGUS AND UROTHELIAL CARCINOMA

A. Ierardi, A. Strangio, M. Leotta, R.C. Santoro

Haemostasis Unit, AOU Dulbecco, Catanzaro, Italy

Background. Acquired von Willebrand syndrome (AVWS) is an autoimmune bleeding disorder characterized by the development of autoantibodies against coagulation factors. It has been described in association with autoimmune diseases, the postpartum period, drugs, and malignancies, including solid tumors and hematologic disorders. The aim of this report is to describe a case of von Willebrand syndrome (AVWS) occurring in a patient with monoclonal gammopathy and urothelial carcinoma, and to explore the possible pathogenetic link between coagulation factor inhibitors and underlying proliferative disease.

Case Report. We report a single case of a 71-year-old male patient with known monoclonal gammopathy and urothelial carcinoma. The diagnosis of a coagulation disorder suggestive of acquired hemophilia was made during pre-operative hospitalization for surgical removal of the urothelial neoplasm. Standard coagulation tests were performed, including activated partial thromboplastin time (aPTT), factor VIII activity, and specific assays for coagulation factor inhibitors, together with laboratory assessment of underlying hematologic and oncologic conditions. The patient exhibited prolonged aPTT (ratio 1.42), reduced factor VIII activity (38%), and markedly decreased VWF functional activity (VWF:RCo 16%), consistent with an acquired defect of the VWF–FVIII axis. Although no classical FVIII or VWF-neutralizing antibodies were detected, the coexistence of MGUS suggests a paraprotein-related mechanism of VWF dysfunction. Two non-mutually exclusive hypotheses are proposed: (i) functional inhibition of VWF by monoclonal immunoglobulin through steric hindrance or epitope masking, and/or (ii) accelerated clearance or adsorption of VWF–FVIII complexes mediated by immunoglobulin–VWF interactions. The concomitant urothelial carcinoma may have acted as a trigger for immune dysregulation amplifying paraprotein pathogenicity. Following tumor resection, progressive normalization of coagulation parameters and reduction of the monoclonal component were observed.

Conclusions. This case supports a mechanistically plausible association between MGUS-associated paraproteinemia and AVWS, potentially mediated by functional interference or enhanced clearance of VWF rather than classical neutralizing inhibitors. The temporal resolution of both monoclonal gammopathy burden and hemostatic abnormalities after tumor removal suggests a dynamic, tumor-driven modulation of paraprotein pathogenicity. These findings reinforce the concept that AVWS in plasma cell disorders may extend beyond antibody-mediated inhibition to include structural and kinetic disruption of VWF function.

XIX CONVEGNO TRIENNALE
VERONA
15, 16, 17 e 18 OTTOBRE 2026
Camera di Commercio di Verona
AICE Associazione Italiana Centri Emofilia

XIX Convegno Triennale sugli Aspetti Clinici e Sociali dell'Emofilia
ABSTRACT N. CO-85

3.04 Acquired coagulation disorders

ACQUIRED HEMOPHILIA A IN LIVER CIRRHOSIS: BALANCING HEMOSTASIS BETWEEN HIGH HEMORRHAGIC AND THROMBOTIC RISKS

N. Portesi, G. Martini

ASST Spedali Civili di Brescia, Italy

Background. Acquired hemophilia A (AHA) is a rare, life-threatening bleeding disorder caused by autoantibodies against factor VIII (FVIII). Diagnosing AHA alongside pre-existing bleeding etiologies is challenging, as emerging symptoms are easily misattributed to baseline conditions, delaying treatment. Furthermore, liver cirrhosis induces alterations in pro- and anti-coagulant pathways, resulting in an unstable hemostatic equilibrium that maximizes risks for localized hemorrhage and systemic thrombosis.

Case Report. We report a 75-year-old male with Child-Pugh B7 alcoholic-metabolic cirrhosis complicated by portal hypertension (F2 blue esophageal varices, congestive gastropathy, mild thrombocytopenia) with multiple comorbidities (see table 1). Following seven months of recurrent bleeding episodes requiring 25 packed red blood cell (PRBC) units despite normal baseline coagulation times, he was readmitted with severe anemia (Hb 5.0 g/dL). His aPTT ratio was 1.52 upon admission and progressively lengthened; AHA was suspected when it reached 2.76, accompanied by extensive truncal ecchymoses and a large subscapular hematoma requiring near-daily transfusions (totaling 35 PRBC units). Assays confirmed FVIII deficiency (FVIII:C 4%) and a 5.0 Bethesda Unit inhibitor. Hemostasis was initiated with an activated prothrombin complex concentrate (aPCC, 50 U/kg q12h) and rapidly switched to recombinant porcine FVIII (rpFVIII, 50 U/kg q12h). Strict FVIII:C monitoring enabled safe dose tapering to 25 U/kg/day and successful discontinuation after three weeks; tranexamic acid (1 g q12h) was maintained until discharge. Immunosuppression began with prednisone (1 mg/kg/day); due to early steroid resistance, cyclophosphamide (50 mg/day for 5 weeks) was added, successfully eradicating the inhibitor. Transfusion requirements dropped after starting rpFVIII. Clinical improvement of ascites was observed. Treatment-related complications included severe glycemic flare, oral candidiasis, and intercostal Herpes Zoster reactivation. A temporary fibrinogen drop occurred post-hemostatic therapy (nadir 1.06 g/L), returning to baseline (3.10 g/L) at discharge. Long-term octreotide (10 mg/month) was introduced for intestinal angioectasias.

Conclusions. Pre-existing bleeding phenotype can confound AHA diagnosis, especially in liver cirrhosis where prolonged coagulation times can be overlooked. In this case, the sequential use of bypassing agents and monitored rpFVIII achieved safe hemostasis without inducing thrombotic events. In patients with tight thromboembolic and hemorrhagic thresholds, monitorable agents represent a crucial asset to navigate narrow therapeutic windows. Concomitant improvement in ascites may reflect the emerging role of FVIII in vascular permeability regulation.

Table 1. Baseline comorbidities and overlapping clinical risk profiles of the patient

Thrombosis risk	Child-Pugh B7 Cirrhosis	Thrombosis risk	Coronary Sclerosis
Bleeding risk	F2 Blue Esophageal Varices with red signs	Thrombosis risk	Active Smoking
Bleeding risk	Congestive Gastropathy	Thrombosis risk	Dyslipidemia
Bleeding risk	Chronic Thrombocytopenia	Thrombosis risk + Treatment complication risk	Type 2 Diabetes Mellitus
Bleeding risk	Chronic Multifactorial Anemia (with recorded Iron-Deficiency)	Thrombosis risk + Treatment complication risk	Hypertension
Bleeding risk	History of Gastric Ulcer & Hematemesis	Treatment complication risk	Severe Chronic Obstructive Pulmonary Disease
Bleeding risk	*Intestinal Angioectasia**	-	Polyneuropathy
-	*Severe Aortic Stenosis**	-	Subclinical Hypothyroidism
-	Colonic Diverticulosis	-	Mild Monoclonal Gammopathy of Undetermined Significance
-	Benign Prostatic Hyperplasia		

Key Legend: Thrombosis risk; Bleeding risk; Treatment complication risk

** Initial suspect of Heyde syndrome, but von Willebrand Factor levels above normal*

Abstracts printing tool powered by pagepress.org

XIX CONVEGNO TRIENNALE
VERONA
15, 16, 17 e 18 OTTOBRE 2026
Camera di Commercio di Verona
AICE Associazione Italiana Centri Emofilia

XIX Convegno Triennale sugli Aspetti Clinici e Sociali dell'Emofilia

ABSTRACT N. CO-86

3.04 Acquired coagulation disorders

A RARE CASE OF ACQUIRED HEMOPHILIA A ASSOCIATED WITH MYELOPROLIFERATIVE NEPLASM

A. Ierardi, A. Strangio, M. Leotta, R.C. Santoro

Hemophilia, Hemostasis and Thrombosis Unit, Azienda Ospedaliero Universitaria Renato Dulbecco, Catanzaro, Italy

Introduction. Acquired hemophilia is a rare bleeding disorder characterized by the development of inhibitors against factor VIII, with idiopathic cases accounting for approximately half of all occurrences. The association between acquired hemophilia and chronic myelomonocytic leukemia (CMML) is less common. CMML is an aggressive clonal stem cell disorder categorized among myelodysplastic/ myeloproliferative overlap neoplasms with distinct molecular and clinical profiles and is often associated with various hematological abnormalities.

Case Report. We present the case of an 85-year-old female patient with a complex medical history, including chronic respiratory failure, hypertension, and cerebral cavernomas, accompanied by epilepsy and essential tremor. The patient was admitted for anemia and widespread hematomas, during which she was diagnosed with acquired hemophilia. A computed tomography (CT) scan of the brain revealed an ischemic focus in the pericapsular area. The day prior to the diagnosis, the patient experienced a cardiac arrest that required defibrillation.At presentation, factor VIII levels were at 3.8%, and the inhibitor level was 2.4 Bethesda Units (BU). Treatment included porcine recombinant factor VIII at a dosage of 100 mg/kg for a total of 10 administrations, along with immunosuppressive therapy using steroids (prednisone 1 mg/kg/day). This treatment led to a rapid resolution of both the hematomas and the inhibitor, with the latter disappearing after 30 days of immunosuppressive therapy. Recombinant factor VIIa (rFVIIa), activated prothrombin complex concentrate (aPCC), or recombinant porcine factor VIII (rpFVIII) are generally used for managing bleeding in AHA patients. In this case, we opted for rpFVIII due to the patient's high thrombotic risk.

Discussion. The mechanism behind secondary acquired hemophilia A (AHA) due to the presence of chronic myelomonocytic leukemia (CMML) or myelodysplastic syndromes (MDS) remains unclear. In cases of hematological malignancies complicated by AHA, lymphoid malignancies—including lymphoma, chronic lymphocytic leukemia, and macroglobulinemia—are more commonly observed than myeloid malignancies. However, it is still possible for myeloid malignancies to infrequently complicate with AHA. This could be due to elevated levels of inflammatory cytokines such as interleukin-6 (IL-6) or tumor necrosis factor-alpha, which may activate autoimmune processes. Nevertheless, the precise mechanism responsible for this phenomenon is not well understood.

Abstracts printing tool powered by pagepress.org

SPONTANEOUS HEMATOMA IN A PATIENT WITH POLYCYTHEMIA VERA: A CASE OF ACQUIRED VON WILLEBRAND DISEASE?

A. Strangio, A. Ierardi, M. Leotta, R.C. Santoro

Hemophilia center, AOU Renato Dulbecco, Catanzaro, Italy

Background. Polycythemia vera (PV) is a chronic myeloproliferative neoplasm associated with both thrombotic and hemorrhagic complications. Bleeding events may occasionally be related to acquired von Willebrand disease (AvWD). We report a case of spontaneous rectus sheath hematoma in a patient with JAK2-positive PV, raising suspicion of concomitant AvWD.

Case Report. A 60-year-old woman affected by JAK2-positive polycythemia vera, receiving treatment with Ruxolitinib and low-dose Aspirin, presented to the Emergency Department on May 1st, 2025, complaining of acute abdominal pain following a coughing episode. Abdominal ultrasound revealed a large rectus sheath hematoma measuring approximately 13 cm. Contrast-enhanced abdominal CT scan demonstrated active bleeding from a branch of the epigastric artery. The patient subsequently underwent right iliac axis angiography with successful embolization of the ipsilateral inferior epigastric artery. Hemostatic investigations performed at our center demonstrated normal factor VIII levels, ristocetin cofactor activity at the lower limit of normality, very reduced collagen-binding activity (4%). However, platelet function analyzer testing (PFA/ADP and PFA/EPI) was within normal range, as was the analysis of high-molecular-weight von Willebrand factor multimers. Notably, collagen-binding activity normalized after five months of follow-up.

Conclusions. This case highlights the diagnostic challenge of spontaneous bleeding in patients with polycythemia vera and underlines the importance of investigating acquired von Willebrand disease in the setting of unusual hemorrhagic complications. Although laboratory findings were not fully consistent with AvWD, the altered von Willebrand factor profile raises questions regarding subclinical hemostatic abnormalities in patients with myeloproliferative neoplasms. In the literature, only one case of AvWD caused by an antibody directed against the glycoprotein Ib-binding domain of von Willebrand factor has been described [1]. Moreover, the hemorrhagic event itself may have been favored by additional contributing factors, including concomitant pharmacological treatment. Early recognition and multidisciplinary evaluation may significantly impact therapeutic management and bleeding risk assessment.

References

1. P J van Genderen et al, Acquired von Willebrand disease caused by an autoantibody selectively inhibiting the binding of von Willebrand factor to collagen, Blood. 1994 Nov 15;84(10):3378-84.

XIX CONVEGNO TRIENNALE
VERONA
15, 16, 17 e 18 OTTOBRE 2026
Camera di Commercio di Verona
AICE Associazione Italiana Centri Emofilia

XIX Convegno Triennale sugli Aspetti Clinici e Sociali dell'Emofilia ABSTRACT N. CO-88

3.04 Acquired coagulation disorders

TRANSIENT IDIOPHATIC ACQUIRED VON WILLEBRAND DISEASE: A RARE CHALLENGING CONDITION WITH A POSSIBLE RAPIDLY AND FAVOURABLE EVOLUTION

G. Murante[1|2|3], S. Bergonzi[1|2|3], M. Capetta[1|2|3], F. Valeri[1|2], C. Dainese[1|2], A. Valpreda[4], R. Pastorino[1|3], F. Bocchi[1|3], B. Bruno[2|3], A. Borchiellini[1|2]

[1]Regional Centre for Hemorrhagic and Thrombotic Diseases, AOU Città della Salute e della Scienza of Turin, Italy; [2]Division of Hematology, AOU Città della Salute e della Scienza, University of Turin, Italy; [3]Dep. of Molecular Biotechnology and Health Sciences, University of Turin, Italy; [4]Central Lab. Baldi and Riberi, AOU Città della Salute e della Scienza of Turin, Italy

Background and Aims. The AvWD is a rare but probably understimated bleeding disorder characterized by laboratory findings and clinical presentations similiar to those of inherithed vWD. However, unlike the inherited disease, AvWS occurs in adults with no personal or family history of bleeding diathesis. Although AvWS is particularly frequent in lymphoproliferative or myeloproliferative disorders, it can also be associated with solid tumors, immunologic and cardiovascular disorders, and other miscellaneous conditions. The aim of this abstarct is to demonstrate the significance of follow-up in cases of AvWS without a recognised underlying cause, given the possibility of spontaneous clinical and laboratory resolution of the haemorrhagic condition.

Case Report. We present a case of a 56 years-old woman that was referred to our centre in 2024 due to multiple episodes of epistaxis and easy bruising. She exhibited negative bleeding histories even in trigger conditions (surgery, childbirth) and no family history of bleeding diathesis. No comorbidities were present at diagnosis and both autoimmune evaluation and cancer screening were negative. One year after diagnosis, a complete clinical and laboratory resolution was observed. As rare disease, the diagnostic process is complex and involves multiple steps, requiring an experienced and specialized laboratory. Despite pathological laboratory results, confirming the acquired nature of this disorder remains a significant diagnostic challenge. The first step routine coagulation tests and vWF screening were performed: factor VIII(FVIII:C) dosage, VWF Antigen(vWF:Ag), VWF activity (VWF:Ac), VWF ristocetin cofactor activity (VWF:RCo) and collagen binding assay (CBA). Afterwards, dilution and subsequent in vivo recovery test with plasma derived von Willebrand factor concentrate were performed. A genetic test was performed. Dilution and in vivo recovery tests strongly suggested an acquired form. Genetic analysis was inconclusive. One year after diagnosis, no more antibodies were found.

Conclusions. The AvWS is a rare bleeding disorder with a diagnostic work-up and optimal treatment highly individualized. The management remains challenging, particularly when discrepancies arise between laboratory findings and the patient's medical history. For this reason, especially in cases without an underlying cause, it is important to perform close follow-up for the possibility of rapid favorable resolution of the condition.

Parameter	2024	2025
FVIII:C	35%	120%
vWF Antigen (vWF Ag)	33%	90%
vWF Ristocetin Cofactor (vWF RCo)	8%	75%
vWF Collagen Binding Activity (vWF CBA)	22%	70%

XIX CONVEGNO TRIENNALE
VERONA
15, 16, 17 e 18 OTTOBRE 2026
Camera di Commercio di Verona
AICE Associazione Italiana Centri Emofilia

XIX Convegno Triennale sugli Aspetti Clinici e Sociali dell'Emofilia

ABSTRACT N. CO-89

3.04 Acquired coagulation disorders

FEMORAL FRACTURE SURGERY IN AN ELDERLY, FRAIL PATIENT WITH ACQUIRED HEMOPHILIA A RECEIVING EMICIZUMAB PROPHYLAXIS: A CASE REPORT

C. Simion[1|2], E. Zanon[1|2], B. Stocco[1|2], F. Sartorello[1], C. Bulato[1], G. Saggiorato[1], P. Simioni[1|2]

[1]First Chair of Internal Medicine and Thrombotic and Haemorrhagic Diseases Unit, Department of Medicine, Padova University Hospital, Italy; [2]Hemophilia Center, Padova University Hospital, Italy

Background. Acquired hemophilia A (AHA) is a rare autoimmune bleeding disorder predominantly affecting elderly and frail patients. Although emicizumab was developed for congenital hemophilia A, its use has progressively expanded to selected patients with AHA. However, evidence supporting perioperative management during major surgery remains scarce. We describe the clinical course and perioperative management of an elderly woman with AHA who underwent urgent femoral fracture surgery while receiving emicizumab prophylaxis.

Case Report. An 80-year-old woman with AHA experienced recurrent spontaneous hematomas and laboratory instability despite treatment with prednisone and cyclophosphamide. FVIII activity fluctuated widely (<1%–66%), while inhibitor levels progressively increased, reaching 37 BU/mL. Due to refractory disease, cumulative immunosuppressive toxicity, and severe clinical frailty (body weight 29 kg), emicizumab prophylaxis was initiated using an individualized reduced regimen consisting of a single 90 mg dose followed by 60 mg every two weeks, without a loading phase. This approach resulted in clinical stabilization. Emicizumab plasma concentrations reached 10.4 µg/mL after 3 weeks and remained stable at 11.0 µg/mL after 5 weeks. In September 2025, the patient sustained a femoral fracture requiring urgent orthopedic surgery. Emicizumab prophylaxis was continued, and perioperative hemostatic management was based on recombinant activated factor VII (rFVIIa, 90 µg/kg per bolus; 3 mg per dose) administered according to a predefined tapering protocol over seven days, for a total cumulative dose of 96 mg. Tranexamic acid (500 mg three times daily) was added on postoperative day 3 because of anemia. Although a postoperative decline in hemoglobin required transfusion support with packed red blood cells, the patient remained hemodynamically stable, with no major bleeding, hematoma formation, or thrombotic complications. At day 10 follow-up, hemoglobin was 11.6 g/dL. A laboratory relapse occurred in January 2026 without clinical bleeding.

Conclusions. This case illustrates that major orthopedic surgery can be successfully performed in selected elderly and frail patients with AHA receiving emicizumab prophylaxis, using individualized dosing strategies and structured rFVIIa-based perioperative management. In the absence of specific recommendations for this clinical scenario, detailed case reporting may help inform clinical decision-making in high-risk patients.

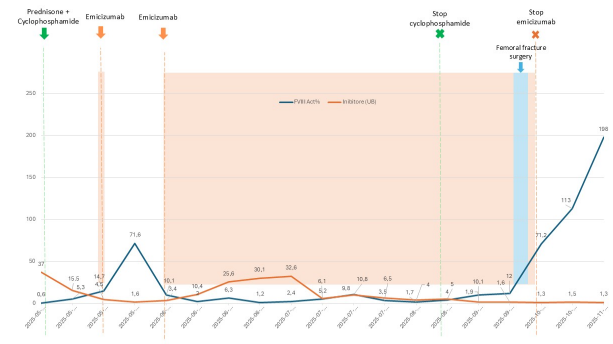


Figure 1. *Clinical and laboratory timeline of an elderly patient with acquired hemophilia A treated with emicizumab undergoing femoral fracture surgery.* FVIII activity and inhibitor levels over time. FVIII and inhibitor measurements were used descriptively to illustrate the disease course.

Abstracts printing tool powered by pagepress.org