Article

The American Surgeon
00(0) 1–5

DOI: 10.1177/0003134820950303
journals.sagepub.com/home/asu
SAGE

Administering DVT Prophylaxis Sooner Than 48 Hours Does Not Increase Failure of Nonoperative Management of High-Grade (Grades III-V) Splenic Injuries

Jared Griffard, MD[1], Bethany Sappington, MD[1], Megan Griffard, MEd, MSJ[1], Reagan Bollig, MD[1], James McMillen, PharmD, MBA[1], Amanda McKinney, PharmD[1], Lou Smith, MD[1], and Brian Daley, MD, MBA[1]

Abstract

Splenic injuries are mostly treated with nonoperative management (NOM) with observation to monitor for continued hemorrhage and holding early chemical DVT prophylaxis to reduce the risk of NOM failure. Eberle et al demonstrated chemoprophylaxis prior to 72 hours didn't increase failure rate of NOM. We chose to extrapolate this finding and compare outcomes in high-grade splenic injuries (HGSI) with chemoprophylaxis before and after 48 hours. From January 2013 to December 2017, 104 patients with HGSI received chemoprophylaxis with unfractionated heparin (UH) or low molecular weight heparin (LMWH) within 72 hours of diagnosis. Of these, 8 patients received chemoprophylaxis within 24 hours, 46 between 24 and 48 hours, and 50 patients between 48 and 72 hours. This population consisted of 70 males and 34 females, with an average age of 40.1 years. The average ISS was 23 and the majority (77%) were grade 3 injuries. We observed 6 failures of NOM: 1 in the <24 hour group, 3 in the 24-48 hour group, and 2 in the 48-72 hour group. There was no statistically significant difference between the <24 hour and >24 groups or between the <48 hour and 48-72 hour groups. A linear regression analysis created a model describing the time to initiation of DVT prophylaxis using age, sex, splenic injury grade, and ISS; the failure rate decreased by 0.00002% for each hour prior to giving DVT prophylaxis, with a *P* value of .111. We conclude a noninferiority statement that DVT prophylaxis prior to 48 hours does not increase the risk of NOM failure.

Keywords
DVT prophylaxis, nonoperative management, high-grade splenic injuries

Background

Abdominal trauma contributes a significant amount to healthcare-associated costs both in the US and worldwide, with 30% of polytraumatized patients having an intra-abdominal injury.[1] Of these injuries, more than half of them involve the spleen, and more than 40 000 splenic injuries occur annually in the US.[2] If the patient is hemodynamically stable and has no evidence of ongoing bleeding, the standard treatment is observational with nonoperative management (NOM).[3,4] Based on current literature, the success rate of NOM approaches 90% in most trauma populations.[5] One of the primary goals assessed by observation in NOM is the absence of ongoing bleeding and allowing the injury to form a clot and heal spontaneously. However, this is in direct opposition to preventing deep venous thrombosis (DVT) or pulmonary embolism in trauma patients.

Trauma populations have been extensively studied and are known to enter a hypercoagulable state secondary to

[1]University of Tennessee Medical Center Knoxville, Knoxville, TN, USA

Corresponding Author:
Jared Griffard, MD, University of Tennessee Medical Center Knoxville, 1954 Alcoa Highway, Knoxville, TN 37920, USA.
Email: jgriffard@utmck.edu

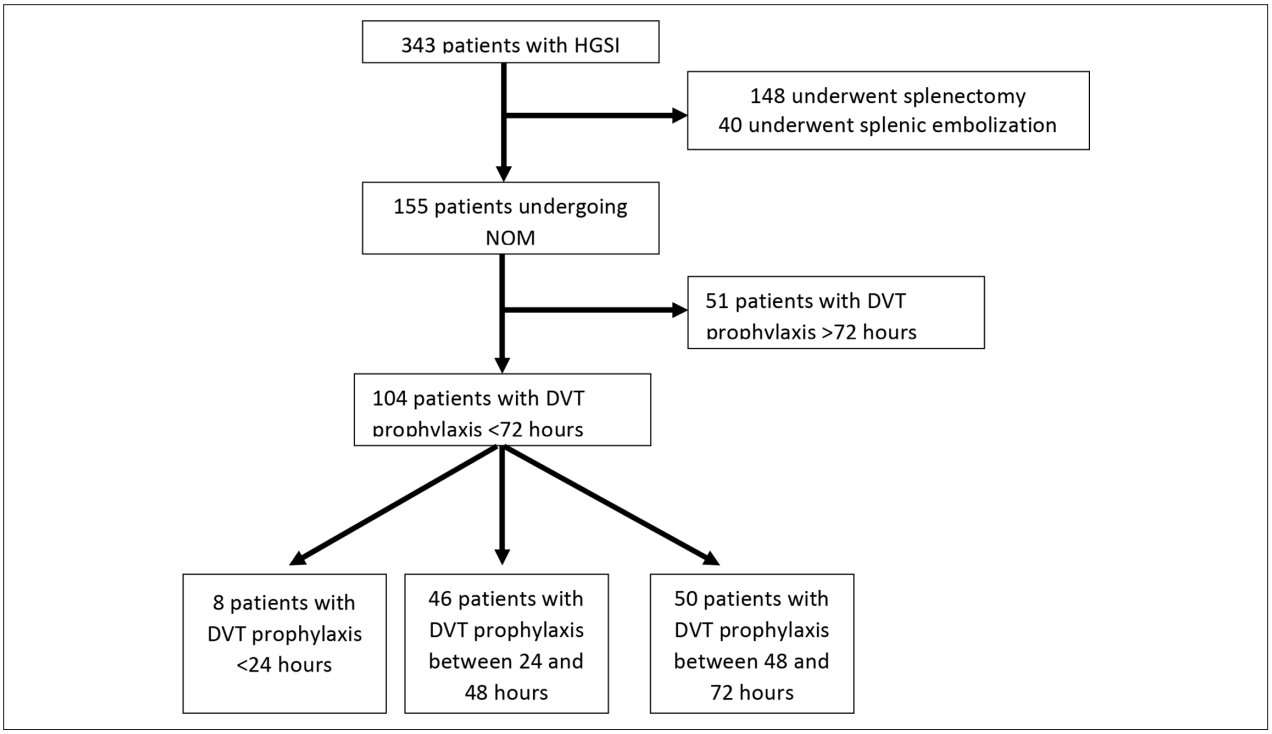

Figure 1. Table 1 Study outline. DVT, deep venousthrombosis; HGSI, high-grade splenic injuries; NOM, nonoperative management.

alterations in Virchow's triad, with rates of DVT cited as 12%-65%.[6] A Cochrane review found that chemical prophylaxis for DVTs with either unfractionated heparin (UH) or low molecular weight heparin (LMWH) reduced the number of DVTs in trauma populations, but did not demonstrate a decrease in mortality or incidence of pulmonary embolism.[7] This supports current guidelines from Eastern Association for the Surgery for Trauma and American College of Chest Physicians recommending thromboprophylaxis in trauma patients. However, the timing of initiation of thromboprophylaxis has not been determined. Eberle et al demonstrated that initiating LMWH before 72 hours did not increase the failure rate of NOM or blood transfusion requirements.[8] This was consistent with a previous analysis that compared early initiation within 48 hours to later initiation after 48 hours.[9]

Due to the paucity of studies evaluating the initiation of chemical thromboprophylaxis, we chose to change our institutional protocols and evaluate our patient population to determine if <48 hours from initial trauma was a safe time period for initiating chemical thromboprophylaxis. We specifically examined outcomes for high-grade splenic injuries (HGSI), grade 3-5, as they are at higher risk of NOM failure. We hypothesized that initiating chemical thromboprophylaxis with either LMWH or UH in patients less than 48 hours after initial trauma in patients with HGSI would not increase the failure rate of NOM.

Methods

Patient Selection

We changed our institution's protocol in January 2013 of holding DVT prophylaxis with either UH or LMWH in patients with HGSI for 72 hours after injury to an abbreviated time frame of less than 48 hours after injury if they were medically cleared to receive DVT prophylaxis, or sooner if determined clinically appropriate by the attending surgeon. Concurrently, a 4-year nonrandomized open study was conducted on patients with the abbreviated DVT prophylaxis protocol. These patients were collected prospectively through our institution's trauma quality improvement program (TQIP) database based on the following criteria: splenic injury grades 3-5 diagnosed on computed tomography (CT) scan, aged 18-99. The amount of anatomical disruption and hemorrhage was not quantified for inclusion into this study.

Exclusion Criteria

We excluded patients with grades 1-2 splenic injuries diagnosed on diagnostic imaging and patients who were taken immediately to the operating room or interventional radiology, defined as within 4 hours of arrival to the hospital.

Table 1. Estimates for Failure Rates of Spleen DVT for Time of Treatment.

	Model number				
	(1)	(2)	(3)	(4)	(5) Robust
Time	–.0008273	–.0024982	–.0022571	–.002243	–.002243
	(.0007724)	(.0016056)	(.0015315)	(.0015359)	(.0013943)
Age, years		.0019004	.0017008	.0016501	.0016501
		(.0013489)	(.0012866)	(.0012925)	(.0011868)
Sex (1 = male, 0 = female)		.0129402	.0405433	.0400967	.0400967
		(.049191)	(.0475913)	(.0477305)	(.0532192)
Injury grade			.1192958	.1077483	.1077483
			(.0357147)	(.0397997)	(.0564186)
ISS				.001545	.001545
				(.0023222)	(.0023802)
Constant	.1004816	.088422	–.3347917	–.3299467	–.3299467
	(.0472741)	(.088422)	(.1574912)	(.1581042)	0.2176346
N	104	104	104	104	104
R^2	.02	.04	.14	.14	.14

Abbreviations: DVT, deep venous thrombosis; ISS, Injury Severity Score.

Study Design

All patients with HGSI who are hemodynamically stable (vital signs consistent with grade I hemorrhagic shock) were admitted with a NOM protocol that included intensive care unit (ICU) observation, frequent laboratory monitoring, close clinical monitoring, and physical examination. Depending on their other traumatic injuries, they would be eligible to receive DVT prophylaxis after 48 hours if they remained hemodynamically stable and their laboratory and clinical exam did not warrant interventional procedures to treat continued splenic hemorrhage. If they remained clinically and hemodynamically stable, then they were discharged after at least 72 hours of observation in the hospital with close clinic follow-up (Figure 1).

Our primary endpoint was failure of NOM in patients who had already received DVT prophylaxis, and we compared 2 population groups in our initial patient population: patients who received DVT prophylaxis less than 48 hours after injury and patients who received DVT prophylaxis later than 48 hours after injury. Our secondary endpoints were age, average injury severity score (ISS), splenic grades, and gender. We defined failure of NOM as operative or interventional radiology procedures greater than 6 hours after admission to the hospital.

Statistical Analysis

Statistical significance ($P < .05$) was tested through both a t test analysis and χ^2 analysis comparing the failure rates between patients who received DVT prophylaxis within 48 hours of admission and those who received it between 48 and 72 hours. Similar analyses were conducted comparing the failure rates between patients receiving DVT prophylaxis less than 24 hours, between 24 and 48 hours, and between 48 and 72 hours. Failure of NOM was defined as a patient requiring a splenectomy or splenic artery embolization. Lastly, a simple linear regression was used to create a model to describe the time to initiation of DVT prophylaxis, using age, sex, splenic injury grade, and ISS as covariates. This analysis was performed with STATA software.

Results

During our study period of January 2014 to July 2017, a total of 343 patients were identified with HGSI; 148 (43.1%) proceeded to splenectomy within 4 hours of admission, and 40 (11.7%) of them proceeded to splenic artery embolization by our interventional radiology colleagues. This resulted in 155 patients (45.2%) remaining in the initially managed NOM group. This group was further separated into a group that received DVT prophylaxis within 72 hours and a group receiving DVT prophylaxis after 72 hours, as we wanted to focus on earlier initiation of DVT prophylaxis. The group who received DVT prophylaxis within 72 hours of admission resulted in 104 patients; 8 patients received DVT prophylaxis within 24 hours of admission, 46 patients between 24 and 48 hours, and 50 patients between 48 and 72 hours. The decision for the timing of initiation was based on the patient's clinical picture and the discretion of the attending surgeon.

Our patient population consisted of 104 patients who received DVT prophylaxis less than 72 hours from diagnosis of a HGSI, 70 (67.3%) were males and 34 (32.7%) were females. The average age was 40.1 years old; the average age for males was 38.9 years and the average age for females was 42.5 years. The average ISS was 23, and the average splenic injury grade was 3.37. There were 74 (71.1%) grade 3 splenic injuries, 22 (21.2%) grade 4 splenic injuries, and 8 (7.7%) grade 5 splenic injuries.

The failures consisted of 1 (12.5%) patient in the <24-hour group, 3 (6.5%) in the 24-48-hour group, and 2 (4%) in the 48-72-hour group. A t test analysis of the failure rates between the <24-hour group and the >24 hour group were not statistically significant (*P* value of .40). In comparing the failure rates of patients receiving DVT prophylaxis in less than 48 hours and between 48 and 72 hours, there was a failure rate of 7% and 4%, respectively.

A chi square analysis of the failure rates between patients receiving DVT prophylaxis <48 hours and between 48 and 72 hours demonstrated a *P* value of .457. The failure rates of patients receiving DVT prophylaxis <24 hours and >24 hours were also not statistically significantly different (*P* value of .395).

A linear regression analysis was performed, creating a model for the estimates for failure rates using age, sex, injury grade, and ISS as covariates. The fifth model created demonstrated an R^2 of 0.14, and identified a decrease in failure rate by .0002% for each hour that passed prior to giving DVT prophylaxis, with a *P* value of .111. (Table 1)

Discussion

This study evaluated the safety of DVT prophylaxis in HGSI in less than 48 hours. Through statistical analyses, we demonstrated that there was no statistically significant difference between failure rates of patients receiving DVT prophylaxis in less than 48 hours and 48-72 hours. From this, we propose a noninferiority statement that initiation of DVT prophylaxis within 48 hours does not increase the rate of failure when compared to patients receiving DVT prophylaxis between 48 and 72 hours. We split our patient population into a subgroup and evaluated the rate of failure in patients who had DVT prophylaxis initiated in less than 24 hours compared to those initiated between 24 and 72 hours, and this also resulted in a non-statistically significant difference.

Our linear regression model demonstrated that the rate of failure only decreased by .002% for each hour that passed prior to initiating DVT prophylaxis in HGSI. This suggests that the timing of DVT prophylaxis initiation is not strongly correlated with increased rate of failure and implies that there is a negligible difference prolonging DVT prophylaxis initiation to 48 hours or later.

One of the limitations in our study is our sample size. With only 104 patients, it limits our ability to generalize it to the trauma population as a whole. The low rate of failures after initiating DVT prophylaxis observed at our institution also limits the power of our study. Further studies can continue to observe a larger sample size of patients to elucidate the true safety of initiating DVT prophylaxis prior to 48 hours, and even within 24 hours of injury.

Another limitation is the selection bias created by determining failure of NOM based on procedural intervention, which was determined based on the surgeon's decision to pursue such measures. These decisions were not made based on specific criteria endpoints, but rather based on the patient presentation as a whole with their vital signs and laboratory values, leading to variability in timing and occurrence of interventions.

Our findings correlate and reaffirm those previously documented by Alejandro et al[9] and similar results in the literature.[10,11] Based on these studies and our own data, we suggest that DVT prophylaxis can be safely given to patients with HGSI prior to 48 hours after injury. We also postulate that it might be safe to give within 24 hours of injury, but this requires further research to evaluate, as we had a small sample size for the <24 hour group.

Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

The author(s) received no financial support for the research, authorship, and/or publication of this article.

References

1. Raza M, Abbas Y, Devi V, et al. Non operative management of abdominal trauma - a 10 years review. *World J Emerg Surg*. 2013;8(1):14. doi:10.1186/1749-7922-8-14
2. Zarzaur BL, Kozar R, Myers JG, et al. The splenic injury outcomes trial: an American association for the surgery of trauma multi-institutional study. *J Trauma Acute Care Surg*. 2015;79(3):335-342. doi:10.1097/TA.0000000000000782
3. Pothmann CEM, Sprengel K, Alkadhi H, et al. Abdominal injuries in polytraumatized adults:systematic review. *Unfallchirurg*. 2018;121(2):159-173. doi:10.1007/s00113-017-0456-5
4. Coccolini F, Montori G, Catena F, et al. Splenic trauma: WSES classification and guidelines for adult and pediatric patients. *World J Emerg Surg*. 2017;12:40. doi:10.1186/s13017-017-0151-4
5. Fodor M, Primavesi F, Morell-Hofert D, et al. Non-operative management of blunt hepatic and splenic injury: a time-trend and outcome analysis over a period of 17

years. *World J Emerg Surg*. 2019;14:29. doi:10.1186/s13017-019-0249-y

6. Hoffman M, Monroe DM. A cell-based model of hemostasis. *Thromb Haemost*. 2001;85(6):958-965.
7. Barrera LM, Perel P, Ker K, et al. Thromboprophylaxis for trauma patients. *Cochrane Database Syst Rev*. 2013; 3:CD008303.
8. Eberle BM, Schnüriger B, Inaba K, et al. Thromboembolic prophylaxis with low-molecular-weight heparin in patients with blunt solid abdominal organ injuries undergoing nonoperative management: current practice and outcomes. *J Trauma*. 2011;70(1):141-147. doi:10.1097/TA.0b013e3182032f45
9. Alejandro KV, Acosta JA, Rodríguez PA. Bleeding manifestations after early use of low-molecular-weight heparins in blunt splenic injuries. *Am Surg*. 2003; 69(11):1006-1009.
10. Norwood SH, McAuley CE, Berne JD, et al. A potentially expanded role for enoxaparin in preventing venous thromboembolism in high risk blunt trauma patients. *J Am Coll Surg*. 2001;192(2):161-167. doi:10.1016/S1072-7515(00)00802-4
11. Norwood SH, McAuley CE, Berne JD, et al. Prospective evaluation of the safety of enoxaparin prophylaxis for venous thromboembolism in patients with intracranial hemorrhagic injuries. *Arch Surg*. 2002;137(6):696-702. doi:10.1001/archsurg.137.6.696