Direct Oral Anticoagulants vs Low-Molecular–Weight Heparin for Thromboprophylaxis in Nonoperative Pelvic Fractures

Mohammad Hamidi, MD, Muhammad Zeeshan, MD, Joseph V Sakran, MD, FACS, Narong Kulvatunyou, MD, FACS, Terence O'Keeffe, MD, Ashley Northcutt, MD, El Rasheid Zakaria, MD, PhD, Andrew Tang, MD, FACS, Bellal Joseph, MD, FACS

BACKGROUND: Patients with pelvic fractures are prone to venous thromboembolic (VTE) complications. Recent literature shows superiority of direct oral anticoagulants (DOACs) over low-molecular–weight heparin (LMWH) for thromboprophylaxis in patients undergoing orthopaedic operations. The aim of our study was to compare in-hospital outcomes for DOACs vs LMWH in patients with nonoperative pelvic fractures.

STUDY DESIGN: We performed a 2-year (2015 to 2016) analysis of the American College of Surgeons-Trauma Quality Improvement Program (ACS-TQIP) database. We included all adult patients with isolated blunt pelvic fractures who were managed nonoperatively and received thromboprophylaxis with either LMWH or DOACs (Factor-Xa inhibitor or direct thrombin inhibitor). Patients were divided into 2 groups based on receipt of DOACs vs LMWH and were propensity-score-matched in a 1:2 ratio to control for possible confounding factors. Primary outcomes were deep venous thrombosis (DVT) and/or pulmonary embolism (PE). Secondary outcomes were pRBC transfusions, intervention for hemorrhage control, and in-hospital mortality after initiation of thromboprophylaxis.

RESULTS: We identified 20,692 patients with pelvic fractures. There were 7,312 patients with isolated pelvic fractures included, 852 of whom were matched (DOACs: 284; LMWH: 568). Mean age was 43.2 ± 15 years, median Injury Severity Score was 14 (range 10 to 18). Matched groups were similar in demographics, vital signs, injury parameters, and timing of initiation of thromboprophylaxis. Overall, 5.2% of patients had DVT, 1.4% PE, and 1.3% died. Patients who received DOACs were less likely to develop DVT (1.8% vs 6.9%, $p < 0.01$) compared with LMWH. There was no difference in PE ($p = 0.85$) or in-hospital mortality ($p = 0.79$) between the 2 groups. Similarly, there was no difference in post-prophylaxis blood transfusion, and post-prophylaxis intervention for hemorrhage control.

CONCLUSIONS: In patients with nonoperative pelvic fractures, DOACs were associated with a reduced rate of DVT vs LMWH without increasing the risk of bleeding complications. No association was found between the type of thromboprophylactic agent and rates of PE or in-hospital mortality. (J Am Coll Surg 2019;228:89–97. © 2018 by the American College of Surgeons. Published by Elsevier Inc. All rights reserved.)

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From the Division of Trauma, Critical Care, Emergency Surgery, and Burns, Department of Surgery, College of Medicine, University of Arizona, Tucson, AZ (Hamidi, Zeeshan, Kulvatunyou, O'Keefe, Northcutt, Zakaria, Tang, Joseph) and the Division of Acute Care Surgery, Department of Surgery, Johns Hopkins Hospital, Baltimore, MD (Sakran).

Correspondence address: Bellal Joseph, MD, FACS, University of Arizona, Department of Surgery, Division of Trauma, Critical Care, and Emergency Surgery, 1501 N Campbell Ave, Room 5411, PO Box 245063, Tucson, AZ 85724. email: bjoseph@surgery.arizona.edu

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Abbreviations and Acronyms

ACS-TQIP = American College of Surgeons Trauma Quality Improvement Program
AIS = Abbreviated Injury Scale
DOAC = direct oral anticoagulants
DVT = deep venous thrombosis
ED = emergency department
LMWH = low-molecular–weight heparin
PE = pulmonary embolism
pRBCs = packed red blood cells
VTE = venous thromboembolic

Trauma patients with pelvic fractures are at an increased risk of developing venous thromboembolic (VTE) complications, including deep venous thrombosis (DVT) and/or pulmonary embolism (PE).[1-3] The incidence of DVT or PE varies according to patients' age, sex, preexisting comorbidities, and type of pelvic fracture. Methods for detecting emergent VTE complications vary, and undertaking thromboprophylaxis to prevent such complications is also pivotal.[4] The consequences of trauma-related VTE vary from asymptomatic DVT to a sudden cardiac death caused by a saddle-pulmonary embolus. The reported incidence of DVT and PE in patients who sustain pelvic or acetabular fractures varies between 10% to 61% and 2% to 8%, respectively.[5,6]

The American College of Chest Physicians and the Eastern Association for the Surgery of Trauma (EAST) recommend the use of low-molecular–weight heparin (LMWH) for the prophylaxis of VTE in patients with pelvic fractures that require operative management or prolonged bed rest.[6,7] Additionally, Jehan and colleagues[8] reported that early initiation of thromboprophylaxis with LMWH in patients with pelvic fractures that are managed nonoperatively is associated with a decreased risk of DVT. Direct oral anticoagulants (DOACs), including direct thrombin inhibitors and direct factor Xa inhibitors, have evolved rapidly over the past decades. Compared with LMWH, DOACs more directly and selectively target and inhibit specific protein components in the coagulation cascade. They are administered orally in fixed doses with no need for sophisticated monitoring, and they are associated with fewer drug-drug and/or drug-food interactions than vitamin K antagonists.[9] The American College of Chest Physicians recommends 10 to 14 days of prophylaxis after total hip arthroplasty (THA) or total knee arthroplasty (TKA) with LMWH, fondaparinux, apixaban, dagibatran, rivaroxaban, low dose unfractionated heparin, adjusted dose vitamin K antagonist, aspirin, or intermittent pneumatic device. However, since these recommendations were issued in 2012, not all DOACs are included in these recommendation, eg edoxaban and betrixaban, which did not receive FDA approval until 2015 and 2017, respectively. Additionally, among the DOACs, only apixaban and rivaroxaban have been approved by the FDA for use in VTE prophylaxis after total hip arthroplasty or total knee arthroplasty, and dabigatran has been approved only for use after total hip arthroplasty.[7]

Several randomized clinical trials showed that direct oral Xa inhibitors (apixaban and rivaroxaban) are more effective as a chemical thromboprophylaxis after total knee or hip replacement, whereas the efficacy of direct thrombin inhibitors (dabigatran) is equivalent to that of LMWH.[10-16] However, the role of DOACs compared with LMWH in trauma patients with pelvic fractures that are managed nonoperatively remains unclear. The aim of our study was, therefore, to assess the association between the type of thromboprophylactic agent (ie DOACs vs LMWH) and outcomes in these patients. We hypothesized that DOACs are associated with lower rates of VTE complications than LMWH in trauma patients with pelvic fractures managed nonoperatively.

METHODS

Study design and population

We analyzed data from the American College of Surgeons Trauma Quality Improvement Program (ACS-TQIP) database over 2 years (2015 to 2016). Patients who had a diagnosis of pelvic fractures and were managed nonoperatively were identified using ICD-10 diagnosis codes. With more than 775 participating trauma centers from across the United States, TQIP is elevating the quality of care for trauma patients. Trained data abstractors collect more than 100 data items, including patient demographics (age, sex, race); comorbidities; injury parameters (type and mechanism of injury, Injury Severity Score [ISS], Abbreviated Injury Scale [AIS]); prehospital and emergency department (ED) vitals; in-hospital course (diagnosis procedures, transfusion, in-hospital complications, and mortality); and discharge disposition. The TQIP started collecting data regarding VTE prophylaxis in 2013, and TQIP validators and external audits ensure the quality and standardization of data abstraction. Institutional Review Board (IRB) approval was not needed because the TQIP database contains only de-identified data.

Inclusion and exclusion criteria

We included all adult trauma patients ($\geq$18 years old) admitted to ACS-TQIP participating hospitals (2015 to 2016), who had an isolated pelvic fracture (pelvic Abbreviated Injury Score $\geq$ 3 and any other body region AIS $<$ 3), underwent nonoperative management and

received pharmacologic thromboprophylaxis with either DOACs (Xa-inhibitor and direct-thrombin-inhibitor) or LMWH. We excluded patients who were transferred from other facilities, dead on arrival, or had a hospital length of stay less than 2 days.

Variables analyzed

We extracted the following variables for each patient: demographics (age, sex, race); injury parameters (mechanism of injury, Injury Severity Score [ISS], and body regions Abbreviated Injury Scale score [AIS]); emergency department vitals (Glasgow Coma Scale, temperature, heart rate, and systolic blood pressure [SBP]); timing of initiation of thromboprophylaxis; type of thromboprophylactic agent used (LMWH vs DOACs); comorbidities (COPD, diabetes mellitus, hypertension, history of cardiovascular disease (congestive heart failure/ischemic heart disease), cerebrovascular accident, renal failure, smoking history), operative interventions and angioembolization; hospital length of stay; transfusion; in-hospital complications, and mortality.

Patients were divided into 2 groups based on the type of agent used for pharmacologic thromboprophylaxis: those who received direct oral anticoagulants (DOACs group) and those who received low-molecular—weight heparin (LMWH group).

Outcomes

The primary outcomes of our study were rates of DVT and/or PE in each group (ie DOACs vs LMWH). Our secondary outcome measures were post-prophylaxis packed red blood cell (pRBC) transfusion, post-prophylaxis surgery and/or angioembolization for hemorrhage control, and in-hospital mortality. Post-prophylaxis pRBC transfusion and surgery/angioembolization were considered surrogate markers for any bleeding complications because the TQIP does not provide information about bleeding secondary to thromboprophylaxis.

Statistical analysis

We performed propensity score matching using nearest-neighbor matching without replacement to match the 2 patient groups in 1:2 ratio for DOACs vs LMWH. Propensity scores were calculated using a logistic regression model with anticoagulant use (DOACs vs LMWH) as the dependent variable. Possible confounding factors (including patient demographics, comorbidities, injury parameters, ED vitals, type of pelvic fracture, hospital length of stay, and time of initiation of thromboprophylaxis) were included as adjustment variables in the propensity model. We then matched each patient in the DOAC group with 2 patients in the LMWH group, such that the matched subjects had similar propensity score. The propensity score is a balancing score, and the baseline confounding variates will be similar between the matched patients at a particular score. We then verified that covariates were balanced across the 2 groups and the groups were well matched. Finally, area under the receiver operator characteristics curve was used to confirm the discrimination ability of the model.

All categorical variables are summarized as proportions, continuous normally distributed variables as mean (standard deviation) and continuous variables without normal distribution as median (interquartile range). We used Pearson's chi-square test to compare categorical variables; the Student's *t*-test and the Mann-Whitney U test were used to analyze the continuous normally distributed and non-normally distributed data, respectively. In our analysis, alpha was set at 5% and a value of $p < 0.05$ was considered statistically significant. All statistical analyses were performed using the Statistical Package for Social Services (SPSS, version 24; SPSS, Inc).

Missing data analysis

Missing data were treated as missing completely at random (MCAR). Multiple imputation using a missing value analysis technique to account for the missing values was performed. For multiple imputation, the original dataset was analyzed for random missing data points using Little's MCAR test. Then the Markov Chain Monte Carlo method was used for multiple imputations. This method refers to a collection of methods for simulating random draws from nonstandard distributions. Less than 2% of the data was missing, and due to this low percentage, it would not be expected to have caused any bias in our analysis.

RESULTS

We identified a total of 20,692 patients with pelvic fractures who were managed nonoperatively; 13,767 patients had isolated pelvic fractures. Of those, 987 patients were discharged or died within the first 2 days of admission. Additionally, 5,468 patients were excluded because they did not receive any thromboprophylaxis, received chemical thromboprophylaxis with agents other than LMWH or DOACs, or had missing VTE complications data. Subsequently, 7,312 patients were included in our final analysis. Five percent (359 of 7,312) of these patients received DOACs for thromboprophylaxis. Figure 1 shows the flow diagram that summarizes the patient selection process. Pre-matched data summaries of patient characteristics for the 2 patient subgroups are presented in Table 1. There were statistically significant differences between the 2 groups regarding demographics, injury parameters, ED vitals, and comorbidities in the pre-matched comparisons.

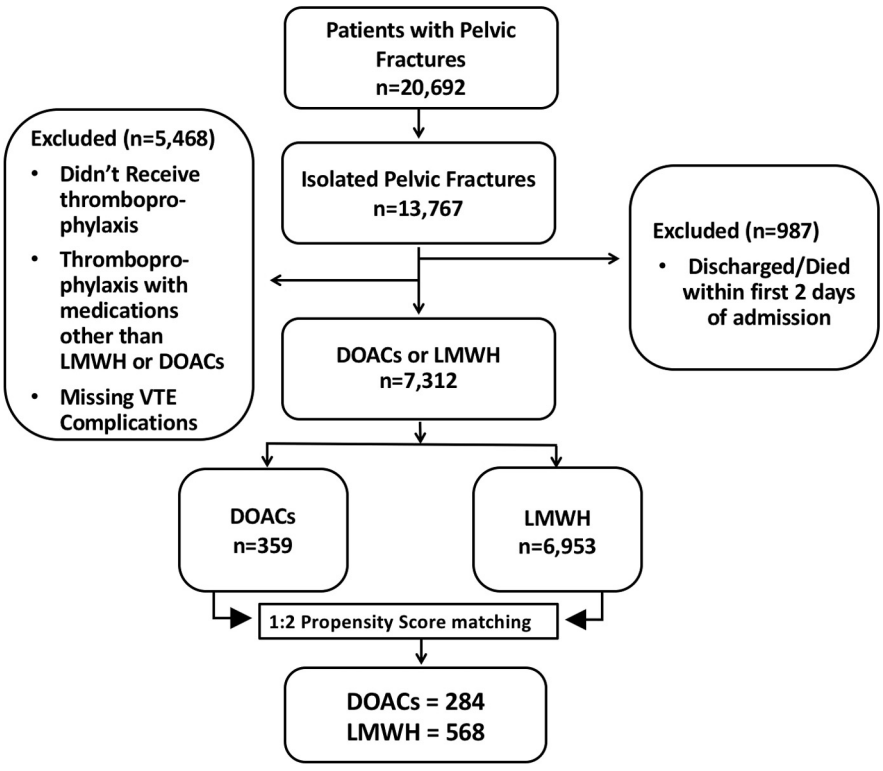

Figure 1. Flow diagram summarizing the patient selection process. DOAC, direct oral anticoagulants, LMWH, low-molecular–weight heparin; VTE, venous thromboembolic.

Using propensity score matching, a total of 852 patients were matched in a 1:2 ratio (DOACs: n = 284 vs LMWH: n = 568). The demographics, ED vitals, and injury parameters of the matched patient subgroups are shown in Table 2. There was no statistically significant difference between the 2 groups regarding age, sex, race, ED systolic blood pressure, ED heart rate, ED Glasgow Coma Scale, Injury Severity Score, pelvic-AIS, hospital length of stay, mechanism of injury, or time to initiation of thromboprophylaxis. These results suggest that our propensity score matching was successful. The injury pattern for pelvic fractures is shown in Table 2. There was no statistically significant difference between the 2 groups regarding the pattern of fractures.

Outcomes of our analysis are reported in Table 3. The overall rates of DVT and PE were 5.2% and 1.4%, respectively. Patients who received DOACs for thromboprophylaxis had lower rate of DVT (1.8% vs 6.9%, $p < 0.01$) compared with DVT rates in those who received LMWH. However, there was no statistically significant difference between the 2 groups regarding the rate of PE and in-hospital mortality. The overall rates of post-prophylaxis pRBC transfusion, angioembolization, and operative interventions for hemorrhage control were 1.9%, 1.5%, and 0.5%, respectively. On comparison, there was no difference between the 2 groups regarding the rate of post-prophylaxis pRBCs transfusion, angioembolization, or operative intervention for hemorrhage control. We performed a sub-analysis of patients who received DOACs and divided them into 2 sub-groups based on the type of DOACs (Xa-Inhibitor: n = 197 vs thrombin inhibitor: n = 87). There was no statistically significant difference between the rates of DVT and PE among patients who received Xa-inhibitors vs those who received thrombin inhibitors, as shown in Table 4.

DISCUSSION

The purpose of this study was to evaluate the differences in outcomes in patients who received chemical thromboprophylaxis after sustaining pelvic fractures. Our results suggest that in patients with nonoperatively managed pelvic fractures, use of DOACs was associated with lower rates of DVT compared with the use of LMWH. However, there was no significant difference between the 2 groups regarding in-hospital mortality or rates of PE. These results were obtained from the analysis after propensity score matching that controlled for possible confounding factors: demographics, injury parameters,

Table 1. Patient Characteristics for the Pre-Matched Data (American College of Surgeons Trauma Quality Improvement Program 2015–2016)

Variable	DOAC (n = 359)	LMWH (n = 6,953)	p Value
Age, y, mean ± SD	48.2 ± 14	41.8 ± 15	<0.01
Male, n (%)	195 (54.3)	3,942 (56.7)	0.32
White race, n (%)	306 (85.2)	5,124 (73.7)	<0.01
Vital parameter			
GCS, median (IQR)	15 (14–15)	15 (14–15)	0.68
ED SBP, mmHg, mean ± SD	134 ± 26	126 ± 25	0.02
ED HR, bpm, mean ± SD	89 ± 13	92 ± 16	0.03
Injury parameter			
ISS, median (IQR)	13 (11–19)	14 (10–20)	0.04
Pelvic-AIS, median (IQR)	3 (3–4)	3 (3–4)	0.67
In-hospital course			
Hospital length of stay, d, median (IQR)	5 (3–8)	6 (3–9)	0.05
Time to thromboprophylaxis, h, median (IQR)	46.7 (24.1–71.5)	47.4 (24.6–95.7)	0.53
Mechanism of injury, n (%)			
Motor vehicle collision	182 (50.7)	3,699 (53.2)	0.38
Fall	153 (42.6)	2,614 (37.6)	0.01
Other	24 (6.7)	640 (9.2)	0.10
Details of pelvic fracture, n (%)			
Pubic rami	243 (67.7)	4,749 (68.3)	0.77
Pubic body	67 (18.7)	1,349 (19.4)	0.78
Iliac fracture	79 (22.0)	1,564 (22.5)	0.79
Sacral fracture	161 (44.8)	3,351 (48.2)	0.21
Acetabular fracture	28 (7.8)	368 (5.3)	0.07
Comorbidity, n (%)			
COPD	11 (3.1)	194 (2.8)	0.74
Diabetes mellitus	30 (8.4)	508 (7.3)	0.46
Hypertension	56 (15.6)	834 (12.0)	0.04
History of cardiovascular disease (CHF/IHD)	22 (6.1)	348 (5.0)	0.32
Cerebrovascular accident	7 (1.9)	85 (1.2)	0.21
Smoker	28 (7.8)	355 (5.1)	0.03

AIS, Abbreviated Injury Scale; BPM, beat per minute; CHF, congestive heart failure; DOAC, direct oral anticoagulants; ED, emergency department; GCS, Glasgow Coma Scale; HR, heart rate; IHD, ischemic heart disease; IQR, interquartile range; ISS, Injury Severity Score; LMWH, low-molecular–weight heparin; SBP, systolic blood pressure.

admission vitals, and hospital course. We believe that this study will be a significant addition to the growing literature about the use of DOACs as thromboprophylactic agents for pelvic fractures.

Patients with pelvic fractures have a substantial risk of developing VTE complications. Without prophylaxis, the incidence of DVT in such patients can be as high as 34%, and the risk of developing PE can reach up to 12%.[17] According to the ACS-TQIP Best Practices in the Management of Orthopaedic Trauma, early initiation of thromboprophylaxis is recommended in patients with pelvic fractures as quickly as possible.[17] For the nonoperative management of such an injury, Jehan and associates[8] reported that the window of safe initiation of thromboprophylaxis is within 24 hours. Based on an extensive literature review, the American Academy of Orthopaedic Surgeons recommended the use of pharmacologic or mechanical prophylaxis for patients undergoing elective hip and knee arthroplasty.[18] However, it does not provide clear guidelines in terms of thromboprophylaxis for pelvic fractures that are managed nonoperatively, which is an area that needs more research and clinical trials. This is supported by Slobogean and coworkers' systematic review,[19] which concluded that early administration of LMWH resulted in reduction of risk for DVT and PE in patients with pelvic and acetabular fracture; however, this conclusion was based on a single study of 100 patients.[20] This same review also revealed a significant lack of data from well-designed studies, highlighting the need for further

Table 2. Patient Characteristics for the Matched Data (American College of Surgeons Trauma Quality Improvement Program)

Variable	DOAC (n = 284)	LMWH (n = 568)	p Value
Age, y, mean ± SD*	43.4 ± 16	42.9 ± 14	0.16
Male, n (%)*	157 (55.3)	317 (55.8)	0.59
White race, n (%)*	223 (78.5)	440 (77.5)	0.49
Vital parameter*			
GCS, median (IQR)	15 (14–15)	15 (14–15)	0.23
ED SBP, mmHg, mean ± SD	129 ± 23	128 ± 22	0.19
ED HR, bpm, mean ± SD	90 ± 12	91 ± 15	0.27
Injury parameter*			
ISS, median (IQR)	13 (10–17)	14 (10–18)	0.21
Pelvic-AIS median (IQR)	3 (3–4)	3 (3–4)	0.34
In-hospital course*			
Hospital LOS, d, median (IQR)	4 (2–7)	4 (3–7)	0.53
Time to thromboprophylaxis, h, median (IQR)	46.9 (24.2–71.7)	47.1 (24.1–72.0)	0.60
Mechanism of injury, n (%)*			
Motor vehicle collision	147 (51.8)	296 (52.1)	0.94
Falls	112 (39.4)	224 (39.4)	
Others	25 (8.8)	48 (8.5)	
Details of pelvic fracture, n (%)*			
Pubic rami	194 (68.3)	387 (68.1)	0.93
Pubic body	54 (19.0)	109 (19.2)	0.92
Iliac fracture	63 (22.2)	129 (22.7)	0.93
Sacral fracture	131 (46.1)	268 (47.2)	0.82
Acetabular fracture	20 (7.0)	39 (6.9)	0.88
Comorbidity, n (%)*			
COPD	7 (2.5)	13 (2.3)	0.89
Diabetes mellitus	22 (7.7)	39 (6.9)	0.67
Hypertension	41 (14.4)	77 (13.6)	0.75
History of cardiovascular disease (CHF/IHD)	16 (5.6)	29 (5.1)	0.50
Cerebrovascular accident	4 (1.4)	5 (0.9)	0.49
Smoker	20 (7.0)	38 (6.9)	0.88

*Variables used for propensity score matching.
AIS, Abbreviated Injury Scale; BPM, beat per minute; CHF, congestive heart failure; DOAC, direct oral anticoagulants; ED, emergency department; GCS, Glasgow Coma Scale; HR, heart rate; IHD, ischemic heart disease; IQR, interquartile range; ISS, Injury Severity Score; LMWH, low-molecular–weight heparin; SBP, systolic blood pressure.

Table 3. Primary and Secondary Outcomes

In-hospital outcome	DOAC (n = 284)	LMWH (n = 568)	p Value
Primary, n (%)			
Deep venous thrombosis	5 (1.8)	39 (6.9)	<0.01
Pulmonary embolism	4 (1.4)	8 (1.4)	0.85
Secondary, n (%)			
Post-prophylaxis pRBCs transfusion received	5 (1.8)	11 (1.9)	0.79
Post-prophylaxis angioembolization	4 (1.4)	9 (1.6)	0.82
Post-prophylaxis surgical hemorrhage control	1 (0.4)	3 (0.5)	0.89
In-hospital mortality	3 (1.1)	8 (1.4)	0.75

DOAC, direct oral anticoagulants; LMWH, low-molecular–weight heparin; pRBCs, packed red blood cells.

Table 4. Venous Thromboembolic Complications Comparing Oral Xa-Inhibitors and Direct Thrombin Inhibitors

Outcome	Xa-inhibitor* (n = 197)	Thrombin inhibitor* (n = 87)	p Value
Deep venous thrombosis, n (%)	3 (1.5)	2 (2.3)	0.64
Pulmonary embolism, n (%)	3 (1.5)	1 (1.1)	0.92

*Sub-analysis of all the patients who received direct oral anticoagulants in the matched cohort.

research to prevent thromboembolism in this high-risk group of patients.

Over the past few decades, there has been substantial debate about which pharmacologic prophylactic agent (LMWH, unfractionated heparin, or warfarin) achieves the best balance between the efficacy for VTE prophylaxis and the safety profile.[21] In the past few years, the focus has shifted to defining the optimal timing of thromboprophylaxis initiation.[22,23] Consequently, the results of our study were obtained after controlling for the timing of initiation of thromboprophylaxis in our propensity model. Recently, DOACs, particularly oral Xa inhibitors, have emerged as the thromboprophylactic agent of choice after orthopaedic surgery.[24] In comparison with LMWH, our study found that the use of DOACs was associated with a lower risk of developing DVT in patients with pelvic fractures who were managed nonoperatively. Additionally, there was no statistically significant difference between the 2 groups regarding the rates of PE and in-hospital mortality. Similarly, several randomized controlled trials have concluded that DOACs, and specifically oral Xa inhibitors, are more effective thromboprophylactic agents against VTE complications than LMWH in patients undergoing orthopaedic procedures.[10-14] However, in our study, there was no difference between oral Xa inhibitors and direct thrombin inhibitors. This result may be due to a small sample size when we performed the subgroup analysis to compare specific drug categories of the DOACs group. However, prospective analysis with a larger sample size may provide answers about the difference of factor Xa and direct thrombin inhibitors.

Pelvic fractures are commonly associated with severe hemorrhage due to the extensive blood supply to the region.[25,26] Massive retroperitoneal hemorrhage may result from bony fragments and lacerated blood vessels, leading to coagulopathy and exsanguination.[27] The safety of an intervention is as important as its efficacy. Therefore, it is imperative that a new intervention has a reasonable benefit-risk relationship. In our analysis, we used post-prophylaxis pRBC transfusions received, post-prophylaxis angioembolization, and post-prophylaxis surgical hemorrhage control as surrogate markers for safety. The use of these markers has been well reported in the literature.[22,23] In their clinical trial, Fuji and coworkers[28] reported that the incidences of major bleeding complications in patients who are receiving oral Xa inhibitors compared with LMWH after elective or semi-elective orthopaedic surgery are 1.1% and 0.3%, respectively, which is comparable to our analysis. Additionally, as we found, they concluded that oral Xa inhibitors and LMWH have similar safety profiles in terms of major bleeding and clinically relevant nonmajor bleeding complications. The DOACs are easier to administer through an oral route, do not require regular follow-up with international normalized ratio, and have fewer drug-drug reactions compared with other thromboprophylactic drugs.

Currently, andexanet alfa is FDA approved for the reversal of apixaban and rivaroxaban in the setting of life-threatening or uncontrolled hemorrhage. Furthermore, idarucizumab is FDA approved for the reversal of direct thrombin inhibitors. Although these reversal agents for DOACs are expensive, they are efficient for the rapid reversal of DOAC's action.[29,30] The better safety profile, availability of rapid reversal agents, along with a more efficacious role in reducing VTE events, indicate a promising future for DOACs to be used as thromboprophylactic agents. Further prospective randomized clinical trials are warranted to investigate the use of DOACs for thromboprophylaxis in trauma patients.

The results of our study should be interpreted in the context of its limitations; our study has the inherent limitations of a retrospective study. We were not able to control for additional confounding factors, including, but not limited to, mechanical prophylaxis, dosage and frequency of LMWH or DOACs, post-discharge events (complications, readmission, compliance, etc), and the day of diagnosis of VTE events. Additionally, we referred to post-prophylaxis pRBCs transfusions, post-prophylaxis angioembolization, and post-prophylaxis surgical hemorrhage control as surrogate markers for safety. Furthermore, there were different limitation factors concerning the TQIP participating institutions. First, we were not able to account for DVT screening protocols at different institutions participating, which may have introduced a detection bias to our analysis. Second, we were not able to determine whether DVTs were symptomatic or asymptomatic at time of diagnosis. Third, there is a potential that some institutions predominantly use LMWH rather than DOACs for prophylaxis, which may have skewed the data. Although our study has the usual limitations

of all retrospective database research, it has significant strength because of the high quality of the TQIP database, which is an adequate representative of the trauma population in the US. It has also been used extensively in the trauma literature. Moreover, the reliability of data is ensured by the intensive training mechanisms for the data extractors as well as interrater reliability audits of the participating sites. Despite these limitations, we believe that this study will pave the way for further prospective clinical studies to provide a stronger evidence-based recommendation.

CONCLUSIONS

In patients with nonoperative pelvic fractures, direct oral anticoagulants were associated with a reduced rate of DVT compared with LMWH, without increasing the risk of bleeding complications or in-hospital mortality. However, there was no association between the type of thromboprophylactic agent and the rate of pulmonary embolism. Prospective clinical trials should evaluate the role of DOACs as prophylactic pharmacologic agents for thromboprophylaxis in patients admitted after trauma.

Author Contributions

Study conception and design: Hamidi, Zeeshan, Sakran, Kulvatunyou, O'Keeffe, Zakaria, Joseph

Acquisition of data: Hamidi, Zeeshan, Kulvatunyou, O'Keeffe, Northcutt, Zakaria, Tang, Joseph

Analysis and interpretation of data: Hamidi, Zeeshan, O'Keeffe, Northcutt, Zakaria,Tang, Joseph

Drafting of manuscript: Hamidi, Zeeshan, Sakran, Kulvatunyou, O'Keeffe, Northcutt, Zakaria,Tang, Joseph

Critical revision: Hamid, Zeeshan, Sakran, Kulvatunyou, Northcutt, Tang, Joseph

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