Clinical Pathology Selected Abstracts, 12/13

Clinical pathology abstracts editor: Deborah Sesok-Pizzini, MD, MBA, associate professor, Department of Pathology and Laboratory Medicine, Perelman School of Medicine, University of Pennsylvania, Philadelphia, and medical director, Blood Bank and Transfusion Medicine, Children's Hospital of Philadelphia.

Impact of blood product ratios in massively transfused pediatric trauma patients

Few studies have included pediatric patients when analyzing the impact of plasma/packed red blood cell (PRBC) ratios during massive transfusions. The implications of changing to a 1:1 plasma/PRBC ratio are significant and relate to additional product exposure, transfusion reaction-related risk, and product wastage. The evidence supporting a 1:1 ratio is largely based on retrospective studies in adults. The authors conducted a study in a level-one trauma center and included children 18 years of age and younger who required massive transfusion, defined as transfusion of 50 percent or more of total blood volume. The study, which included 6,675 trauma patients, of whom 105 were considered massively transfused, evaluated the impact of plasma and platelet ratios on mortality. The authors' findings showed that plasma/PRBC or platelet/PRBC ratios were not significantly associated with mortality. The only factor that proved to be an independent predictor of mortality was severe neurologic impairment at admission. The authors concluded that use of aggressive blood product transfusion (higher plasma/PRBC ratios) for injured pediatric patients requires further prospective evaluation. Of note in this study was that blood product ratios were not associated with increased survival. The authors also stated that in their institution, specific provisions for pediatric patients are not included in the massive transfusion protocol, and component therapy is administered based on physician preference.

Nosanov L, Inaba K, Okoye O, et al. The impact of blood product ratios in massively transfused pediatric trauma patients [published online ahead of print]. *Am J Surg.* doi:10.1016/j.amjsurg.2013.07.009.

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Integrated clinico-metabolomic model improves prediction of death from sepsis

Sepsis, an infection resulting in systemic inflammatory response syndrome, is the 10th leading cause of death in the United States. Although mortality from sepsis has decreased during the past decade due to improved treatment protocols, the appropriate treatment is not always apparent or easy to implement. For example, some patients may present with only mild clinical symptoms yet rapidly progress to a critical septic illness. Understanding the molecular processes behind sepsis may result in more appropriate treatments being deployed to patients earlier. The authors conducted a study to predict patient survival in sepsis. They examined the clinical features and plasma metabolome and proteome of patients with and without community-acquired sepsis on those patients' arrival in the emergency room and 24 hours later. The authors enrolled 1,152 patients with suspected community-acquired sepsis in the prospective trial, which ran from 2005 to 2009. They then performed metabolomic and proteome analysis measurements and developed a predictive model representative of the clinical and molecular findings and compared survivors and nonsurvivors at 28 days. The authors showed that there were robust and reproducible differences in host responses to sepsis between survivors and nonsurvivors. They noted that a molecular signature that appeared to differentiate these groups as early as the time of hospital arrival was detected. The authors concluded that a molecular signature of the energy-producing fatty acid catabolism was associated with survival in sepsis. In contrast, the metabolomes and proteomes of surviving patients with mild sepsis did not differ from those of survivors with severe sepsis or septic shock. The authors suggested that a test developed around this molecular profile may help guide decisionmaking in the emergency room.

Langley RJ, Tsalik EL, van Velkinburgh JC, et al. An integrated clinico-metabolomic model improves prediction of

death in sepsis. *Sci Transl Med.* 2013;5:1–17.

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Fecal hemoglobin concentration and severity of colorectal neoplasia

Guaiac fecal occult blood tests are used to screen patients for colorectal neoplasia. However, fecal immunochemical tests (FIT) are beginning to replace this test because they are more specific for human fecal hemoglobin concentration (f-Hb). Using a quantitative FIT, the f-Hb concentration may be used as a cutoff to select those who should undergo additional investigative measures, such as colonoscopy. A commentary published with this study suggested that there may be a continuum of increasing risk for colorectal neoplasia as the f-Hb increases from zero. The authors examined this hypothesis via an observational study assessing colonoscopy and pathology findings in patients who were above the f-Hb cutoff for FIT. This will help to determine the test's usefulness for first-line screening. The authors examined f-Hb from 38,720 subjects who ranged in age from 50 to 75 years. Additional colonoscopy findings and pathology data were collected on the 943 subjects with an f-Hb of 400 ng Hb/mL or greater. Of the 814 participants with outcome data available, 39 had cancer, 190 high-risk adenoma, and 119 low-risk adenoma. Median f-Hb concentration was higher in those subjects with cancer compared to those with no neoplasia or those with low-risk adenoma. Of interest, 74.4 percent of the subjects with cancer had an f-Hb greater than 1,000 ng Hb/mL compared with 58.4 percent with high-risk adenoma and 44.1 percent with no pathology. The authors concluded that f-Hb is related to severity of colorectal neoplastic disease in an average-risk population. Therefore, this study has implications for selecting the appropriate cut-off concentration for bowel cancer screening programs. However, the authors noted that a limitation of the study was that f-Hb could not be fully assessed since the upper analytical limit was 1,000 ng Hb/mL. This must be taken into consideration as subjects with large cancers may have had f-Hb far higher than 1,000 ng Hb/mL.

Digby J, Fraser CG, Carey FA, et al. Faecal haemoglobin concentration is related to severity of colorectal neoplasia. *J Clin Pathol.* 2013;66:415–419.

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