



## Journal Club

Simon Stanworth, Richard Haspel, and Jeannie Callum, *Abstract Editors*

### Safety of endoscopic interventions in patients with thrombocytopenia.

Krishna SG, Rao BB, Thirmurthi S, et al. *Gastrointest Endosc* 2014; 80: 425–34.

There is a growing realization that not all patients with coagulation abnormalities require preprocedure transfusions to prevent excess bleeding. Much of the data supporting a limited transfusion approach comes from “negative” cohort studies. That is, a description of patients with low platelet counts and/or an elevated prothrombin times who successfully underwent procedures without receiving platelet or plasma transfusions. Krishna et al add to this valuable literature by investigating the safety of gastrointestinal (GI) endoscopy in patients with thrombocytopenia.

The authors performed a retrospective analysis of consecutive oncology patients with platelet counts of less than 50/ $\mu\text{L}$  who underwent either esophagogastroduodenoscopy, sigmoidoscopy, or endoscopy. Patients who underwent biopsies were included. Given the retrospective nature, there was limited consistency in transfusion practice. Patients essentially always received a platelet transfusion if the count was less than 10/ $\mu\text{L}$ . Otherwise, the decision to transfuse was at the discretion of the primary team or the GI consultant. A platelet count was considered preprocedure if it was obtained within 8 hours before the endoscopy. Importantly, posttransfusion platelet counts were not routinely checked, making this laboratory value the most commonly missing data (23% of procedures) with statistical imputation of the missing values. Patients with preprocedure posttransfusion platelet counts greater than 75/ $\mu\text{L}$  were excluded from the analysis.

A total of 395 patients having 617 endoscopic procedures (351 esophagogastroduodenoscopies, 90 colonoscopies, and 176 sigmoidoscopies) with 398 including biopsies were included in the analysis. Most patients (84%) had hematologic malignancies, with most procedures performed on inpatients (87%). The most common indications for endoscopy were suspected graft vs host disease (47%) and GI bleeding (37%).

Patients undergoing biopsy had a mean preprocedure platelet count of 38/ $\mu\text{L}$ . For approximately 35% of these 398 procedures, a preprocedure platelet transfusion was not given. A total of 6 patients had biopsy-related bleeding (2 from each type of procedure). Five of these patients had bleeding during the procedure, which was managed by clip placement or epinephrine. The other patient had delayed bleeding managed by subsequent clip placement. Five of the patients with biopsy-related bleeding had not received preprocedure platelet transfusions and had a mean preprocedure platelet count of 38/ $\mu\text{L}$ . In regard to polypectomy, 45 polyps were removed in 17 colonoscopies with a mean preprocedure platelet count of 40/ $\mu\text{L}$  and 11 of these patients had received a platelet transfusion. There was no significant difference in hemoglobin values prepolypectomy and postpolypectomy. Only 2 patients had immediate bleeding, which was controlled by epinephrine and clips (platelet counts of 48/ $\mu\text{L}$  and 53/ $\mu\text{L}$ ).

The authors also demonstrate the importance of actually performing the procedures in these patients and not shying away due to thrombocytopenia. For the biopsy procedures, 62% had significant pathology, with graft vs host disease being the most common diagnosis. In addition, 89% of the polyps removed were precancerous and 2 of these had high-grade dysplasia. For the 68 endoscopies with evidence of active GI bleeding, an intervention was performed in 41. For these patients, there was a 51% reduction in packed red cell transfusions in the 72 hours before and after transfusion (approximately 4 to 2 units,  $P < .001$ ).

Taken together, the data suggest that both polypectomy and biopsies can be safely performed in patients with platelet counts below 50/ $\mu\text{L}$ , and if transfusion is given, it is not necessary to religiously follow post-transfusion counts. In addition, it is important to perform endoscopy in these patients for both diagnostic and therapeutic reasons. Krishna et al should be commended for this essentially negative study suggesting that a platelet count less than 50/ $\mu\text{L}$  is not an absolute contraindication to GI endoscopy. (RH)

### Consistency of thromboelastometry analysis under scrutiny: Results of a systematic evaluation within and between analysers. Nagler M, ten Cate H, Kathriner S, et al. *Thromb Haemost* 2014; 111:1161–1166.

Many of us have more interest in viscoelastic technologies including thromboelastometry analysis using the ROTEM device, a point-of-care test comparable to thromboelastography (TEG). Potential advantages include the ability to monitor coagulopathy closer to the patient bedside. A separate review in this section describes a systematic review of the overall value of viscoelastometric testing devices to manage hemostasis clinically. This article picks up on another point, which is the consistency of the analysis, but one that deserves more attention. As hematologists, we are familiar with quality assurance schemes. The national external quality assurance scheme in the United Kingdom continues to highlight, for example, inconsistencies in the reporting of standard coagulation tests on common blood samples. Clearly, limitations in reproducibility can seriously reduce the value of any medical test.

The purpose of this study was to assess whether thromboelastometry measurements were reproducible in different clinically relevant situations. The authors evaluated the consistency of thromboelastometry parameters, within individual tests, between different analysers, between different channels of the same analyzer, between morning and afternoon measurements (to assess circadian variation), and when measured 4 weeks apart (to assess day-to-day variation). In this prospective study, citrated whole blood samples were taken from 40 healthy young volunteers and evaluated with 2 ROTEM analyzers in parallel. These individuals did not have any known diseases and were not taking any medication with effects on hemostatic parameters, and also had no history of bleeding

or thromboembolic events. The analysis used a Bland-Altman comparison, and “homogeneity” of variances was tested using the Pitmen test.

The results revealed some surprisingly large differences for some thromboelastometry parameters and a lack of homogeneity for many measures. Indeed, less than half of all comparisons made showed high homogeneity of variances; in about a fifth of the comparison, data distributions were quite heterogeneous. Differences appeared not only between analysers but also between the different channels of the same analyzer, between morning and afternoon measurements, and when samples were measured 4 weeks apart. Moreover, there was an inconsistency within individual tests and parameters, although there were suggestions of more homogeneity of measurements for some parameters, for example, maximum clot firmness.

In summary, the findings indicate variable results that lead onto key questions regarding exact reproducibility of ROTEM. The strength of this study was the systematic approach; the limitation was the collection of blood samples from only healthy volunteers rather than mixed populations including hospital inpatients. To my mind, these results do have implications for further multicentre study designs to evaluate different algorithms. (SJS)

**Omitting pre-operative coagulation screening tests in hip fracture patients: Stopping the financial cascade.** Salar O, Holley J, Baker B, et al. *Injury* 2014; 45: 1938–41.

It is a well-known fact to laboratory technologists and physicians that preoperative coagulation testing is unnecessary unless it is clinically indicated by history (preferably a validated bleeding history questionnaire). Of course, this provision of better care takes time and resources on the clinical side. The continued ordering of preoperative coagulation testing is taking place because it is an engrained practice by the ordering physicians, the ordering physicians have no idea when they are supposed to order these tests, and it is cognitively easier to order it on everyone than triaging patients to testing vs no testing. Even orthopedic guidelines recommend against coagulation testing unless clinically indicated (eg, on anticoagulation therapy). Despite clear recommendations in the literature, this single-center report from the United Kingdom finds near universal coagulation screening for hip fracture patients at considerable costs and no observed benefits. Perhaps we need to add this to a future “Choosing Wisely” list: Don’t routinely order preoperative coagulation testing unless clinically indicated (followed by behavior modification of surgeons).

This report comes from Queens Medical Centre, a major trauma hospital in the United Kingdom. They reviewed the use of coagulation testing for 814 patients in 2012 who were admitted with a spontaneous hip fracture. Patients were divided into 4 groups: (1) no testing (n = 70; 8.6%); (2) testing performed, normal results (n = 580; 71.3%); (3) testing performed, abnormal results, on warfarin (n = 55; 6.8%); (4) testing performed, abnormal results, no warfarin (n = 109; 13.4%). I was surprised that not a single patient was on one of the new oral anticoagulant drugs (anti-Xa or anti-IIa inhibitors) in the year 2012. Remarkably, no patient in group 4 received either blood products or vitamin K in response to the abnormal test result. No details on the management of the warfarin reversal strategy for the warfarinized group were provided. There were no differences in intraoperative blood loss, red cell transfusion rates, hematoma formation, or GI hemorrhage when patients with abnormal results (not on warfarin) were compared with patients with normal results. Similarly, the abnormal result did not impact on rates of regional (as compared with general) anesthesia. The degrees of elevation of the coagulation results were not provided. The authors estimated a potential savings of up to US \$648 375 if coagulation testing was omitted for such patients across the United Kingdom, presuming their estimates of inappropriate testing reflect what is occurring in other institutions.

So why did the surgeons (or anesthesiologist or emergency physicians) caring for these patients order coagulation testing? Is this part

of an order set in their computer system or on a written physician order set? Is it part of the blood work ordered by the nurses in the emergency department when the patient arrives? Perhaps no physician actually orders these test. Alternatively, are the surgeons or anesthesiologists forced to order this as part of a policy requiring patients planned for regional anesthesia to have normal coagulation test results on their chart? We are also not told any details about the degree of derangement or the etiology of the derangement, so we can make some sense of what is going on at this hospital. And lastly, and most interestingly, why does it appear that no one “sees” these abnormal results? There were no blood products ordered to “correct” the values, and there was no impact on decision making regarding regional anesthesia. This article provides a very cursory look at the problem. They (and probably you are in the same boat at your hospital) need to do a process map of when, by whom, and how this test gets ordered. In the meantime, flip this article to your head of orthopedics with the subject header—“We don’t do this at our hospital do we?” It might just open up an important conversation at your hospital. (JC)

**Changing patterns of in-hospital deaths following implementation of damage control resuscitation practices in US forward military treatment facilities.** Langan NR, Eckert M, and Martin MJ. *JAMA Surg* 2014; 149: 904–12.

Based on military data, there was a significant shift to “damage control resuscitation” (DCR) in civilian hospitals. That is, early administration of plasma and platelets in addition to red cells in equal amounts (“1:1:1”). Subsequent studies have shown some significant issues, such as survival bias, with the military data. Lagan et al review a registry of military trauma cases and attempt to provide additional data to support DCR.

The authors used the data from the Joint Theater Trauma Registry (JTTR), which prospectively captured all data on patients treated at forward military treatment facilities (MTFs) in the war in Afghanistan and Iraq. Data collected include vital signs, laboratory values, injuries, interventions including amounts of fluid, and blood products. Data from 2001 to 2011 were analyzed, and the periods before and after DCR implementation were compared (pre- and post-January 2006). Deaths were defined as killed in action (KIA; died before reaching the MTF) or died of wounds (DOW; presented at MTF with recorded vital signs and subsequently died). The case-fatality rate represents all KIA and DOW deaths as a percentage of all wounded patients.

A total of 57 129 patients were admitted to MTFs and recorded in the registry. Of these, 902 and 1663 died in the pre- and post-DCR periods, respectively. It is clear that DCR was successfully implemented. Crystalloid use was cut in half (approximately 6 to 3 L), with a very large increase in plasma use (3.2 to 10.1 units). There was also a significant increase in red cell usage (8.4 to 11.4 units) but not for platelets and cryoprecipitate. The mean ratio of red cells to plasma also changed from 2.6:1 to 1.4:1.

Of course, the key question is whether this change in practice made a difference. Patients who died in the post-DCR period had worse injuries (eg, significantly increased injury severity score [ISS]), and the authors make the claim that because the patients dying in the post-DCR period were sicker, there was “a decrease in the number of deaths among potentially salvageable patients.” There is, however, minimal analysis of the patients who survived. Although the authors note that the average injury severity score of all patients did not change over the period, a specific analysis of surviving patients and their ISS would seem to be a more straightforward approach to get at the core question (ie, did the average ISS of surviving patients increase?).

In addition, the authors note that there were many other interventions during the periods investigated. Most notably, the time from injury to arriving at a MTF dropped from 2 hours in the early years of the analysis to 45 minutes more recently. Other possible differences between the 2 periods are suggested in the graphs tracking KIA rate and

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