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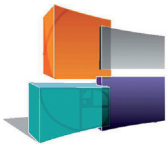

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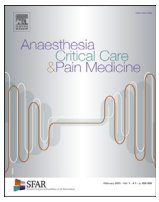

Éditorial

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

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Massive haemorrhage remains the first cause of preventable death after severe trauma [1]. Reducing haemorrhage-induced fatality requires prompt diagnosis of ongoing bleeding, early recognition of trauma-induced coagulopathy (TIC) and close monitoring of haemostatic strategies. In this current issue of Anaesthesia Critical Care and Pain Medicine, Guth et al. [2] report the results of a monocentric before/after study suggesting that the implementation of a bundle of care including damage control resuscitation, thromboelastometry-guided haemostatic therapy and administration of tranexamic acid, could both decrease the use of blood products and need for massive transfusion, and improve survival rates.

Viscoelastic tests (VETs) were developed to assess – online in real time – the mechanical properties (viscosity and elasticity) of whole blood as the haemostatic process goes on and clot is building up [3]. VETs principles rely on the continuous transformation of a complex physico-chemical process (haemostasis and building of the clot) into a graphical and straightforward representation. In a glimpse, the clinician in charge can therefore easily assess the initiation of the coagulation process, its actual speed, clot strength and stability and eventually the clot lysis process. Unlike standard coagulation tests [Quick Time (QT), activated Partial Thromboplastin Time (aPTT) and the fibrinogen test], which are performed on platelet-poor plasma and focus on isolated coagulation factors, VETs are performed on whole blood and include erythrocytes, platelets and leukocytes, reproducing the physiological process of global haemostasis. Three VETs devices are commercially available: thromboelastography (thromboelastogram [TEG^{TM}], Haemonetics, Braintree, MA, USA), thromboelastometry (ROTEM, Tem International GmbH, Munich, Germany), and more recently sonorheometry (Quantra^{TM}, HemoSonics, Charlottesville, VA, USA). Most recent devices (TEG 6S, rotational thromboelastometry [ROTEM^{TM}] σ and Quantra) are fully automatised, do not require any supplemental human action and rely on dedicated cartridges, which allow their use both in central lab and in the clinical arena as point-of-care assays. Due to the simultaneous development of haemostatic resuscitation [4] and VETs [5], two strategies eventually challenge each other: the first is a VET-driven "theragnostic strategy" in which the results of VETs continuously determine transfusion practice, facing the other, ratio-driven, massive transfusion strategy in which the transfusion of blood products is based on predefined ratios.

From a diagnostic perspective, many VETs-derived variables (either TEG- or TEM-derived) accurately predict subsequent red blood cell transfusion [6], massive transfusion [7] and mortality [8]. Hypofibrinogenemia is also accurately detected by VETs. Moreover, VET-derived variables of hypofibrinogenemia are closely correlated with plasma fibrinogen concentration, measured with the gold standard Clauss technique [9]. Hyperfibrinolysis is one of the cornerstones of trauma-induced coagulopathy and, as such, deserves specific emphasis [10]. This is all the more true as VETs outperform conventional coagulation tests in diagnosing hyperfibrinolysis and as the early delivery of tranexamic acid [11] is widely recommended [Grade 1A] [12]. Equipoise persists as to whether the administration of tranexamic acid should be either liberal and empiric, or VET-based and therefore restricted to the bunch of patients who actually demonstrate a VET-defined "fibrinolytic spectrum" of trauma-induced coagulopathy [13]. Platelet dysfunction [impaired aggregation to agonists (arachidonic acid and ADP)] also participates in trauma-induced coagulopathy and its VET-based diagnosis (TEG^{TM} platelet mapping) was recently emphasised [14]. We still do not know whether platelet transfusion cures platelet dysfunction, but it may partially correct hyperfibrinolysis (by providing an additional source of plasminogen activator inhibitor-1 [15]) and was recently shown to reduce mortality in a retrospective cohort of severe traumatic brain injury patients suffering VET-defined platelet dysfunction [16]. New developments in VET devices (custom-made cartridges) nowadays allow the diagnosis of coagulopathy associated with direct-acting oral anticoagulants (DOACs), their class effect (either direct thrombin inhibitors or direct factor Xa inhibitors) and, potentially, the accurate monitoring of their reversal [17]. As DOACs have different mechanisms of action, effects on conventional coagulation assays, and reversal strategies, rapid, VET-based identification of DOACs in whole blood may allow timely reversal of factor Xa and direct thrombin inhibitors in trauma patient on DOAC therapy pre-injury.

From a therapeutic point of view, meta-analysis suggest that, as opposed to conventional strategy, VET-based haemostatic resuscitation of the bleeding patient may be associated with reduced mortality [OR: 0.52; 95%CI (0.28–0.95)] and a reduced incidence of transfusion (red blood cells, fresh frozen plasmas and platelets)

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[18]. However, most of these results were obtained in cardiac surgery under cardiopulmonary bypass with low-quality evidence. In the setting of severe trauma, a recent monocentric prospective randomised controlled trial compared VET-based haemostatic resuscitation and a strategy driven by conventional tests [19]. Trauma patients meeting criteria for activation of the local massive transfusion protocol ($n = 111$) were randomised to be managed either by TEG ($n = 55$), or by conventional coagulation assays (i.e., international normalised ratio, fibrinogen, platelet count, $n = 55$). Primary outcome was 28-day survival. Mortality was lower in the TEG group (19.6%) than in the conventional coagulation assays group (36.4%; $P = 0.049$). The survival gain was mainly due to a reduced incidence of early deaths (within the first 6 hours: 7.1% vs. 21.8%; $P = 0.032$). Survivors in the TEG group also benefited from more ICU-free and ventilator-free days. The more individualised approach in the TEG group also resulted (counter-intuitively) in a reduction of transfused blood products (less units of plasma and platelets in the first 2 hours of resuscitation). The observed survival benefit may therefore result from a timelier administration of blood products in the TEG group. A larger, multicentric (8 European Trauma Centres) randomised controlled trial is under way to confirm or dismiss these preliminary findings. The iTACTIC trial will compare the haemostatic effect of an evidence-based VET-guided versus an optimised conventional coagulation tests-guided transfusion algorithm in haemorrhaging trauma patients (clinical signs of haemorrhagic shock, activation of the local massive haemorrhage protocol and initiation of first blood transfusion) [20]. The primary endpoint is the proportion of patients alive and free of massive transfusion (less than 10 units of red blood cells) at 24 h. Secondary endpoints include organ failure, total hospital and intensive care lengths of stay, health care resources needed, mortality and a quality of life at day 90 (EuroQol EQ-5D).

Taken as a whole, recent advances in the field of VET now represent major value-based breakthroughs: robust physiological rationale, ease of use, rapid online availability, provision of a comprehensive visual profile of clot formation and breakdown, dedication to all components of trauma-induced coagulopathy and to newer DOACs, potential to drive haemostatic resuscitation in a more efficient way than conventional coagulation tests. Ongoing clinical trials will address the last knowledge gaps (optimal algorithms for transfusion and coagulation adjuncts) but European Guidelines recommend their use from now [12].

Disclosure of interest

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Author contributions

All authors attest that they meet the current International Committee of Medical Journal Editors (ICMJE) criteria for Authorship.

Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at https://doi.org/10.1016/j.accpm.2019.07.012.

References

[1] Girard E, Jegousso Q, Boussat B, François P, Ageron FX, Letoublon C, et al. Preventable deaths in a French regional trauma system: A six-year analysis of severe trauma mortality. J Visc Surg 2019;156:10–6. http://dx.doi.org/10.1016/j.jviscsurg.2018.05.002.

[2] Guth C, Vassal O, Friggeri A, Wey PF, Inaba K, Decullier E, et al. Effects of modification of trauma bleeding management: A before and after study. Anaesth Crit Care Pain Med 2019. http://dx.doi.org/10.1016/j.accpm.2019.02.005 [S2352-5568(18)30213-3].

[3] Roullet S, de Maistre E, Ickx B, Blais N, Susen S, Faraoni D, et al. Position of the French Working Gr0up on Perioperative Haemostasis (GIHP) on viscoelastic tests: What role for which indication in bleeding situations? Anaesth Crit Care Pain Med 2018. http://dx.doi.org/10.1016/j.accpm.2017.12.014 [S2352-5568(17)30283-7].

[4] Stensballe J, Ostrowski SR, Johansson PI. Haemostatic resuscitation in trauma. Curr Opin Crit Care 2016;22:591–7. http://dx.doi.org/10.1097/MCC.0000000000000359.

[5] Baksaas-Aasen K, Van Dieren S, Balvers K, Juffermans NP, Næss PA, Rourke C, et al. Data-driven Development of ROTEM and TEG Algorithms for the Management of Trauma Hemorrhage. Ann Surg 2018;1. http://dx.doi.org/10.1097/SLA.0000000000002825.

[6] Roullet S, de Maistre E, Ickx B, Blais N, Susen S, Faraoni D, et al. Position of the French Working Group on Perioperative Haemostasis (GIHP) on viscoelastic tests: What role for which indication in bleeding situations? Anaesth Crit Care Pain Med 2018. http://dx.doi.org/10.1016/j.accpm.2017.12.014.

[7] Holcomb JB, Minei KM, Scerbo ML, Radwan ZA, Wade CE, Kozar RA, et al. Admission rapid thrombelastography can replace conventional coagulation tests in the emergency department: experience with 1974 consecutive trauma patients. Ann Surg 2012;256:476–86. http://dx.doi.org/10.1097/SLA.0b013e3182658180.

[8] Veigas PV, Callum J, Rizoli S, Nascimento B, da Luz LT. A systematic review on the rotational thrombelastometry (ROTEM®) values for the diagnosis of coagulopathy, prediction and guidance of blood transfusion and prediction of mortality in trauma patients. Scand J Trauma Resusc Emerg Med 2016;24:1127. http://dx.doi.org/10.1186/cc13721.

[9] Rugeri L, Levrat A, David JS, Delecroix E, Floccard B, Gros A, et al. Diagnosis of early coagulation abnormalities in trauma patients by rotation thrombelastography. J Thromb Haemost 2007;5:289–95. http://dx.doi.org/10.1111/j.1538-7836.2007.02319.x.

[10] White NJ. Mechanisms of trauma-induced coagulopathy. Hematol Am Soc Hematol Educ Program 2013 2013;660–3. http://dx.doi.org/10.1182/asheducation-2013.1.660.

[11] CRASH-2 trial collaborators, Shakur H, Roberts I, Bautista R, Caballero J, Coats T, et al. Effects of tranexamic acid on death, vascular occlusive events, and blood transfusion in trauma patients with significant haemorrhage (CRASH-2): a randomised, placebo-controlled trial. Lancet 2010;376:23–32. http://dx.doi.org/10.1016/S0140-6736(10)6083-5.

[12] Spahn DR, Bouillon B, Cerny V, Duranteau J, Filipescu D, Hunt BJ, et al. The European guideline on management of major bleeding and coagulopathy following trauma: fifth edition. Crit Care 2019;23:98. http://dx.doi.org/10.1186/s13054-019-2347-3.

[13] Walsh M, Shreve J, Thomas S, Moore E, Moore H, Hake D, et al. Fibrinolysis in Trauma: "Myth," "Reality" or "Something in Between". Semin Thromb Hemost 2017;43:200–12. http://dx.doi.org/10.1055/s-0036-1597900.

[14] Wohlauer MV, Moore EE, Thomas S, Sauaia A, Evans E, Harr J, et al. Early Platelet Dysfunction: An Unrecognized Role in the Acute Coagulopathy of Trauma. J Am Coll Surg 2012;214:739–46. http://dx.doi.org/10.1016/j.jamcollsurg.2012.050.

[15] Vulliamy P, Gillespie S, Gall LS, Green L, Brohi K, Davenport RA. Platelet transfusions reduce fibrinolysis but do not restore platelet function during trauma hemorrhage. J Trauma Acute Care Surg 2017;83:388–97. http://dx.doi.org/10.1097/TA.0000000000001520.

[16] Furay E, Daley M, Teixeira PG, Coopwood TB, Aydelotte JD, Malesa N, et al. Goal-directed platelet transfusions correct platelet dysfunction and may improve survival in patients with severe traumatic brain injury. J Trauma Acute Care Surg 2018;85:881–7. http://dx.doi.org/10.1097/TA.0000000000002047.

[17] Dias JD, Lopez-Espina CG, Ippolito J, Hsiao H, Zaman F, Muresan AA, et al. Rapid point-of-care detection and classification of direct-acting oral anticoagulants (DOACs) with the TEG® 6s: implications for trauma and acute care surgery. J Trauma Acute Care Surg 2019. http://dx.doi.org/10.1097/TA.0000000000002357.

[18] Wikkelsø A, Wetterslev J, Møller AM, Afshari A. Thromboelastography (TEG) or rotational thromboelastometry (ROTEM) to monitor haemostatic treatment in bleeding patients: a systematic review with meta-analysis and trial sequential analysis. Anaesthesia 2017;72:519–31. http://dx.doi.org/10.1111/anae.13765.

[19] Gonzalez E, Moore EE, Moore HB, Chapman MP, Chin TL, Ghasabyan A, et al. Goal-directed hemostatic resuscitation of trauma-induced coagulopathy: A pragmatic randomized clinical trial comparing a viscoelastic assay to conventional coagulation assays. Ann Surg 2016;263:1051–9. http://dx.doi.org/10.1097/SLA.0000000000001608.

[20] Baksaas-Aasen K, Gall L, Eaglestone S, Rourke C, Juffermans NP, Goslings JC, et al. iTACTIC - implementing Treatment Algorithms for the Correction of Trauma-Induced Coagulopathy: study protocol for a multicentre, randomised

controlled trial. Trials 2017;18:486. http://dx.doi.org/10.1186/s13063-017-2224-9.

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