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Journal Club

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Let technology do the work: Improving prediction of massive transfusion with the aid of a smartphone application. Mina MJ, Winkler AM, Dente CJ. *J Trauma Acute Care Surg* 2013;75:669–5.

The blood bank technologists will be happy to hear that this research group from Atlanta has developed a smartphone "app" to tell trauma surgeons when they need to activate the massive transfusion protocol (MTP). Over triaging a patient to an MTP results in unnecessary preparation/wastage of plasma and cryoprecipitate, excessive cross-matching of red blood cells, mobilization of unneeded human resources (runners and on-call blood bank technologists), and possibly even results in medically unnecessary transfusions. It may even be inflating the inventory needs for red cells and thawed plasma at trauma centers. On the flip side, failure to activate the MTP early in a true massive hemorrhage situation can lead to inferior patient outcomes. We need to be able to get this right. We do have predictive tools for massive transfusion, but their widespread use is limited by their mathematical complexity (who is realistically going to complete an 8-variable Trauma Associated Severe Hemorrhage score and then put the result into a logistic equation to get the probability of massive transfusion at 2 in the morning when a patient is crashing?).

This group used data from 13 961 trauma activations, of whom 394 were treated with their hospital MTP, to develop their statistical model using a regression algorithm termed *least absolute shrinkage and selection operator* or LASSO for short. This technique "shrinks" less important variables to knock them out of the model to improve simplicity (we cannot have residents imputing 15 variables at the bedside). They used 80% of their data to train the computer and left the final 20% for validation of the model.

Of their 394 MTP activations, 77 (20%) were false alarms (they kindly termed them *early bleeder controls*). The remaining "appropriate" MTP activation patients received a mean of 23 U of red cells in the first 24 hours. These false alarm patients were less severely injured (lower injury score) and less shocky (less severe base deficit, higher blood pressure). The greatest proportion of false activations occurred with stab wounds (10/27, 37%), as compared to blunt (27/189, 14%) and gunshot injuries (40/178, 22%).

Their model was mathematically complex (lots of *e* and *ln*—complicated enough to require a degree in mathematics to compute). The model allowed incorporation of continuous variables, rather than only dichotomous variables (eg, actual heart rate rather than heart rate above or below a cut off). The trauma surgeon in the final model was only required to know 4 variables. The mechanism of injury was entered as 1 of 3 buttons (gunshot, blunt, stab). The 3 continuous variables (base deficit, heart rate, and blood pressure) were entered with a toggle bar. The risk of massive transfusion was then displayed at the bottom of the screen as an absolute percentage and as 4 risk groups (very low, low, moderate, high).

The model performance was exceptional with a very high sensitivity and specificity (area under the receiver operator curve of 0.96). The model was very good at properly predicting the false activations, with only 14% incorrectly reported as "high" risk for massive transfusion. The model was best for "ruling out" the need for massive transfusion, as compared to "ruling in," although performed far better than the available "simple" scores currently in clinical practice. What was most impressive was that the computer has the ability to readjust its model after every new trauma case recorded in the system. Every time the system is used the machine gets a little bit smarter at predicting who is likely to go on to need a massive transfusion. The group is now prospectively validating their app at their center so clearly more studies on this app will follow. I also wondered whether this app would perform as well in centers with few penetrating injuries, where 1 variable would be the same for all patients (blunt). In addition, I wonder if other variables would dominate the model in other centers, for example, at my center, we have many traumas that require more than 1 hour of transport time by air ambulance from remote areas. Let us hope these apps can be designed to learn center-specific variables for optimal performance.

The only thing I wondered about was how receptive patients, who are fortunate to be in alert in the trauma room, were to their physicians using a smartphone app. "Don't you think you should be looking after me instead of playing with your phone?", "Not to worry, I am just checking to see if we are going to have to transfuse you a lot of blood", "Shouldn't you know if I need a transfusion?", "Unfortunately my phone is vastly smarter than me when it comes to deciding this." (JC)

Potassium changes associated with blood transfusion in pediatric patients. Olson J, Talekar M, Sachdev M, et al. *Am J Clin Pathol* 2013;139:800–5.

There have been approximately a dozen case reports of transfusion-associated hyperkalemia in children. The practice of washing units for pediatric patients to prevent this complication varies among blood banks, and a number of studies measuring potassium in red cell products suggest that such manipulation is not always warranted. Olson et al add to this literature.

The authors measured potassium concentration of red cell units and segments. Hematology-oncology patients recruited for the study had their potassium level checked pretransfusion and then an hour

posttransfusion of these units. All units were prepared in AS-5 (Adsol), irradiated within 24 hours of transfusion, leukoreduced, and infused no faster than 150 mL/h. To reduce discomfort from blood sampling, all participants had central lines. Ten leukoreduced (but not irradiated) units were also selected to measure changes in potassium concentration over time. Aliquots were removed from these units every 7 days using a neonatal aliquot system to avoid puncturing the bag.

Not surprisingly, red cell unit potassium increased with day of storage from a mean concentration of 1.4 mmol/L on day 0 up to 51 mmol/L on day 42. In regard to in vivo studies, 17 products were infused into 9 patients who were 1 to 14 years old and weighed between 8.8 and 57 kg. All subjects had normal glomerular filtration rates and were transfused volumes between 140 and 450 mL.

The average 1-hour posttransfusion potassium increase was .08 mmol/L with a maximum increase of 0.5. Units had an average age of 26.5 days (38 days maximum) with an average potassium concentration of 54.9 mmol/L translating to an average of 0.6 mmol/kg infused. There was no correlation between amount of potassium infused or unit age with change in posttransfusion patient potassium result. Of note, segment potassium concentrations were significantly different than the unit values ranging up to 8.6 mmol/L higher to 28.4 mmol/L lower than the parent unit (average absolute difference of 9 mmol/L). This result serves as a reminder that what is in the segment does not always accurately reflect what is in the bag.

Checking that there was not a clinically significant higher potassium level immediately posttransfusion and including patients with abnormal renal function or other factors leading to potentially increased risk may have further helped assuage fears regarding nonwashed products. Still, the data from Olson et al and previous studies suggest that washing products to reduce potassium levels may not be necessary for all pediatric patients. Perhaps even more convincing would be larger data sets from centers that do not wash products for all pediatric transfusions and demonstration that there has not been a resulting epidemic of transfusion-related hyperkalemia.

Washing products is time consuming, may lead to cell loss, and shortens the product outdate. All centers should critically review the available literature and practice at other institutions to reach evidence-based conclusions regarding washing products for their pediatric patients. (RH)

Measuring clinical bleeding using a standardized daily report form and a computer algorithm for adjudication of WHO bleeding grades. Middelburg R A, Ypma P F, van der Meer P F et al. *Vox Sanguinis* 2013;105:144–9.

This article reinforces messages about what should be a simple objective—the measurement of bleeding in clinical studies. This is well recognized in many fields including platelet transfusion research. Anyone who now tries to review the results and compare findings between clinical studies will be struck by very different results reported for bleeding outcomes. Work has been progressing on agreement and consensus and validation of bleeding scales, for example, one published in Canada, and there is ongoing work through the Biomedical Excellence for Safer Transfusion Collaborative to try and agree on an internationally standardized case report form (CRF). This article addresses how the results from a bleeding assessment CRF can be converted into a grade or score. Traditionally, researchers might have considered an adjudication system of the CRFs by (preferably blinded and independent) researchers, but the alternative approach is to develop and test a computer algorithm. This was the approach taken in the PLADO trial and the TOPPS trial.

In this short article, the researchers for the PREPAReS study group designed and published the bleeding assessment form they were using. In this pilot study, 3 adjudicators independently assigned the bleeding grades into the WHO scoring system. Discrepancies between adjudicators were identified by the data manager, and a consensus meeting was held to then agree a final score. Alongside this work, a computer algorithm was developed and designed on the basis that any day was considered bleeding grade zero unless shown otherwise. A series of successive steps were then followed in which, depending on the data entered from the CRF into the database, the algorithm assigned grade 1, 2, 3, or 4 bleeds. Adjudication by researchers and adjudication by algorithm were then compared. Some of the results of the analysis of just over 1000 bleeding days confirmed, not surprisingly, problems of incorrect completion of CRFs. Some discrepancies between the human adjudicators (reflecting human errors) were not (correctly) identified as errors by the computer algorithm.

The authors are to be commended for publishing the details of their proposed bleeding assessment CRF and for publishing work addressing an aspect of validating the computer algorithm by comparison to human adjudication, which has traditionally been considered the criterion standard. The results are not surprising in that a computer algorithm can more consistently convert findings into a grade. The authors also indicate that there is a considerable saving on time. There are some minor queries about the strength of this study given that, for example, some higher grade bleeds were very uncommon.

For me, the main other question is whether all the information on the bleeding assessment form needs to be documented. What are the clinical significances of some of the more minor bleeds? There is remarkably little evidence in the literature to indicate whether the patient perception of the different bleeds has been considered. Obtaining consensus on the options for a minimum data set for collection of data on bleeding remain a key objective in the next year or so, which could be of immense benefit to researchers not just in the field of platelet transfusions but in other areas. For example, a bleeding assessment tool has now been published for use in the neonatal care setting. Although originally developed for use in the context of a platelet transfusion trial to neonates, a recent publication in Transfusion has shown how this could be adapted for use to assess coagulopathy and fresh frozen plasma use. No one doubts the importance of collecting some data on clinical bleeding; the question is how to do this in a uniform manner, which is more widely applicable and accepted in transfusion research. (SJS)

Cryoprecipitate use in the PROMMTT study. Holcomb JB, Fox EE, Zhang X, et al. *J Trauma Acute Care Surg* 2013;75:S31-9.

There continues to be “massive confusion” about when to give cryoprecipitate during a “massive transfusion.” Country-based reports on the use of cryoprecipitate find highly variable use and clearly unnecessary cryoprecipitate transfusions. The PRospective Observational Multicenter Major Trauma (PROMMTT) study group has published widely on a prospectively collected data set of 1245 traumas patients in 10 US level I trauma centers. This particular analysis looks at how these very large trauma centers use this blood component. Huge variability was observed; one center used it on 7% of patients, and another center used in 82% of patients. These medical technologists deserve merit awards for managing to get cryoprecipitate out for almost every patient, in addition to the other components! In general, the most common transfusion practice was to reserve this product for the very sickest of patients and to give it late in the game.

In the introduction to this report, the authors state that in the Joint Theater Trauma System, clinical practice guidelines for damage control resuscitation (US military) suggest that 10 U cryoprecipitate (or 2 g of fibrinogen concentrates) should be transfused early with the first units of red blood cells (RBCs). So I went to the US Military Institute for Surgical Research Web page and read this guideline. The guidelines state that, if the massive transfusion protocol is activated, in the first blood box with 4 RBCs also comes 10 U of cryoprecipitate