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Abstract: Summary Standard laboratory coagulation tests (SLTs) such as prothrombin time/international normalized ratio or partial thromboplastin time are frequently used to assess coagulopathy and to guide haemostatic interventions. However, this has been challenged by numerous reports, including the current European guidelines for perioperative bleeding management, which question the utility and reliability of SLTs in this setting. Furthermore, the arbitrary definition of coagulopathy (i.e. SLTs are prolonged by more than 1.5-fold) has been questioned. The present study aims to review the evidence for the usefulness of SLTs to assess coagulopathy and to guide bleeding management in the perioperative and massive bleeding setting. Medline was searched for investigations using results of SLTs as a means to determine coagulopathy or to guide bleeding management, and the outcomes (i.e. blood loss, transfusion requirements, mortality) were reported. A total of 11 guidelines for management of massive bleeding or perioperative bleeding and 64 studies investigating the usefulness of SLTs in this setting were identified and were included for final data synthesis. Referenced evidence for the usefulness of SLTs was found in only three prospective trials, investigating a total of 108 patients (whereby microvascular bleeding was a rare finding). Furthermore, no data from randomized controlled trials support the use of SLTs. In contrast, numerous investigations have challenged the reliability of SLTs to assess coagulopathy or guide bleeding management. There is actually no sound evidence from well-designed studies that confirm the usefulness of SLTs for diagnosis of coagulopathy or to guide haemostatic therapy.

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Usefulness of standard plasma coagulation tests in the management of perioperative coagulopathic bleeding: is there any evidence?

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Editor's key points

- The authors review the evidence for the continued use of standard laboratory tests of coagulation.
- They conclude that there is minimal evidence for the use of standard laboratory tests in guiding the management of perioperative bleeding.

Summary. Standard laboratory coagulation tests (SLTs) such as prothrombin time/international normalized ratio or partial thromboplastin time are frequently used to assess coagulopathy and to guide haemostatic interventions. However, this has been challenged by numerous reports, including the current European guidelines for perioperative bleeding management, which question the utility and reliability of SLTs in this setting. Furthermore, the arbitrary definition of coagulopathy (i.e. SLTs are prolonged by more than 1.5-fold) has been questioned. The present study aims to review the evidence for the usefulness of SLTs to assess coagulopathy and to guide bleeding management in the perioperative and massive bleeding setting. Medline was searched for investigations using results of SLTs as a means to determine coagulopathy or to guide bleeding management, and the outcomes (i.e. blood loss, transfusion requirements, mortality) were reported. A total of 11 guidelines for management of massive bleeding or perioperative bleeding and 64 studies investigating the usefulness of SLTs in this setting were identified and were included for final data synthesis. Referenced evidence for the usefulness of SLTs was found in only three prospective trials, investigating a total of 108 patients (whereby microvascular bleeding was a rare finding). Furthermore, no data from randomized controlled trials support the use of SLTs. In contrast, numerous investigations have challenged the reliability of SLTs to assess coagulopathy or guide bleeding management. There is actually no sound evidence from well-designed studies that confirm the usefulness of SLTs for diagnosis of coagulopathy or to guide haemostatic therapy.

Keywords: bleeding; blood; coagulation; coagulopathy; transfusion

Perioperative management of coagulopathic bleeding requires timely haemostatic intervention using allogeneic blood products, administration of coagulation factor concentrates, or both. To guide these interventions, fast laboratory workup is essential. If it comes to the question which laboratory test should be performed to assess haemostasis, current guidelines usually refer to standard plasma coagulation tests (SLTs), that is, prothrombin time (PT)/international normalized ratio (INR) and activated partial thromboplastin time,^{1–7} while viscoelastic tests (i.e. thrombelastography) are less commonly advocated.⁷ Although the complete panel of standard coagulation testing almost always covers additional measurements of fibrinogen and platelet count, interpretation of SLTs is most frequently used to assess coagulopathy. Generally

speaking, coagulopathy is presumed when SLTs are prolonged by more than 1.5-fold, although the evidence to support this degree of prolongation as diagnostic of coagulopathy is limited.

However, there are major limitations to these SLTs. These tests are time-consuming (with turnaround times sometimes longer than 60 min)⁸ and, as a consequence, they are often omitted in situations of severe bleeding, where prompt treatment must be ensured. In addition, if the results of PT/aPTT are more than 1.5 times prolonged, the treatment options range from transfusion of fresh-frozen plasma (FFP) to administration of coagulation factor concentrates such as prothrombin complex concentrates (PCC) or activated recombinant factor VII. Notably, all these treatment options may be linked

to serious side-effects, and their administration should be rigorously justified.

More importantly, we need to question what information we obtain from a PT or aPTT. In routine clinical practice, PT and aPTT are commonly used either for bleeding risk assessment before an invasive procedure or, as will be the focus in this review, for the assessment of the haemostasis profile with respect to detection of underlying coagulopathy and guiding subsequent blood component therapy. In fact, PT/INR and aPTT are plasma-based coagulation tests that were basically designed to monitor vitamin K antagonists and heparin, respectively,⁹ and to assess coagulation factor deficiencies. These latter assays were not intended to monitor perioperative coagulation disorders, predict bleeding, or to guide bleeding therapy in the perioperative setting.^{10–14}

This review aims to assess the evidence for using SLTs in the perioperative setting or massive bleeding management for diagnosis of coagulopathy and guidance of bleeding therapy, and also to assess the evidence for using the widely accepted trigger of ≥ 1.5 -fold prolongation of SLTs.

Methods

Ovid Medline (between 1950 and November 2013) was searched for suitable studies using the following search terms: 'standard laboratory tests' or 'international normalised ratio' or 'international normalized ratio' or INR or prothrombin time or 'activated partial thromboplastin time' or aPTT and (guid* or transfus*). Only English language, non-animal studies were included. The following terms were excluded from the search: heparin or warfarin or coumadin or coumarin or acenocoumarol or anticoagula*. An initial screen was carried out, which involved reading titles only and rejecting papers based on topic: haemophilia/hemophilia, (chronic) liver disease, liver transplantation, cirrhosis, leukaemia, hepatitis, thalassaemia, lupus, inherited/congenital, and carcinoma. The second screen involved reading the abstracts of the papers that made it through the initial screen. Papers were included if PT, INR, or aPTT were measured, a threshold for the results of the SLTs was given to determine coagulopathy or the results were used to guide treatment, and the outcomes of interest for this review (blood loss, time to haemostasis, transfusion requirements, mortality) were reported. This screen removed 278 hits leaving 109 hits to be included in the final screen, which involved reading the full papers. In addition, Ovid Medline was checked for bleeding management guidelines from national Societies or Boards. Special focus was set at the referenced literature that supports the ongoing recommendations to use SLT and the coupled trigger levels.

The literature search was conducted by Meridian Health-Comm Ltd (Plumley, UK) and thereafter independently screened by two authors (H.S. and T.H.). Disparities in the literature search were resolved by consensus.

Results

The initial search revealed 1123 records for SLTs and 18 for bleeding management guidelines. After refining the search

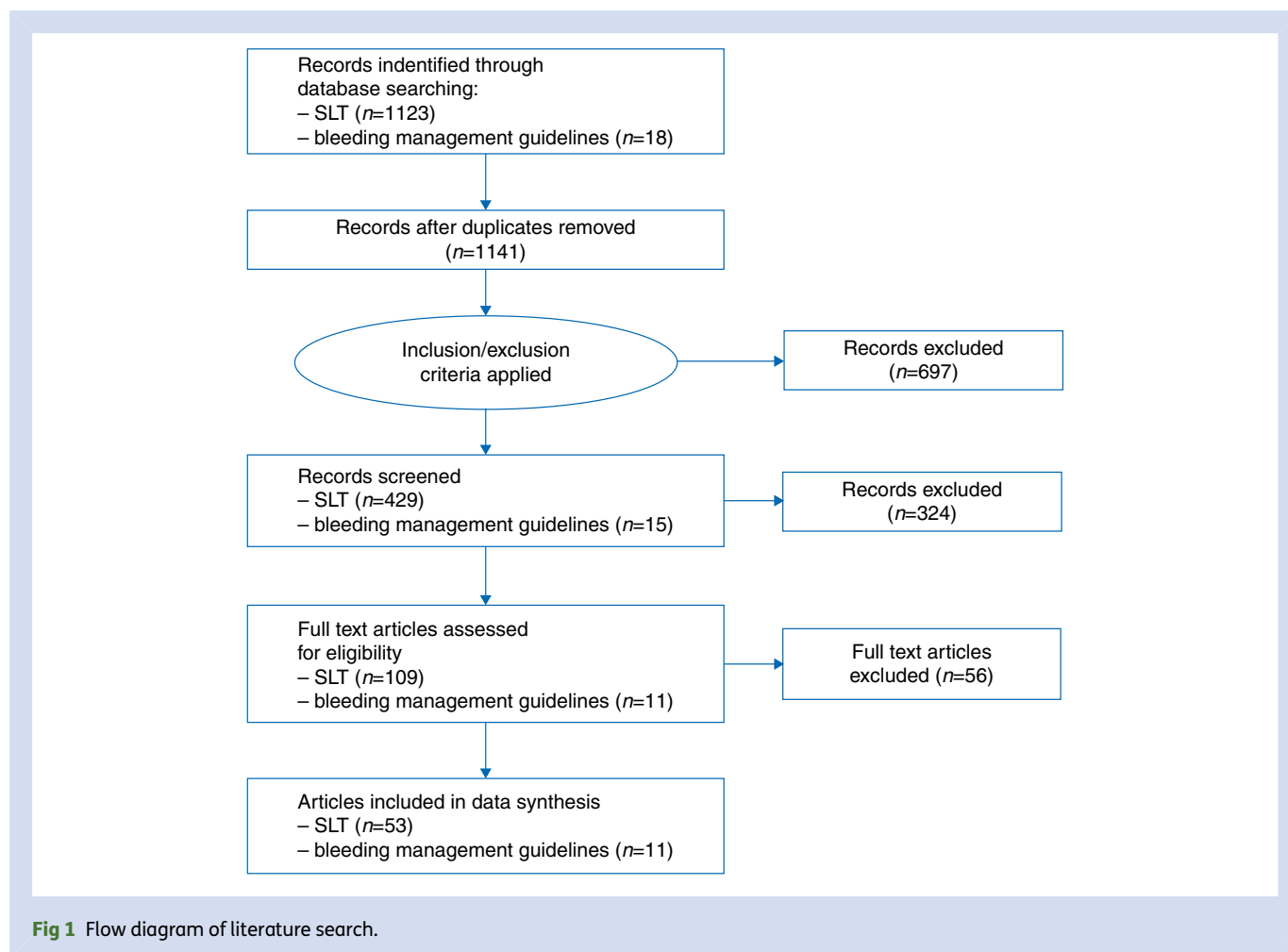
by applying exclusion criteria and further screening by full paper reading, a total of 64 studies were included for final data synthesis. The full process of literature search was displayed in Figure 1.

The recommended methods of monitoring/diagnosing coagulopathy in major haemorrhage using laboratory coagulation tests and the recommended bleeding management within the 11 identified current bleeding management guidelines are summarized in Table 1. The referenced literature for supporting these recommendations is given in Table 2.

The traditional trigger of using a ≥ 1.5 -fold prolongation of aPTT/PT as a transfusion trigger was identified in six out of the 11 published guidelines for bleeding management. Screening of referenced literature within these guidelines revealed that these triggers were not based on high-quality prospective data but rather on retrospective data analysis (Table 2). Eight publications in total were referenced within these guidelines to justify the traditional SLT trigger. Two of them were review papers without original data;^{27 29} one reported recommendations from a national expert panel,²⁸ two provided data from retrospective observational data analyses of a trauma registry and medical charts, respectively,^{20 22} and finally, three provided data from prospective observational studies.^{21 23 31} In those three prospective studies, data were reported from a total of 108 patients (72 who underwent major surgery and 36 trauma patients after admission to the hospital) were investigated, but of these, only nine patients experienced diffuse microvascular bleeding and a prolonged PT/aPTT ≥ 1.8 . Analysing data from patients who underwent major surgery revealed that in one study, only two patients showed PT/aPTT > 1.5 -fold prolonged, while no thresholds for PT/aPTT were given in the second study.

Discussion

Numerous guidelines and publications encourage the use of SLTs for diagnosis of coagulopathy during perioperative and massive bleeding and to base transfusion therapy upon prolonged thresholds of these SLTs.^{1–6 15 30 33 34} This concept, however, has been challenged by more recently published data questioning the usefulness of SLTs and especially the proposed triggers to initiate transfusion therapy in these settings.^{11 18 24 26 35–42} Based on the data of the present review, there is no high-quality evidence to support that the traditionally applied trigger levels of ≥ 1.5 -fold prolongation of aPTT/PT or INR are of great help to diagnose whether a patient suffers from coagulopathic bleeding or if any bleeding therapy should be initiated. Notably, all referenced evidence within the guidelines recommending the use of SLTs were either cross-referenced between guidelines without providing clear data, or relate to very sparse, low-quality published literature. The most frequently referenced evidence of all screened literature is a prospective study from Ciavarella and colleagues²¹ who investigated haemostasis in 36 patients after admittance to the emergency room in 1986. In that study, diffuse microvascular bleeding was observed in nine out of 36 patients only, while four of these nine patients experienced fibrinogen levels



$<0.5 \text{ mg dl}^{-1}$, whereby valid interpretation of the results of SLTs seemed to be impossible. However, the authors concluded that if fibrinogen levels were adequate, PT or PTT ratios prolongation ≥ 1.8 is a reliable predictor of FV or FVIII levels $<20\%$.

In fact, it seems as if the rationale for using PT/INR or aPTT triggers stem mostly from trauma databases that demonstrated that prolonged SLTs were frequently correlated with increased mortality. In a large retrospective analysis of more than 35 000 trauma patients admitted to the emergency room, an INR of ≥ 1.3 was linked to a 6.3-fold increased risk of in-hospital mortality.²⁰ However, it was not addressed if those prolonged SLTs were associated with increased bleeding or transfusion requirements. Using the trigger of 1.5-fold prolongation of SLTs, data from a retrospective study in adult trauma patients ($n=3646$)⁴³ and prospective data in paediatric trauma patients ($n=102$)⁴⁴ demonstrated that prolongations of SLTs were correlated with higher transfusion requirements and mortality. Similar observations were made in critically ill patients, whereby prolonged PT was independently associated with greater intensive care unit mortality.⁴⁵ However, the actual reason for the increase in mortality cannot be answered by an abnormal baseline test.

SLTs are poor predictors of bleeding and PT/aPTT values >1.5 -fold are not highly correlated to clinically relevant

bleeding.^{31 46 47} The PT and aPTT evaluate quantities of coagulation factors and do not evaluate thrombin potential, which is arguably a better predictor of bleeding risk. A single coagulation factor deficiency of $<30\%$ (0.30 IU ml^{-1}) will lead to prolongation of the PT or aPTT, but when multiple factors are diminished, the PT and aPTT become variably and less predictably prolonged.^{21 48–50} Massive bleeding can be characterized as acquired deficiency of more than just one coagulation factor, and multiple factor deficiency is accountable for greater prolongation of SLTs than single factor deficiencies.^{48 51} Another major determinant of measuring SLTs is fibrinogen level below 80 mg dl^{-1} that may result in prolonged SLT results.⁵² This is of great importance as fibrinogen deficiency occurs early during treatment of massive blood loss and thus may have frequent impact on the results of SLTs.³⁰

There are various other well-known limitations that should be emphasized for interpretation of SLTs: all these tests are performed in plasma without platelets or red cells at a standardized temperature, and may not be able to correctly diagnose complex settings of fibrinogen deficiency, heparin effects, or fibrinolysis.⁵³ In addition, using different commercially available reagents for SLTs, it has been demonstrated that the least sensitive combination of reagents used for PT and aPTT testing

Table 1 Recommended laboratory coagulation testing in current guidelines

Guideline (year)	Recommended monitoring for coagulopathy	Recommended bleeding management
American Society of Anesthesiologists Task Force on Perioperative Blood Transfusion and Adjuvant Therapies (2006) ¹	Platelet count, PT or INR, aPTT. Other tests may include fibrinogen level, assessment of platelet function, thromboelastogram, D-dimers, and thrombin time	Transfusion of FFP for correction of excessive microvascular bleeding in the presence of: <ul style="list-style-type: none"> • PT > 1.5 times normal • INR > 2.0 • aPTT > 2 times normal
Guidelines Blood transfusion and the anaesthetist: management of massive haemorrhage. Association of Anaesthetists of Great Britain and Ireland (2010) ¹⁵	Full blood count, PT and aPTT, Clauss fibrinogen. ROTEM [®] or TEG [®] if available. Fibrinogen level is more sensitive than the PT and aPTT to a developing dilutional or consumptive coagulopathy	PT and aPTT > 1.5 times normal is predictive of microvascular bleeding. Transfusion of FFP to prevent microvascular bleeding if senior clinician anticipates a massive haemorrhage
Guidelines on the management of massive blood loss. British Committee for Standards in Haematology (2006) ⁶	Full blood count, PT, aPTT, thrombin time, Fibrinogen (Clauss method)	Administration of FFP to maintain PT and aPTT < 1.5 times control
Guidelines for the use of fresh-frozen plasma, cryoprecipitate and cryosupernatant. British Committee for Standards in Haematology, Blood Transfusion Task Force (2004) ⁵	Traditional clotting tests (PT, aPTT, thrombin time), platelet count, and near-patient tests such as the thromboelastogram	Whether and how much FFP should be used for treating a patient with major blood loss should be guided by timely tests of coagulation (including near-patient tests); however, no clear thresholds given because of paucity of data
Coagulation management in trauma-related massive bleeding. Recommendations of the Task Force for Coagulation of the Austrian Society of Anesthesiology, Resuscitation and Intensive Care Medicine (2010) ¹⁶	Viscoelastic tests recommended (e.g. ROTEM [®] or TEG [®]), and platelet count (function)	Targeted administration of purified coagulation factors based on ROTEM [®] or TEG [®] ; PT (Quick's value < 30%) may be alternatively used to guide administration of PPC/FFP
Scandinavian guidelines—'The massively bleeding patient' (2008) ¹⁷	Thromboelastogram (TEG [®]) superior with regard to identifying and treating clinically relevant coagulopathies	Targeted administration of FFP/coagulation factor concentrates based on TEG [®]
German Medical Association. Cross-sectional guidelines for therapy with blood components and plasma derivatives (2009) ²	PT, aPTT, fibrinogen, platelet count	FFP transfusion if PT (Quick's value) < 50% or aPTT > 45 s in the presence of diffuse microvascular bleeding
Management of severe perioperative bleeding. Guidelines from the European Society of Anaesthesiology (2013) ¹⁸	Thromboelastometry should be preferably used to identify coagulopathy and guide treatment during obstetric bleeding, cardiovascular surgery, emergency radiological/surgical interventions, orthopaedic surgery and neurosurgery, visceral and transplant surgery, and paediatric surgery. Platelet count (and function). PT/INR/aPTT prolongation can be misleading in patients with chronic liver disease	Recommendation to substitute fibrinogen if plasma concentration is < 1.5–2.0 g litre ⁻¹ or functional fibrinogen deficit in ROTEM/TEG. Prolonged INR/PT alone is not an indication for PCC. In VKA-treated patients, INR > 1.5 with life-threatening bleeding should trigger administration of PCC and Vit K. Otherwise, coagulation therapy should be based on ROTEM/TEG
Recommendations for the transfusion management of patients in the intraoperative period. Italian Society of Transfusion Medicine and Immunohaematology (2011) ⁴	Monitoring of platelet count, PT, aPTT, fibrinogen, antithrombin, D-dimer	FFP should be transfused for correction of microvascular bleeding if PT or aPTT, expressed as a ratio is > 1.5
Management of bleeding and coagulopathy following major trauma: an updated European Guideline (2013) ⁷	Measurement of PT, aPTT, fibrinogen and platelets. Viscoelastic measurements should be also performed	No trigger levels for PT/aPTT/INR given
Australian Patient Blood Management Guidelines: Module 1 (2011) ¹⁹	Platelet count, PT/INR, aPTT, fibrinogen	Values indicative of critical physiological derangement include: PT/aPTT > 1.5 normal, INR > 1.5

would have suggested coagulopathy in only two out of 16 patients, while the most sensitive set of reagents suggested therapy in all patients.⁵⁴

Besides the methodological limitations, the clinically most important problem is that all SLTs are unacceptably time-consuming which may frequently result in omission of SLT measurements or transfusion without laboratory guidance.^{8 55} This may explain why there is a widespread inappropriate use of FFP transfusion,⁵⁶ or the implementation of transfusion

guidelines based on viscoelastic testing (e.g. ROTEM[®]) have lowered transfusion requirements.^{57–59}

Although the time to test results could be sped up by the use of point-of-care devices for measuring PT/INR, there is a high variability in reported results and thus they may not be useful for identification or exclusion of patients with coagulopathy after trauma.^{8 60}

Notably, transfusion of FFP without clear indications is performed frequently in the medical community^{56 61} and people

Table 2 Evidence from references within current guidelines (Table 1)

Guideline (year)	References within guideline
American Society of Anesthesiologists Task Force on Perioperative Blood Transfusion and Adjuvant Therapies (2006) ¹	Recommendations based on a consultant survey response and ASA membership survey response No referenced evidence for usefulness of standard laboratory coagulation tests
Blood transfusion and the anaesthetist: management of massive haemorrhage. Association of Anaesthetists of Great Britain and Ireland (2010) ¹⁵	Hess, <i>Transfusion</i> 2009 ²⁰ INR or activated PTT ratio (aPTTr) increased with increasing injury severity score of 35 322 trauma patients after admission to trauma centre (retrospective analysis). An increase in INR or aPTTr demonstrated stepwise relationship with in-hospital mortality. No clear threshold given
Guidelines on the management of massive blood loss. British Committee for Standards in Haematology (2006) ⁶	Ciavarella, <i>Br J Haematol</i> 1987 ²¹ Microvascular bleeding was associated with severe abnormalities of coagulation factor levels < 20% (PT and aPTT values >1.8 times control). Prospective study in 36 patients admitted to emergency room, which were likely to be massively transfused
Guidelines for the use of fresh-frozen plasma, cryoprecipitate and cryosupernatant. British Committee for Standards in Haematology, Blood Transfusion Task Force (2004) ⁵	Ciavarella, <i>Br J Haematol</i> 1987 ²¹ (See above) Mannucci, <i>Vox Sang</i> 1982 ²² PT > 1.2 times normal or aPTT > 1.25 times normal were found in 93% of patients who underwent major surgery (including cardiopulmonary bypass procedures) and received massive transfusion. Retrospective data analysis of 172 patients
Coagulation management in trauma-related massive bleeding. Recommendations of the Task Force for Coagulation of the Austrian Society of Anesthesiology, Resuscitation and Intensive Care Medicine (2010) ¹⁶	No evidence for usefulness of standard laboratory coagulation tests
Scandinavian guidelines—'The massively bleeding patient' (2008) ¹⁷	No evidence for usefulness of standard laboratory coagulation tests
German Medical Association. Cross-sectional guidelines for therapy with blood components and plasma derivatives (2009) ²	Hiippala, <i>Anesth Analg</i> 1995 ²³ Fibrinogen deficiency develops earlier than any other haemostatic abnormality. No trigger levels for PT/aPTT given. Prospective data from 60 patients undergoing major urologic or abdominal surgery
Management of severe perioperative bleeding. Guidelines from the European Society of Anaesthesiology (2013) ¹⁸	Abdel-Wahab, <i>Transfusion</i> 2006 ²⁴ No correlation with mild abnormalities of PT, aPTT, and risk of bleeding. Correction of mildly prolonged PT/INR by transfusion of FFP fails in 99%. Data from prospective audit from Massachusetts General Hospital after transfusion of 1091 units of FFP, 2004–5 Matevosyan, <i>J Neurosurg</i> 2011 ²⁵ Prolongation of INR up to 1.7 has haemostatically normal levels of coagulation factors. Prospective study in 31 neurosurgical patients de Loyd, <i>Int J Obstet Anesth</i> 2011 ²⁶ Fibrinogen level is most sensitive laboratory parameter for detecting coagulopathy during obstetric bleeding, and PT is an unhelpful test. Retrospective analysis of 18 501 deliveries over 3 yr in a large UK city-based maternity unit
Recommendations for the transfusion management of patients in the intra-operative period. Italian Society of Transfusion Medicine and Immunohaematology (2011) ⁴	<i>American Society of Anesthesiologists Task Force on Perioperative Blood Transfusion and Adjuvant Therapies (2006)</i> ¹ (See above) Calder, <i>Can Med Assoc J</i> 1997 ²⁷ Recommendation of an expert panel. No transfusion triggers were given De Backer, <i>Acta Clin Belg</i> 2008 ²⁸ PT and aPTT are not useful for guidance of FFP transfusion in severe bleeding. Recommendations from a national guideline based on expert opinion Hellstern, <i>Thromb Res</i> 2002 ²⁹ FFP transfusion if PT or aPTT is > 1.5 times prolonged during acute blood loss and massive transfusion. Review article. References to Hiippala ³⁰ and Murray. ³¹ Hiippala, <i>Vox Sanguinis</i> 1998 ³⁰ Probability of coagulopathy increases when aPTT and PT are > 1.5 times normal. Hypofibrinogenaemia develops first during massive blood loss. Review Paper. References to Murray ³¹ and Ciavarella ²¹ Murray, <i>Anesthesiology</i> 1988 ³¹ Massive transfusion was necessary in seven out of 12 patients during major surgery; while only two patients showed PT/aPTT > 1.5. Prospective observational study in 12 patients
Management of bleeding and coagulopathy following major trauma: an updated European Guideline (2013) ⁷	No evidence for usefulness of standard laboratory coagulation tests Only data showing the beneficial use of ROTEM/TEG were referenced

Continued

Table 2 Continued

Guideline (year)	References within guideline
Australian Patient Blood Management Guidelines: Module 1 (2011) ¹⁹	Mitra, <i>Injury</i> 2007 ³² Predictors of mortality: INR (OR=1.62; 95% CI: 1.18, 2.24; $P<0.01$); aPTT: (OR=1.01; 95% CI: 1.01, 1.02; $P<0.01$). Retrospective analysis of 119 adult trauma patients at Australian hospital

seem to trust traditional SLT, but retrospective data analyses have demonstrated that SLT will be normalized in only 34.5% of cases after FFP transfusion.⁶²

It should be noted that due to changes of modern bleeding management seen particularly in Europe, for example, PCC may be used increasingly instead of FFP to treat prolonged SLT results, which could lead to serious side-effects and high costs if the use was not justified.

It should be clearly stated that SLT are not *per se* inappropriate, but have been frequently used to try to answer a question that they were never designed to be able to answer. It seems as if the medical community continues to believe in the usefulness of SLTs to diagnose coagulopathy, as they do for the (not existing) predictive value of SLTs to predict risk of bleeding before invasive procedures.⁶³ However, if no other laboratory test is available, SLTs may be preferable above no testing. Certainly, SLTs have considerable utility in managing ongoing bleeding, when several SLT tests have been taken and a trend in the change of blood tests can guide further therapy. This is in fact hard to answer and will be eventually based on local standards of treatment.

Neither PT/INR nor aPTT were designed to accurately portray the complex interaction of coagulation factors and inhibitors. SLTs may often incorrectly be thought to provide information about overall thrombin generation (TG). A common assumption is that as procoagulant factors decline, TG declines too. Important inhibitors such as antithrombin or protein C, which are involved in overall TG, are not adequately represented in SLTs.⁶⁴ But, PT and aPTT measurements terminate when only 5% of thrombin is generated.⁶⁵ Therefore, SLTs provide information only about the very initial process of TG. Studies have revealed that haemodilution results in a lesser degree of TG than was expected by the decline of procoagulant factors.⁶⁶ Dunbar and Chandler⁶⁷ observed that dilution of all plasma proteins to 40% of normal resulted in an increase in tissue factor-stimulated TG. This finding is related to a simultaneous dilution of both procoagulant and anticoagulant proteins. Shaz and colleagues⁶⁸ investigated 371 trauma patients on ER admission. Patients were grouped in those with prolonged PT suggestive of trauma-induced coagulopathy (TIC) and those with normal PT. Despite the fact that FV, FVII, and FXIII were lower in the TIC group, no difference in markers of TG (prothrombin fragment 1–2 and thrombin–antithrombin complexes) could be observed. Again this observation might be explained by a simultaneous decrease in both procoagulants and inhibitors, which is not adequately reflected by SLTs. However, the question about whether prolonged SLTs are indicative of the requirement for specific haemostatic therapy

needs to be addressed with adequately powered studies. Analogous findings have been reported from patients with liver failure. These patients are able to maintain normal TG as a result of a simultaneous decrease in both pro- and anticoagulant factors.⁶⁹ In another study on patients with liver cirrhosis and prolonged PT/INR, Gatt and colleagues⁷⁰ investigated TG parameters in cirrhotic patients. Despite a prolonged PT/INR, TG parameters were consistent with a hypercoagulable profile. The authors stated that the PT/INR test should not be used to assess bleeding risk and as a guidance for prophylactic transfusion of clotting factors.

In conclusion, there are significant shortcomings of SLTs in the perioperative and major bleeding management setting. First, these tests were neither designed to accurately reflect compromised TG nor to guide coagulation therapy. In addition, the applied trigger levels of ≥ 1.5 -fold prolongation of aPTT/PT or INR > 1.5 to initiate bleeding therapy were not supported by evidence-based data but rather on historically established habits. In general, SLTs are widely available and frequently used, but there is no sound evidence from well-designed studies that confirm that SLTs are useful for diagnosis of coagulopathy or to guide haemostatic therapy. Secondly, the turnaround times of SLTs are too protracted for emergency scenarios, where quick decision-making is mandatory. Alternatives, such as viscoelastic analysers, provide data much more quickly and provide a more comprehensive overview of the whole coagulation process. However, more well-designed studies in different clinical settings are needed to confirm that these tests are preferable over standard tests. Thus, it seems questionable how long physicians are willing to continue using (late) results of SLTs as marker of coagulopathy or guidance for bleeding management. But as always, old and even bad habits die hard.

Authors' contributions

T.H.: data collection and analysis and writing of the paper; D.F., K.A.T., and L.A.: data analysis; N.S.C.: data analysis and writing of the paper; H.S.: data collection and analysis and writing of the paper.

Declaration of interest

T.H. has received speaker fee and travel support from CSL Behring GmbH, Octapharma AG, TEM International, Fresenius Kabi, and B Braun AG. D.F. has received study funding, payments, and travel funding for overseas lectures from Austrian National Bank, AOP Orphan, Pfizer, Astra Zeneca, Baxter, Braun, Biotest, CSL Behring, Fresenius, Glaxo, Haemoscope, Hemogem, Lilly, LFB, Mitsubishi Pharma, NovoNordisk,

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