Injury, Int. J. Care Injured xxx (2016) xxx–xxx

Contents lists available at ScienceDirect

Injury

journal homepage: www.elsevier.com/locate/injury

Thrombocytosis in splenic trauma: In-hospital course and association with venous thromboembolism

Tze L. Chia, MD[a,1], Tyler R. Chesney, MD MSc[b,1], David Isa, MD[c], Gevork Mnatzakanian, MD[a], Errol Colak, MD[a], Caio Belmont, MD[d], Dhruvin Hirpara, BHSc[e], Precilla V. Veigas, PhD[f], Sergio A. Acuna, MD[g], Sandro Rizoli, MD PhD[b], Joao Rezende-Neto, MD PhD[b,*]

[a] Department of Medical Imaging, St. Michael's Hospital, Toronto, Canada
[b] Department of Surgery, University of Toronto, Toronto, Canada
[c] Division of General Surgery, St. Michael's Hospital, Toronto, Canada
[d] Federal University of Juiz de Fora, Juiz de Fora, Brazil
[e] Institute of Health Policy, Management and Education, University of Toronto, Toronto, Canada
[f] Institute of Medical Science, University of Toronto, Toronto, Canada
[g] Li Ka Shing Knowledge Institute at St. Michael's Hospital, Toronto, Canada

ARTICLE INFO

Keywords:
Trauma
Splenic injury
Platelets
Splenectomy
Thrombocytosis
Venous thromboembolism
Non-operative management
Embolization
Acetylsalicylic acid

ABSTRACT

Introduction: Thrombocytosis is common following elective splenectomy and major trauma. However, little is known about the in-hospital course of platelet count (PC) and incidence of thrombocytosis after splenic trauma. Extreme thrombocytosis ($PC > 1000 \times 10^9$) is associated with increased risk of venous thromboembolism (VTE) in primary thrombocytosis leading to the use of acetylsalicylic acid (ASA) for risk reduction, but the need for this agent in splenic trauma is undefined.

Methods: Retrospective cohort study of all patients with splenic trauma between April 1, 2010 and March 31, 2014. The in-hospital course of PC was assessed based on splenic injury management type. The association of management type with thrombocytosis was evaluated using a multivariable logistic regression model adjusting for potential confounders. The association of thrombocytosis, extreme thrombocytosis, and ASA use for the outcome of VTE was explored.

Results: 156 patients were eligible, PC initially increased in all patients with the highest peak after total splenectomy. The incidence of thrombocytosis was 41.0% (64/156). Thrombocytosis was more likely following splenectomy compared with spleen preserving strategies independent of length of stay, injury grade, ISS, age and transfusion (OR 7.58, 95% CI: 2.26–25.45). Splenectomy was associated with extreme thrombocytosis (OR 10.39, 95% CI: 3.59–30.07).

Conclusions: Thrombocytosis in splenic trauma is more likely after splenectomy than with spleen preserving strategies. Splenectomy is associated with extreme thrombocytosis. There was insufficient data in our study to determine the use of ASA as primary prevention of VTE after splenic trauma.

Introduction

Splenic injury is the commonest solid organ injury following blunt abdominal trauma [1]. The management of splenic trauma ranges from total splenectomy to various spleen preserving strategies including nonoperative management, angioembolization, splenhorrhaphy and partial splenectomy [2,3]. The association of major trauma, splenic injury, and splenectomy with thrombocytosis and thrombotic complications is complex and unclear.

Thrombocytosis, defined as a platelet count (PC) $> 500 \times 10^9$/L, is divided into primary thrombocytosis due to myeloproliferative disorders, and reactive thrombocytosis, which accounts for 80–90% of cases [4]. Reactive thrombocytosis occurs in transient processes such as acute blood loss, infection, and inflammation; or in sustained processes such as iron deficiency, chronic inflammatory disorders, cancer, and asplenia [4–6]. Reactive thrombocytosis is common following elective or urgent splenectomy, but there is a

* Corresponding author. Address: 30 Bond Street, Donnelly Wing Room 3074, St. Michael's Hospital, Toronto, Canada.
E-mail address: rezendenetoj@smh.ca (J. Rezende-Neto).
[1] These authors contributed equally to this publication

http://dx.doi.org/10.1016/j.injury.2016.07.016
0020-1383/

20–30% incidence of thrombocytosis following major trauma regardless of splenectomy [4,7–13].

The risk of venous thromboembolism (VTE) associated with thrombocytosis is complex. Primary thrombocytosis is clearly associated with thrombotic complications in myleloproliforative disorders [10,14–16]. A descriptive cohort identified post-splenectomy reactive thrombocytosis as a possible risk factor for portal vein thrombosis [17]. However, the pathogenesis of VTE following trauma is multifactorial. Therefore, even though reactive thrombocytosis may play a role in the development of VTE in trauma, most available evidence does not support an independent association between reactive thrombocytosis and thrombotic complications [5,8,9,11,12,18].

Extreme thrombocytosis (ET), defined as a PC > 1000×10^9/L, has been thought to impart even greater risk of thrombotic complications [19–21]. Extreme thrombocytosis is more frequently associated with reactive thrombocytosis (66–82%) than with primary thrombocytosis [20,22]. Splenectomy accounts for approximately 20% of ET cases [20]. The incidence of ET after major trauma is 1%, and the rate of subsequent VTE is 4% [11,23]. Higher rates of thrombotic complications in ET secondary to myeloproliferative disorders [20,22]. Therefore, platelet-cytoreductive therapy in that setting is recommended [4]. However, the efficacy of antiplatelet therapies, such as acetylsalicylic acid (ASA) or clopidogrel, as primary prevention of VTE in low-risk, asymptomatic splenic trauma patients with reactive thrombocytosis and ET is unknown.

The primary objectives of our study were to demonstrate the in-hospital course of PC following distinct management strategies of splenic injuries and to evaluate the association of these strategies with thrombocytosis. We verified whether the effect of treatment strategy on thrombocytosis was independent of injury severity, length of stay (LOS), splenic injury grade, age, and receipt of blood transfusion. Secondary objectives were to evaluate the association of treatment strategy with extreme thrombocytosis and VTE, and to evaluate the association of thrombocytosis, extreme thrombocytosis and ASA administration with VTE following spleen trauma independent of treatment strategy.

Methods

Study design and data sources

This retrospective cohort study used trauma registry data from a Level-1 Trauma Centre. The trauma registry prospectively collects data on all trauma activations from standardized trauma records and the electronic medical record. Medical records, including surgical and radiological reports, were reviewed to verify data for all included patients. The St. Michael's Hospital Research Ethics Board approved this research (REB 14-292).

Patients

All patients who sustained splenic trauma from April 1, 2010 to March 31, 2014 were included. Patients younger than 18 years of age, on therapeutic anticoagulation or with known coagulopathy, hematologic disorder, or pregnancy were excluded. All patients received VTE chemoprophylaxis in the form of low molecular weight heparin unless contraindicated.

Data were collected on age, sex, Glasgow Coma Scale (GCS) score, ICU LOS, total hospital LOS from the medical record. ASA administration dates were collected from the Medication Administration Record. Selection criteria for ASA administration include preadmission use, acute coronary syndrome, and vascular injury managed nonoperatively. The Injury Severity Score (ISS) was used to define the severity of trauma [24]. The Abbreviated Injury Scale (AIS) for extremity as well as the proportion of pelvic and femur fractures were collected. The American Association for the Surgery of Trauma Organ Injury Scaling (AAST-OIS) was used to grade splenic injuries [25]. For this, a blinded radiologist retrospectively reviewed all admission CT scans, which used a standardized contrast-enhanced CT examination in a 16-slice multidetector CT scanner (Lightspeed, GE Healthcare, Little Chalfont, UK). Patients with immediate indications for laparotomy did not receive admission CT scans and splenic injury was graded intraoperatively.

Splenic injury management

Splenic injuries were managed using the following strategies: nonoperative management, angioembolization, splenorrhaphy, partial splenectomy, and total splenectomy. These were grouped into two groups: (1) spleen preserving strategy, including nonoperative management, angioembolization, splenorrhaphy, and partial splenectomy; and (2) total splenectomy, the non-spleen preserving strategy, which included those that underwent splenectomy directly from admission or after failure of nonoperative management.

Outcomes

Platelets were measured by impedance (Coulter LH 780 Analyzer, Beckman Coulter, Breas, CA). Platelet counts were assessed daily on each patient beginning at the time of presentation to the trauma bay and followed during the index hospital admission (median 10 days, interquartile range (IQR) 5–22.5 days). Due the retrospective nature of this study, some patients did not have PC measured on some hospital days. 109 patients (69.9%) of patients had no missing PC data. For the 47 patients with missing PC data, this was missing from a median of 2 days (IQR 1–4). Thrombocytosis was defined as PC > 500×10^9/L, and extreme thrombocytosis was defined as PC > 1000×10^9/L.

Diagnosis of VTE was by diagnostic imaging. No screening protocol for VTE was used. Patients received in-hospital imaging to investigate for VTE based on clinical indicators as determined by the treating physician. Pulmonary emboli were confirmed on CT, and upper and lower extremity deep venous thrombosis confirmed on Doppler ultrasound. The composite outcome of VTE included pulmonary embolism, and upper and lower extremity deep venous thrombosis.

Statistical analysis

Patients treated with total splenectomy were compared to patients treated with spleen preserving strategies. Patient characteristics were presented as percentages for categorical variables and as median and interquartile range for continuous variables not normally distributed. Shapiro-Wilk test was used for normality testing. Differences between treatment groups were tested using Chi-square with Yate's correction for continuity for categorical variables and Wilcoxon Rank-Sum Test for continuous variables not normally distributed.

For the primary outcome of thrombocytosis unadjusted odds ratios and 95% confidence intervals (CI) were estimated. A multivariable logistic regression was used to adjust for potential confounders that were determined in advance. Potential confounders included hospital LOS, splenic injury grade, ISS, age, and transfusion. For this analysis, ISS was dichotomized into severe (score >21) or not severe (score of 21 or less). Age was dichotomized using a cutoff of 55. This age was chosen as older guidelines suggested that age greater than 55 years was a contraindication to nonoperative management of blunt splenic injury [2]. Splenic injury grade was grouped into low grade (grade

Please cite this article in press as: T.L. Chia, et al., Thrombocytosis in splenic trauma: In-hospital course and association with venous thromboembolism, Injury (2016), http://dx.doi.org/10.1016/j.injury.2016.07.016