

LABORATORIO E FATTORI PREDITTIVI

ASSESSMENT OF COAGULATION PROFILES IN SEPTIC PATIENTS USING VISCOELASTIC COAGULATION MONITORING AND ROTATIONAL THROMBOELASTOMETRY IN AN INTERNAL MEDICINE SETTING.

G. Gottardi, C. Simion, D. Regazzo, C. Samà, G. P. Arcidiacono, L. Gianesello, E. Campello, P. Simioni.

Department of Medicine - DIMED, University of Padua, Padua.

Background and Aims: Sepsis is a life-threatening organ dysfunction caused by a dysregulated host response to infection. It is frequently associated with coagulopathy, ranging from mild coagulation activation to overt disseminated intravascular coagulation. Standard coagulation tests provide limited information, prompting the use of complementary tools for dynamic assessment. Viscoelastic methods such as rotational thromboelastometry (ROTEM) and the novel Viscoelastic Coagulation Monitoring (VCM) allow for rapid, bedside evaluation of global hemostasis. This study aims to compare VCM and ROTEM in assessing coagulation profiles in septic patients and to evaluate the potential clinical usefulness of VCM in this setting.

Methods: We included adult patients with sepsis, defined by Sepsis-3 Criteria, admitted to the First Chair of Internal Medicine at the University Hospital of Padua. ROTEM and VCM were performed within 48 hours of diagnosis. Patients with active cancer or known inherited thrombophilia were excluded. Based on ROTEM, patients were classified as hypocoagulable (prolonged clotting time [CT] and reduced maximum clot firmness [MCF]), hypercoagulable (increased MCF in EXTEM), or normocoagulable if neither criterion was met. Demographic data, standard laboratory, and conventional coagulation parameters were also collected. Comparisons were made using non-parametric statistical tests. The predictive value of VCM-MCF for hypercoagulability was assessed via receiver operating characteristic (ROC) curve analysis.

Results: Forty-seven patients were enrolled (median age 82 years, IQR 70-88; 62% male). According to ROTEM, 28 patients were normocoagulable and 17 hypercoagulable. Only

two patients (4.4%) showed a hypocoagulable profile and were excluded due to the limited sample size. Hypercoagulable patients showed higher creatinine values (233 $\mu\text{mol/L}$ vs 119 $\mu\text{mol/L}$, $p = 0.005$) and lower hemoglobin levels (93 g/L vs 112.5 g/L, $p = 0.009$). Normocoagulable patients had lower platelet counts (145 vs 241 $\times 10^9/\text{L}$, $p = 0.002$). Notably, only 53% of hypercoagulable patients had a sepsis-induced coagulopathy (SIC) score ≥ 4 , highlighting the limited sensitivity of this score in detecting hypercoagulable states. Clinical and laboratory characteristics of the two groups are summarized in Table 1a. We observed good concordance between VCM and ROTEM in identifying normocoagulable patients (25/28; 89% sensitivity) and moderate concordance in hypercoagulable profiles (9/17; 53% specificity). With a new MCF cut-off of 40.5 mm (Table 1b), VCM-MCF showed good predictive value for hypercoagulability (AUC 0.8, sensitivity 76.5%, specificity 75%).

Conclusions: VCM proved useful in detecting coagulation abnormalities in septic patients and showed good performance in identifying hypercoagulability when compared with ROTEM. The identification of a lower MCF cut-off versus the prior 44 mm upper normal limit set by the manufacturer, improves the test's sensitivity and specificity, allowing for earlier and more accurate detection of hypercoagulable states. This supports the potential role of VCM as a practical and accessible bedside tool for early detection of hypercoagulability in septic patients admitted in internal medicine wards, which may go unnoticed with traditional scores such as SIC score. Due to the small sample size, results are exploratory and warrant further validation.

Email: giovanni.gottardi@studenti.unipd.it

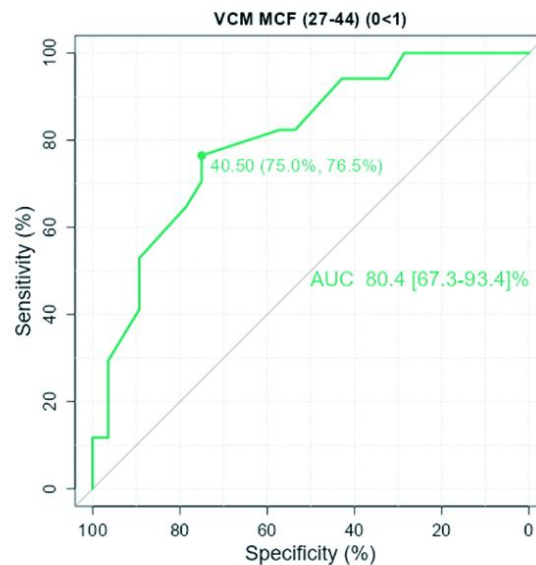
a. Demographic, clinical and laboratory characteristics of the septic population (n=45)

	Normocoagulable	Hypercoagulable	Total	p
Total N (%)	28 (62.2)	17 (37.8)	45	
Age, years	81.5 [71.5-88.0]	84.0 [70.0-87.0]	82.0 [70.0-88.0]	n.s.
Gender - F, n (%)	14 (50.0)	3 (17.6)	17 (37.8)	n.s.
Comorbidities, n (%)				
Hypertension	16 (57.1)	14 (82.4)	30 (66.7)	n.s.
CAD	5 (17.9)	6 (35.3)	11 (24.4)	n.s.
DM II	3 (10.7)	6 (35.3)	9 (20.0)	n.s.
CKD	4 (14.3)	7 (41.2)	11 (24.4)	n.s.
Dyslipidemia	12 (42.9)	11 (64.7)	23 (51.1)	n.s.
Anticoagulation/Antiplatelet therapy				
Heparin prophylaxis	15 (53.6)	11 (64.7)	26 (57.8)	n.s.
Antiplatelet therapy	7 (25.0)	6 (35.3)	13 (28.9)	n.s.
Anticoagulation therapy	7 (25.0)	3 (17.6)	10 (22.2)	n.s.
Source of sepsis, n (%)				
Urinary	12 (42.9)	6 (35.3)	18 (40.0)	n.s.
Pulmonary	7 (25.0)	8 (47.1)	15 (33.3)	n.s.
Abdominal	5 (17.9)	0 (0.0)	5 (11.1)	n.s.
Other	4 (14.3)	3 (17.7)	7 (15.5)	n.s.
SOFA score, median [IQR]	4.0 [3.0-5.0]	5.0 [3.0-6.0]	4.0 [3.0-5.0]	n.s.
SIC ≥4	21 (75.0)	9 (52.9)	30 (66.7)	n.s.
Laboratory findings, median [IQR]				
INR	1.5 [1.3-1.7]	1.5 [1.3-1.6]	1.5 [1.3-1.7]	n.s.
Hb, g/L	112.5 [101.2-137.8]	93.0 [87.0-109.0]	105.0 [91.0-123.0]	0.009
WBC x10 ⁹ /L	11.3 [8.1-17.2]	17.6 [12.3-18.8]	15.2 [9.8-18.6]	0.049
PLTS, x10 ⁹ /L	145 [94-172]	241 [170-317]	154 [119-278]	0.002
CRP, mg/L	111.9 [89.4-244.1]	206.8 [93.3-335.9]	133.7 [92.9-251.1]	n.s.
PCT, ng/mL	8.7 [4.8-37.4]	2.0 [0.8-7.0]	6.3 [1.4-30.5]	0.033
Creatinin, umol/L	119.0 [89.5-170.0]	233.0 [140.0-346.0]	148.0 [114.0-233.0]	0.005
VCM CT, s	393.0 [342.0-491.0]	414.0 [366.0-456.0]	408.0 [342.0-486.0]	n.s.
VCM MCF, mm	37.0 [34.0-40.5]	46.0 [41.0-50.0]	40.0 [36.0-46.0]	0.001
EXTEM CT, s	76.5 [63.2-90.2]	70.0 [67.0-95.0]	73.0 [64.0-94.0]	n.s.
EXTEM MCF, mm	67.0 [61.5-70.0]	76.0 [73.0-80.0]	70.0 [66.0-73.0]	<0.001
INTEM CT, s	178.5 [160.8-200.0]	183.0 [178.0-192.0]	181.0 [168.0-196.0]	n.s.
INTEM MCF, mm	64.5 [57.8-68.2]	74.0 [72.0-78.0]	69.0 [62.0-74.0]	<0.001
FIBTEM MCF, mm	24.5 [21.0-33.2]	41.0 [34.0-42.0]	33.0 [22.0-39.0]	<0.001

Abbreviations: CAD: coronary artery disease; CRP: C-reactive protein; CT: clotting time; Hb: hemoglobin; INR: international normalized ratio; WBC: White blood cells count; MCF maximum clot firmness; N.S.: not significant; PLTS: platelet count; PCT: procalcitonin; SIC: sepsis-induced coagulopathy; SOFA: Sequential Organ Failure Assessment; VCM: viscoelastic coagulation monitoring.

Reference ranges: INR 0.9-1.2; Hb 123-153; WBC 4.00-11.00; PLT 150-450; CRP 0-5; PCT 0-0.5; Creatinin 45-84; VCM CT 312-522; VCM MCF 27-44; EXTEM CT 38-79; EXTEM MCF 50-72; INTEM CT 100-240; INTEM MCF 50-72; FIBTEM MCF 9-25.

b. ROC curve's values for VCM MCF



	AUC	95% CI	Best cut-off	Sensitivity	Specificity	+LR	-LR	Youden index
VCM-MCF, mm	0.804	67.3 - 93.4	40.5	0.765	0.750	3.06	0.31	1.51

Abbreviations: AUC: area under the curve; CI: confidence interval; LR: likelihood ratio.