

Primary Fibrinolysis Lowers Trauma Survival

BY PATRICE WENDLING

FROM THE ANNUAL MEETING OF THE
AMERICAN SURGICAL ASSOCIATION

CHICAGO — Primary fibrinolysis occurs early after severe injury, and is associated with massive transfusion requirements, the presence of coagulopathy, and hemorrhage-related death.

Primary fibrinolysis also is associated with poor clot strength as measured by rapid thrombelastography “G” value, which has emerged as a rapid point-of-care test for such assessments, said Dr. Jeffrey L. Kashuk, lead author of a retrospective analysis of primary fibrinolysis.

Dr. Kashuk reported on 61 consecutive trauma patients treated at Denver Health Medical Center who required transfusion within 6 hours of admission. Penetrating injuries were present in 51% of the patients, and 52% required massive transfusion of more than 10 units. Rapid thrombelastography (r-TEG) was performed by adding tissue factor to uncitrated whole blood.

Primary fibrinolysis (PF) was identified in 11 patients, 34% of whom required massive transfusion. PF was defined by an estimated percent lysis (EPL) greater than 15%, and coagulopathy as clot strength equal to a G value of less than 5.3 dynes/cm². Transient fibrinolysis was found in 28 patients, and no fibrinolysis in 22.

PF occurred early, at a median of 58 minutes postinjury vs. a median of 104

minutes for transient fibrinolysis, said Dr. Kashuk, chief of the acute care surgery section and associate director of the Shock Trauma Center at Penn State University, Hershey.

PF was significantly associated with hypothermia in the emergency department, increased red blood cells, depressed fibrinogen at 1 hour, prolonged partial thromboplastin time in ED and, at 6 hours postinjury, increased international normalized ratio (INR) and lower hemoglobin.

All r-TEG findings were significantly associated with PF and included activated clotting time, clot formation time, alpha angle, maximum amplitude, EPL, and G value—all at a *P* value less than .0001.

A total of 64% of patients with PF died, compared with 29% with transient fibrinolysis and 18% with no fibrinolysis (*P* = .027), Dr. Kashuk said.

For every 1U drop in G-value postinjury, the risk of PF increased by more than 30% and death by more than 10%.

In logistic regression analysis, the best clinical variable to predict PF was presenting temperature in the ED, whereas INR and hemoglobin in the ED were the best laboratory predictors. Among r-TEG values, G-value—or clot strength at 1 hour—had a highly significant correlation with PF (*P* = .02), he said.

“These data warrant renewed emphasis on the precise timing and early diag-

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Major Finding: Mortality was 64% in patients with primary fibrinolysis vs. 29% in those with transient fibrinolysis and 18% with no fibrinolysis.

Data Source: A retrospective analysis of point-of-care testing for primary fibrinolysis in 61 consecutive trauma patients.

Disclosures: Dr. Kashuk and Dr. Hoyt disclosed no conflicts.

nosis of fibrinolysis in the injured patient. Such investigations could allow for timely administration of antifibrinolytic agents in this cohort,” he said.

The study is important because it takes comprehensive point-of-care testing using r-TEG to a “new level” and describes the importance and risks of primary fibrinolysis, said invited discussant Dr. David B. Hoyt, executive director of the American College of Surgeons. The findings also suggest there is a specific group of patients with a primary fibrinolytic state that occurs upon presentation and is associated with the sickest patients postinjury.

“This observation is particularly important as it could be the potential target for intervention at a time when our traditional thinking suggests that inhibition of fibrinolysis might potentially be dangerous and actually enhance coagulopathy,” he said. “This is very important work.”

Dr. Hoyt questioned what is thought to be the cause of the primary fibri-

nolytic state and how practical the r-TEG test is in most trauma centers. Dr. Kashuk said the researchers think fibrinolysis is a normal physiologic response to thrombosis that might be critical for survival under shock and low-flow states. When fibrinolysis is observed early on, it is most likely related to factors associated with shock and endothelial injury rather than to physiologic exhaustion. When consumptive coagulopathy is observed, it follows PF, suggesting that the lytic process is driving the consumption of clotting factors rather than the reverse, he said. Furthermore, because this is happening quite early, there is a window of opportunity for therapy before the consumptive state occurs.

He added that the r-TEG test (Haemonetics Inc.) seems to be the only one rapidly available to both identify and quantify fibrinolysis and that point-of-care testing has the added potential of being able to guide therapy.

Hemorrhagic shock accounts for 50% of deaths worldwide from trauma via exsanguination or postinjury coagulopathy. The mechanistic link between PF and acute coagulopathy of trauma remains to be clearly elucidated, even though the association between PF and shock has been recognized for more than 100 years.

“Fibrinolysis is a complex process, and r-TEG provides us with a blueprint of the clotting process to help decipher this,” Dr. Kashuk said. ■

Rapid Lymphopenia Recovery Predicts Better Outcome

VITALS

Major Finding: Trauma patients who developed lymphopenia within hours of their injury, followed by recovery of their blood lymphocyte level within 4 days of an injury, had a significantly lower mortality rate, 13%, than did patients who did not have a quick blood lymphocyte recovery (22%) or did not have the early drop in blood lymphocytes (18%).

Data Source: Review of prospectively collected data from 2,448 trauma patients at a U.S. trauma center September 2003-September 2008.

Disclosures: Dr. Heffernan said that he and his associates had no disclosures.

BY MITCHEL L. ZOLER

FROM THE SURGICAL INFECTION SOCIETY ANNUAL MEETING

LAS VEGAS — Trauma patients who developed lymphopenia within hours of an injury but recovered their lymphocyte counts over the next 4 days had a better survival rate than patients whose blood lymphocyte levels followed different patterns, a review of more than 2,400 trauma patients treated at one U.S. center found.

“Lymphocytes are not just bystanders following trauma. Persistent lymphopenia [without recovery] was associated with higher mortality and shorter time to death,” Dr. Daithi S. Heffernan said at the annual meeting.

The findings, derived from what he called “the first report detailing the lymphocyte profile in a large trauma population,” suggest that intervention may help patients who fail to recover quickly from lymphopenia. The results also raise the possibility that measuring lym-

phopenia might be a quick and easy way for physicians to assess trauma patients and predict their acute course.

Dr. Heffernan, a trauma surgeon at Rhode Island Hospital and Brown University, Providence, and his colleagues reviewed data prospectively collected from 2,448 patients seen at the Rhode Island Hospital trauma center from September 2003 to September 2008 who survived for at least 3 days and had an Injury Severity Score (ISS) of at least 15 but not as high as 75. Their average age was 52 years, their average ISS was 23, and their average head Abbreviated Injury Scale (AIS) score was 3.8. Two-thirds of the patients were men.

The researchers divided the patients into three groups: 792 who developed early lymphopenia that resolved back to normal over the first 4 days following injury, 817 patients who developed early lymphopenia that did not resolve during those days, and 839 patients who did not have early lymphopenia. The patients with early lymphopenia that then resolved were significantly younger (average age 46 years) and had higher ISS (average 25) and lower head AIS scores (average 3.5) than did the other patients.

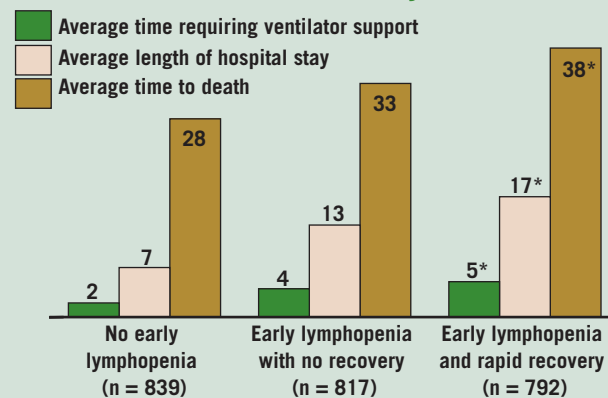
Poorer survival extended not only to patients whose lymphocyte counts failed to recover in 4 days but also to those whose lymphocyte counts never dipped in the hours following traumatic injury. Mortality rates were 13% for patients with early lymphopenia that resolved quickly, 22% for those whose lymphopenia never recovered, and 18% for those who didn’t experience lymphocyte declines. The group

whose lymphopenia resolved also had a significantly longer time to death than did the other patients.

“I don’t think that failure to recover the lymphocyte count is just a marker. It’s a contributing factor” to a poor outcome, Dr. Heffernan said. Lymphocyte concentration in blood usually falls after trauma because the cells “are doing their job,” leaving the bloodstream and entering damaged tissues, he explained. The normal response is for these cells to be quickly replaced by new lymphocytes from bone marrow. “If you can’t get new cells, you can’t fight infection,” Dr. Heffernan said.

“This may help physicians get patients to the ICU earlier. When lymphocyte counts fail to normalize, physicians could know the patient is in trouble.” ■

Quick Lymphopenia Recovery Extends Survival After Trauma (Days)



* Statistically significant difference from comparison groups.
Source: Dr. Heffernan