

MALATTIE EMORRAGICHE CONGENITE E ACQUISITE

INTRACEREBRAL HEMORRHAGE IN HEMOPHILIA A AND B: A 10-YEAR PROSPECTIVE MULTICENTER STUDY IN ITALY (2012-2022).

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Background and Aims: Intracerebral hemorrhage (ICH) is a severe and life-threatening complication in patients with hemophilia, often resulting in high mortality and long-term neurological impairment. Despite its clinical importance, prospective data on ICH incidence, associated risk factors, and outcomes in hemophilia A and B remain scarce. This study aimed to evaluate the prevalence, clinical features, risk factors, and long-term outcomes of ICH in a cohort of patients with hemophilia A and B over a 10-year period.

Methods: This was a prospective, multicenter study conducted in Italian hemophilia centers between 2012 and 2022. All patients with hemophilia A or B (any severity) who experienced at least one ICH during this period were included. Data collected included demographic and clinical characteristics, type and severity of hemophilia, prophylaxis vs. on-demand treatment, cardiovascular risk factors (e.g., hypertension), comorbid infections (e.g., HCV), neuroimaging findings (CT/MRI), and neurological sequelae. Survival was evaluated using Kaplan-Meier analysis, and group comparisons were conducted with appropriate statistical tests.

Results: Thirty-two patients were enrolled: 26 with hemophilia A and 6 with hemophilia B; 21 had severe and 11 mild hemophilia. Adults represented 75% of the cohort, with

a mean age of 45.46 ± 7.58 years. Patients on regular prophylaxis had significantly fewer ICH events compared to those on on-demand therapy (81.2% vs. 18.8%, $p < 0.05$). Hypertension was present in 14 of 24 adults (58.3%) and was more common in mild hemophilia (9/10). Patients with mild hemophilia were significantly older (median 61.3 vs. 42.4 years, $p = 0.018$) and heavier (median 76 vs. 58 kg, $p = 0.010$) than those with severe forms. No significant differences were found in platelet counts (median 214 vs. 219, $p = 0.938$), hemophilia type (A vs. B), or presence of inhibitors. Traumatic ICH was more frequent in severe hemophilia (40% vs. 9.1%, $p = 0.106$). Kaplan-Meier survival analysis showed survival $>75\%$ in both groups up to 60 months, with a steeper decline in severe cases thereafter, though this was not statistically significant ($p = 0.57$, log-rank test) (Fig.1).

Conclusions: Regular prophylaxis significantly reduces the risk of ICH in patients with hemophilia. Mild hemophilia patients were older and more often hypertensive, suggesting that comorbidities related to aging contribute to ICH risk. Although trauma-related ICH was more frequent in severe hemophilia, survival did not differ significantly by disease severity. Continuous monitoring and individualized prevention strategies are essential to reduce ICH-related morbidity and mortality in this population.

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The Kaplan-Meier curves for haemophilia grade. P-value derived from Long rank-test

