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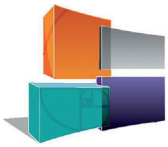

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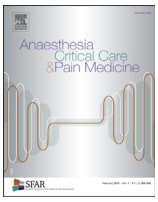

Editorial

Routine use of viscoelastic tests for severe trauma management: The dark side

Routine use of viscoelastic tests for severe trauma management: the dark side.

During the past two decades, the management of severe trauma patients has evolved. The implementation of regional trauma systems and application of damage control strategies improved the survival of trauma patients at risk of major bleeding. As a result, the effect of selected therapeutic interventions among all factors involved in the patient outcome remains uncertain. For instance, in a mature trauma care system, the use of tranexamic acid in the management of severely injured trauma patients failed to demonstrate a reduction of intra-hospital mortality in the total population [1].

In this issue of *Anaesthesia Critical Care and Pain Medicine*, Guth et al. compared two historical cohorts of trauma patients to test the effect of a new protocol including thromboelastometry-based coagulation management on mortality and blood products administration [2]. The first cohort included patients from January 2005 to December 2008 (period 1), and the second cohort included patients from January 2012 to December 2015 (period 2). Between these two periods, new procedures for trauma care were implemented: tranexamic acid administration, damage control resuscitation strategies and haemostatic product administration based on rotational thromboelastometry algorithms. Patients of the two periods were matched according to baseline confounders. The authors reported more use of tranexamic acid, prothrombin complex concentrates and fibrinogen concentrates, and significantly less red blood cells, fresh frozen plasma and platelet consumption in period 2. Survival at day-28 was not different between the two groups. The authors argued that application of a thromboelastometry-based algorithm led to an increased fibrinogen/red blood cells ratio, and was possibly involved in reducing blood product administration. However, the effect of thromboelastometry remains hard to differentiate from the entire bundle of care, and the role of viscoelastic tests in the management of massive bleeding is still debated.

After severe trauma, trauma-induced coagulopathy, a term including acute traumatic coagulopathy and resuscitation coagulopathy, is associated with increased morbidity and mortality. Plasma-based routine coagulation tests, like prothrombin time and activated partial thromboplastin time, may be considered as inappropriate for monitoring coagulopathy [3]. Then, several studies reported the use of viscoelastic tests at hospital admission to detect trauma-induced coagulopathy and predict massive transfusion requirements [4,5]. A great limitation of trauma-induced coagulopathy is the wide range of parameters and threshold values used to define trauma-induced coagulopathy, to predict massive transfusion and guide interventions. Both rotational thromboelastometry and thromboelastography give six parameters to analyse clot initiation, kinetics, strength and stability (lysis). The number of parameters has multiplied because some of these can be measured at different time points with different activators or inhibitors of the coagulation process (Table 1) [6]. Moreover, scores based on clinical and/or simple point-of-care biological parameters achieve high performance for severe haemorrhage prediction [7–10]. Recently, best predictive performance of coagulation tests for massive transfusion was achieved with the thromboelastography lysis parameter (LY30), which is obtained 30 min after maximal amplitude, i.e. 45 min minimum after test initiation[5]. Despite an area under the receiver operating characteristic curve of 0.86 (0.79–0.93), the performance of the LY30 was similar to the TASH score (AUC 0.84 [0.79–0.90]). But more interestingly, the TASH score, based on simple clinical and biological data, is available easily and rapidly, within a few minutes after patient admission.

Underlying mechanisms of trauma-induced coagulopathy remain miscellaneous, complex, and poorly understood. In a recent review, Meledeo et al. compared acute traumatic coagulopathy to "the elephant in a room of blind scientists" [11]. VET give more details to describe different patterns of coagulation abnormalities compared to classical coagulation tests. But those details give little information for etiologic analysis of these coagulation abnormalities. The acute fibrinolysis shutdown may be an example of possible misinterpretation of VET. In the years 1960s and 1970s, some studies identified an inhibition of fibrinolysis after major surgery, especially in case of malignant disease, called fibrinolysis shutdown, and associated to deep venous thrombosis [12]. In 2014, Moore et al. analysed with thromboelastography the percentage of fibrinolysis at 30 min in the early stage of medical care of 180 trauma patients with an Injury Severity Score of 15 or greater admitted in a level 1 trauma centre [5]. They described three different groups of patients based on the fibrinolysis patterns presented. The group with low fibrinolysis activity, defined by a LY30 $< 0.8\%$, represented 64% of the patients. In this group, mortality was higher, compared to the group with a physiologic fibrinolysis pattern, defined by a LY30 from 0.8% to 3%. The authors suggested that the fibrinolysis shutdown previously recognised in postoperative and septic patients was a possible explanation of such differences. In the following years, the concept of fibrinolysis shutdown was

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Table 1
Diagnostic accuracy of coagulation tests for coagulopathy in trauma patients [6].

Study	Parameter + cutoff value	Definition of coagulopathy	Sensitivity	Specificity	PPV	NPV	AUC
Plasmatic coagulation							
Davenport et al. (*Crit Care Med* 2011)	EXTEM CA5 ≤ 35 mm	INR > 1.2	0.70	0.86	0.30	0.97	NR
Woolley et al. (*Injury* 2013)	EXTEM CA5 < 32 mm	EXTEM MCF < 40 mm	0.96	0.58	0.71	0.94	NR
	EXTEM CA10 < 40 mm		1.00	0.70	0.78	1.00	NR
Hagemo et al. (*Crit Care* 2015)	EXTEM CA5 ≤ 37 mm	INR > 1.2	0.66	0.81	0.30	0.95	0.79
	FIBTEM CA5 ≤ 8 mm		0.68	0.79	0.27	0.96	0.80
	Fibrinogen ≤ 1.61 mg/dL		0.73	0.88	0.45	0.96	0.87
	Platelet count ≤ 199×10^9/L		0.62	0.70	0.12	0.97	0.74
Rugeri et al. (*J Thromb Haemost* 2007)	EXTEM CA15 < 32 mm	INR > 1.6 and/or aPTT > 60 s and/or platelet Count < 100 10^9/L and/or fibrinogen < 1 g/L	0.88	1.00	1.00	0.95	0.98
Rizoli et al. (*J Trauma* 2011)	INR (≥1.5)	Clotting factor deficiency (≤50% activity)	0.32	1.00	1.00	0.85	NR
	aPTT (≥45 s)		0.36	1.00	1.00	0.86	NR
	TEG (>2 abnormal parameters)		0.35	0.89	0.40	0.87	NR
Nascimento et al. (*Transfusion* 2012)	INR ≥ 1.3	Vitamin K clotting factor deficiency (≤50% activity)	0.75	0.94	0.62	0.97	NR
	R > 8 min		0.33	0.95	0.92	0.47	NR
Platelet dysfunction							
NR	NR	NR	NR	NR	NR	NR	NR
Fibrinogen concentration							
Meyer et al. (*J Surg Res* 2015)	FF MA < 12.9 mm	Fibrinogen levels < 150 mg/dL	0.60	0.89	0.33	0.96	0.87
	FIBTEM MCF < 10.0 mm		0.80	0.89	0.41	0.98	0.89
Rourke et al. (*J Thromb Haemost* 2012)	EXTEM CA5 < 36 mm	Fibrinogen levels < 150 mg/dL	0.53	0.87	NR	NR	0.80
	FIBTEM CA5 < 9.5 mm		0.78	0.70	NR	NR	0.80
Fibrinolysis							
Levrat et al. (*Br J Anaesth* 2008)	EXTEM CA10 ≤ 10 mm	Euglobin lysis time < 90 min (hyperfibrinolysis)	1.00	NR	NR	NR	1.00
	EXTEM CA15 ≤ 12 mm		1.00	NR	NR	NR	1.00
	EXTEM MCF ≤ 18 mm		1.00	NR	NR	NR	1.00
	EXTEM Li30 ≤ 71%		1.00	NR	NR	NR	0.87

aPTT: activated partial thromboplastin time; AUC: area under the curve; INR: international normaliSed ratio; MA: maximum amplitude; MCF: maximum clot firmness; NR: not reported; NPV: negative predictive value; PPV: positive predictive value; TEG: thromboelastography.

highlighted to explain the 1.4 increase in mortality risk reported in the CRASH-2 trial, when tranexamic acid was given later than 3 hours after injury [13]. The decrease of thromboelastography amplitude did not reflect solely fibrinolysis [14]. It could be due to platelet-mediated clot retraction that pulled away the fibrin fibres connected to the cuvette wall. With the adjunction of abciximab, the authors inhibited platelet function and thromboelastography profile mimicked a low fibrinolysis activity by preventing clot retraction. In 2019, a secondary analysis of the PROPPR trial described the pathophysiology of thromboelastography shutdown in 547 severely injured bleeding patients [15]. They demonstrated that the low TEG LY30 did not mirror a shutdown of fibrinolytic enzymatic activity with a hypercoagulable state, but rather a reduced platelet count and function with moderate fibrinolysis and fibrinogen consumption associated with poor outcome.

Another discrepancy between viscoelastic tests and their therapeutic implication is highlighted in studies assessing administration of early fibrinogen concentrate in trauma patients. To date, despite a strong correlation between hyperfibrinolysis, fibrinogen consumption and mortality, no study showed a benefit in survival associated with the administration of fibrinogen concentrate, even based on a viscoelastic tests-guided procedure [16]. Only one pragmatic randomised clinical trial, by Gonzalez et al., suggested a benefit on mortality of thromboelastography-guided haemostatic resuscitation in 111 patients requiring massive transfusion [17].

The complex physiopathology of post-traumatic coagulopathy hinders the development of viscoelastic tests-based protocols due to a difficult interpretation of numerous and complex results. Although very exciting scientifically, there is little evidence to demonstrate a decrease in mortality of severe trauma patients using viscoelastic tests. These patients need a holistic approach on both diagnostic and therapeutic sides, and fluid therapy, for instance, is often omitted in algorithms focusing on coagulation. Massive transfusion protocols approximating whole blood transfusion are still relevant for the more severe trauma patients. Viscoelastic-targeted therapies should gain in standardisation and validation to become a standard of care.

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