Evaluation of the Relationship Between Fractures and Hyponatremia

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Purpose: Hyponatremia is frequently present in the elderly population. Recent studies show an increased risk of fractures in patients with mild chronic hyponatremia. Hyponatremia upregulates osteoclast-mediated bone resorption. Our study evaluates the relationship between hyponatremia and risk of incident fracture while controlling for bone density, age, and sex.

Methods: A retrospective, matched case-controlled study was performed. Patients ≥45 years old with dual-energy x-ray absorptiometry (DEXA_ scans and serum sodium obtained within a year prior to event of interest (fracture/nonfracture complaint) were included**.** Cases were defined as patients with an incident fracture (vertebra, femur/hip, tibia/fibula, and forearm) between January 2005 and May 2013. The first fracture was used for cases with multiple fractures. Controls were defined as patients with a nonfracture complaint over the same time period, matched 2:1 with cases on age (within 2 years) and sex. Data on disease modifiers including medications and disease conditions that could influence sodium levels and osteoporosis risk were also obtained. Hyponatremia was defined as: absent (>137 mmol/L), low-normal (135-137 mmol/L), mild (130-134 mmol/L), or moderate-severe (<130 mmol/L). Bone density classification was defined as: osteopenia = T-score –1.0 to –2.5, and osteoporosis = T-score <–2.5; univariate and multivariate conditional logistic regression models were used to estimate risk of fracture with hyponatremia and bone density. Odds ratios (ORs) and 95% confidence intervals (CIs) were calculated. ll statistical analysis was performed using SAS v9.3. All tests were two-sided with alpha = 0.05.

Results: We identified 457 cases and 914 controls. Mean age was 73 ± 10 years old and 89% females. Hyponatremia was more prevalent in cases compared to the controls. Univariate logistic regression models showed a significantly higher risk of fracture in hyponatremia ($P < 0.0001$) and osteoporosis/osteopenia ($P < 0.0001$). Vertebral fractures were associated with worsening hyponatremia, compared to nonvertebral fractures (χ^2, $P = 0.0002$). A similar pattern was observed in femur fractures when compared to other nonvertebral fractures (χ^2, $P = 0.04$). On multivariate analysis, controlling for presence of known disease modifiers, the risk was 3-fold higher in mild (OR 3.0; 95% CI: 2.2, 4.2), 4-fold higher in moderate (OR 4.4; 95% CI: 2.8, 7.0) and 11-fold higher in severe hyponatremia (OR 11.1; 95% CI: 4.1, 30.5). A reverse trend was seen among patients with forearm and tibia/fibula fractures who tended to be younger.

Conclusion: Our study shows an increased risk of fractures in patients with varying degrees of hyponatremia irrespective of radiologic bone density changes. In addition the risk of fracture appeared to increase with worsening hyponatremia while controlling for known disease modifiers. This highlights the importance of recognizing and managing hyponatremia and its associated morbidity including fractures.

See pages 99 - 147 for financial disclosure information.

Can Thrombelastography Predict Venous Thromboembolic Events in Patients with Severe Extremity Trauma?

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Background/Purpose: Despite increased bleeding risk during the acute trauma resuscitation, trauma-induced coagulopathy is associated with greater likelihood of hypercoagulability, and eventual venous thromboembolic events (VTEs). Rapid thrombelastography (r-TEG) is a whole-blood assay that identifies both hypo- and hypercoagulable states. Graphical r-TEG results are available within minutes, correlate with conventional coagulation laboratory values, and predict early transfusion requirements. In addition, an elevated maximal amplitude (mA) value on admission can identify general trauma patients with increased risk of VTE. We hypothesized that (1) the risk of VTE traditionally assigned to injury lies specifically in those who sustain major orthopaedic trauma, and (2) an elevated admission mA value could be used to identify patients with major orthopaedic injuries at risk for VTE during initial hospital admission.

Methods: This is a retrospective review of a prospectively collected database of 9090 consecutive trauma patients admitted to an urban Level I trauma center between September 2009 and February 2011. We then evaluated only those patients who met highest-level trauma activation criteria, were 18-85 years of age, and were direct scene transports. Patients with burn wounds greater than 20% total body surface area or who died within 30 minutes of arrival were excluded. Two groups were created, one whose extremity abbreviated injury severity (AIS) score was 2 or greater (ORTHO) and one whose extremity AIS score was <2 (non-ORTHO). VTEs were defined as those pulmonary emboli confirmed by CT angiography and those symptomatic deep vein thromboses confirmed by venous duplex. Univariate analyses were conducted followed by purposeful regression analysis.

Results: 1818 patients met the inclusion criteria (310 ORTHO, 1508 non-ORTHO). While there was no difference in median age (32 vs. 34), ORTHO patients were more likely to be female (29% vs. 21%), white (62% vs. 54%), and blunt trauma (89% vs. 73%); all $P < 0.05$. With the exception of median extremity AIS (3 vs. 0, $P < 0.001$), there were no differences in individual systems AIS scores. ORTHO patients had lower systolic blood pressure (115 vs. 130), higher pulse (107 vs. 95), and worse base deficit (–5 vs. –2) on arrival; all $P < 0.05$. Despite more hypocoagulable r-TEG values on arrival (alpha angle 71 vs. 73 and mA 62 vs. 64, both $P < 0.05$), ORTHO patients had higher rates of VTE (6.5% vs. 2.7%, p<0.001). Time to VTE was similar (5.5 days vs. 5.5 days). Stepwise regression generated four values to predict development of VTE (age, male gender, white race, and ORTHO). After controlling for these variables, admission mA of ³65 (odds ratio 3.66) and ³72 (odds ratio 6.70) were independent predictors of VTEs during hospitalization.

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Conclusion: Admission r-TEG mA values can identify patients with major orthopaedic trauma injuries who present with an increased risk of in-hospital deep vein thrombosis and pulmonary embolism. Patients presenting with admission r-TEG mA value of ³65 are at a 3.6-fold increased risk (and those with mA ³72 at a 6.7-fold risk) for in-hospital VTE. Admission r-TEG values can help to identify patients at greatest risk for VTE and best target those who might benefit from an early, aggressive prophylaxis strategy.

See pages 99 - 147 for financial disclosure information.

Prediction of Pulmonary Embolism in Trauma Patients: A Risk Assessment Model Based Upon 38,000 Patients

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Purpose: Pulmonary embolism (PE) is a rare but sometimes fatal complication of trauma. Many studies have identified risk factors and developed risk stratification models to identify patients at an increased risk of venous thromboembolism; however, they are often complex and difficult to use. The purpose of this research is to develop a risk assessment model, based upon a large sample of trauma patients, which can be easily and quickly used at the time of admission to predict PE.

Methods: Our institutional trauma registry was queried. The National Trauma Registry of the American College of Surgeons (NTRACS) registry system collects voluminous data on each patient registered. We targeted the following information: demographic and injury data, prehospital information, and data on treatments and events during hospitalization. Out of 49,604 patients admitted to our trauma center from 2000-2012, 11,007 (22%) were excluded due to incomplete data. This study used trauma registry data from the remaining 38,597 trauma patients. Of these patients, 239 (0.619%) developed a PE. A multivariate binary logistic regression model was developed to predict the likelihood of developing a PE during each patient's hospitalization. The logistic regression model was developed using a 50%, randomly selected development subsample, and then tested for accuracy of prediction using the remaining 50% validation sample. The two random subsamples did not differ with respect to any demographic, injury, prehospital, or hospital treatment variables examined.

Results: Results from this study suggest there are seven statistically significant predictors of PE, including age, obesity, injury resulting from motorcycle accident, arrival to hospital by helicopter or ambulance, pulse rate upon arrival in emergency room, admission to ICU, and location of injury (thorax, abdomen, and lower extremity). Comparison of predicted PE events to actual PE events resulted in high sensitivity (82%) and specificity (75%). The comparison of odds ratios in the model development and validation samples was nonsignificant ($P = 0.4032$), indicating that predictions from the model do not differ between the two samples.

Conclusion: Using this model, based on data available upon admission, we were able to correctly predict 88.9% of the pulmonary emboli within the top 35% of the model score distribution of our validation subsample. This knowledge will allow us to focus more stringent and earlier thromboprophylactic efforts on those patients at highest risk for PE. In the future, this model will be used to develop an application suitable for smart phone devices, to allow physicians easy and accurate identification of trauma patients at high risk for the development of PE.

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