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Featured Article

Worth looking! venous thromboembolism in patients who undergo preperitoneal pelvic packing warrants screening duplex

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ABSTRACT

Background: Venous thromboembolism (VTE) in patients with major pelvic fractures who undergo preperitoneal pelvic packing (PPP) has not been investigated. We hypothesized that patients who undergo PPP are at high risk for VTE, thus early prophylactic anticoagulation and screening duplex are warranted.

Study design: All patients requiring PPP from 2015 to 2019 were reviewed. Management and outcomes were analyzed.

Results: During the study period, 79 patients underwent PPP. Excluding the early deaths, 17 patients had deep venous thrombosis (DVT) and 6 had pulmonary emboli (PE); 4 patients had both DVT/PE. Overall mortality was 15%. Thirty-two patients underwent screening duplex within 72 h of admission and 10 were positive for DVT.

Conclusion: Patients with complex pelvic trauma undergoing PPP have a 23% incidence of DVT and an additional 8% incidence of PE. 31% of screening ultrasounds are positive. The overall mortality was 15%. With a high incidence of VTE in this patient population, we recommend screening duplex ultrasounds.

Introduction

Venous thromboembolism (VTE) is a recognized cause of morbidity and mortality in severely injured patients with major pelvic fractures. Hemorrhage control, which is crucial to early survival in this severely injured population, is achieved by angioembolization (AE) and/or preperitoneal pelvic packing (PPP).[1–11] Our group has previously demonstrated that PPP reduces mortality in patients with life-threatening pelvic hemorrhage due to pelvic fracture.[1] The incidence of VTE in severely injured trauma patients is reported to be up to 61%, with more current day rates of VTE reported to be 4.3%–16.8% in studies with data specific to patients with pelvic injury.[12–15] Most studies looking at VTE rates do not account for injury severity and none have investigated VTE in patients undergoing PPP. The pelvic trauma population is already known to have endothelial injury and hypercoagulability, two components of Virchow's triad. Pelvic packing may cause the third element of the triad, stasis. Therefore, the VTE risk may be higher in the PPP population.[16–18]

The objective of this study was to investigate the incidence of VTE in PPP patients and to determine the role of screening duplex ultrasonography. We hypothesized that patients with complex pelvic trauma who undergo PPP are at high risk for VTE.

Materials and methods

This was a retrospective evaluation of prospectively collected data at the Ernest E. Moore Shock Trauma Center at Denver Health from September 2015 to October 2019. Denver Health Medical

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Center is American College of Surgeons-verified and state certified level-I urban trauma center. Since September 2004, all pelvic fracture patients with persistent hemodynamic instability despite red blood cell (RBC) transfusion underwent PPP and external fixation (EF), according to our protocol (Fig. 1). Specifically, the indication for PPP is a persistent systolic blood pressure (SBP) < 90 mmHg in the initial resuscitation period despite the transfusion of 2 units of packed RBCs. Initial stabilization of the pelvis is performed in the emergency department (ED) with either pelvic sheeting or pelvic binder. Additionally, resuscitative endovascular balloon occlusion of the aorta (REBOA) can be placed in the emergency department if the patient has blunt trauma with a systolic blood pressure of <70 mmHg and remains hypotensive despite beginning resuscitation. Zone of REBOA placement is determined by the attending trauma surgeon. In the operating room (OR), orthopedics performs EF of the pelvis immediately prior to the trauma team completing PPP. Additional operative procedures such as thoracotomy or laparotomy for hemorrhage are performed at the initial PPP operation as indicated.

Our technique and outcomes of PPP has been described previously.[2,19,20] Angiography is performed for ongoing pelvic bleeding, defined as:

1) greater than 4 units of RBCs after the patient's coagulopathy is corrected or
2) ongoing hemodynamic instability despite PPP/EF.

Restoration of coagulation is guided by thromboelastography (TEG).[21] Pelvic pack removal is performed at 24–48 h once physiologic restoration is complete. Repacking of the pelvis is generally avoided due to infectious risks.

All patients undergoing PPP/EF have been prospectively followed since the initiation of PPP as our primary hemorrhage control technique for unstable pelvic fractures. The study period for this analysis encompassed a 4-year period, when the electronic collection of VTE chemoprophylaxis (VTEp) and VTE rates was initiated. The use of screening duplex ultrasound was at the discretion of the operative surgeon or the surgical intensivist. Patients with pre-hospital arrest or those undergoing ED resuscitative thoracotomy were excluded. Patients with primary pulmonary thrombus on computed tomography (CT) during the initial work up of their traumatic injuries were excluded from VTE analysis as primary VTE events. Early deaths (defined as within 48 h of presentation) were excluded from the VTE analyses.

All ultrasounds (U/S) were performed by a certified ultrasound technologist and interpreted by an attending radiologist. Screening U/S included the examination of bilateral lower extremities. Diagnostic U/S was performed for symptomatic patients and limited to the symptomatic extremity(s). Computed tomography pulmonary angiogram (CTPE) was performed only on patients with signs and symptoms concerning for pulmonary embolus (PE). All imaging was ordered at the discretion of the trauma surgeon or surgical intensivist. If CTPE and U/S were ordered concurrently, completed within 12 h of one another, and both positive, these were considered concurrent DVT/PE diagnosis.

Patient demographics, admission physiology, transfusion requirements, need for angiography, timing and type of VTE prophylaxis, VTE rates, the use of duplex ultrasonography and hospital course were reviewed. The Young and Burgess classification was used to categorize fracture patterns.[22] Student's *t*-test, $\chi 2$ or Fisher's exact test were used as appropriate. $p < 0.05$ was considered statistically significant. The Colorado Multi-Institutional Review Board approved this study.

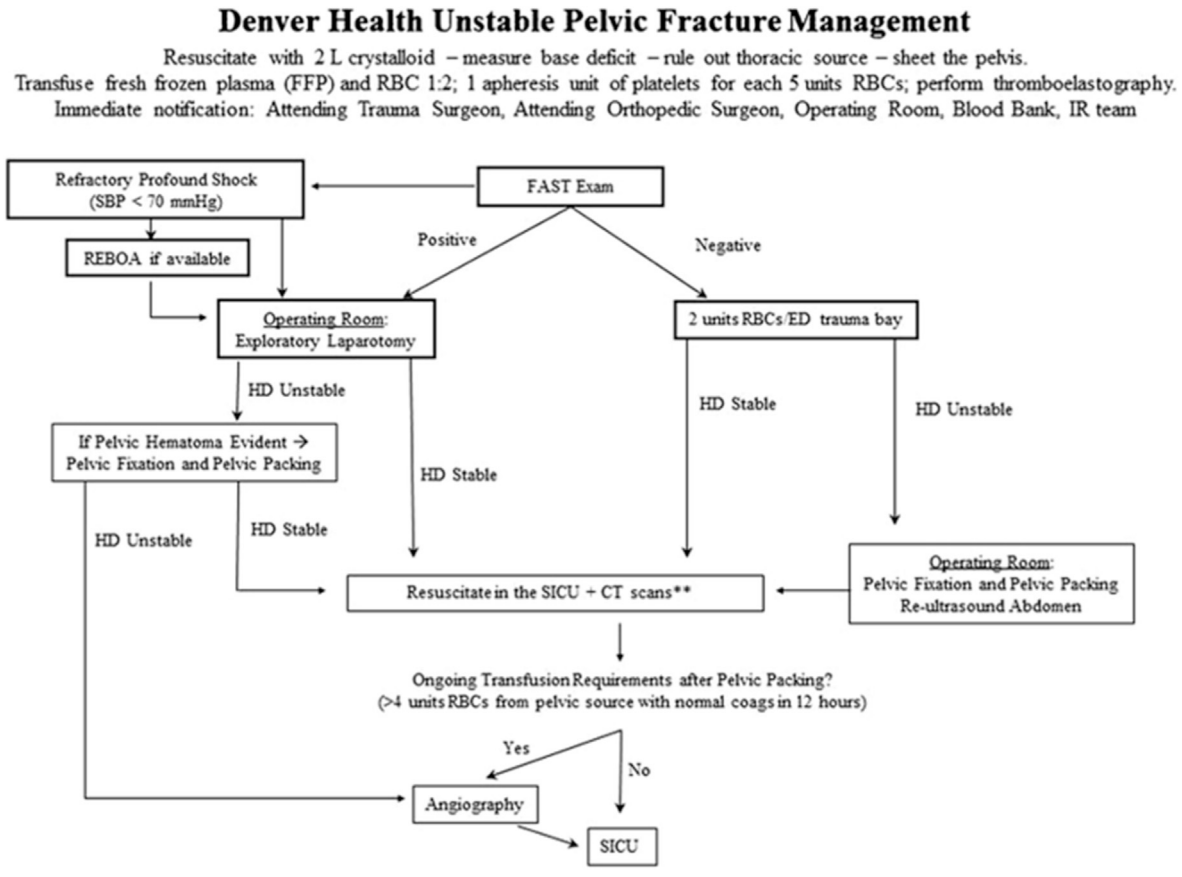

Fig. 1. Denver health unstable pelvic fracture management protocol.

Results

During the 4-year study period, 79 patients underwent PPP. The majority of patients were male (72%), with a mean age of 47±18 years and a mean injury severity score (ISS) of 37±14. The most common mechanism was auto-pedestrian crash (28), followed by motor vehicle collision (23), motorcycle collision (15), fall (4), auto-bicycle crash (3), and other (6).

Overall, mortality was 15% with 74 patients surviving >48 h. Of the five patients who died in the first 48 h, four were due to devastating traumatic brain injury and one was secondary to withdrawal of treatment in congruence with the patient's family's wishes. The 7 late deaths (>48 h) were patients who also had withdrawal of treatment secondary to devastating TBI (5), diffuse ischemic small bowel (1), and embolic cerebrovascular accident with concurrent heart failure (1). No patient died of exsanguination.

VTE rate and risk factors

Excluding the early deaths and one patient with a diagnosis of primary pulmonary thrombus on initial trauma work up, 23/73 (32%) patients developed DVT and/or PE. We did not identify any significant differences in the patients who developed VTE compared to those that did not, including the use of REBOA, the number of packs placed or length of time to pack removal. Two patients required repacking, and both of those patients developed VTE. Five patients required pelvic angioembolization for hemorrhage control, in addition to PPP, and 60% (3/5) of those patients developed VTE. (Table 1).

VTE diagnosis

Of patients who had VTE, 13 had deep venous thrombosis (DVT), 6 had PE, and 4 had both DVT/PE. Excluding patients with PE who did not also have DVT, the DVT rate was 23% (17/74). The majority of patients, 57/74 (77%) had an evaluation for VTE, with 43% (32/74) of patients undergoing a screening ultrasound. The majority (25/42–60%) of patients who did not get a screening U/S had a VTE work up during their hospitalization (diagnostic lower extremity U/S or CTPE) and 52% (13/25) of these were positive. Of the 32 patients who underwent early screening U/S, 14 patients had an additional diagnostic U/S or CTPE for symptoms and 5 PE were diagnosed (Fig. 2).

The median time from admission to VTE diagnosis was 4 days. Screening U/S captured 10 DVTs and 9% (3/32) of these patients were also diagnosed with PE concurrently. For the 3 patients that had a DVT diagnosed on screening U/S and had concurrent PE, both VTEs were diagnosed with pelvic packs in place. 5/13 patients had DVT diagnosed with the pelvic packs still in place. Two patients were diagnosed with DVT after discharge, at 35- and 128-days post-packing. For the final/fourth patient diagnosed with both DVT and PE, diagnosis of the PE was 9 days after the DVT. This patient was on a therapeutic heparin drip but had intermittent suboptimal anti-coagulation. In patients who did not have screening ultrasound, 24% (6/25) were diagnosed with isolated PE. The incidence of PE in patients who had screening U/S compared to those that did not was not statistically different ($p = 0.06$).

Table 1
Patient demographics with and without VTE development.

	VTE N = 23	No VTE N = 50	p-value
Age (years)	50	44	0.22
Sex (% male)	78%	72%	0.46
Mortality	1 (4.3%)	6 (12%)	0.30
Injury Severity Score	39	35	0.40
Pelvic Fracture Type			0.54
APC	8	15	
LC	13	22	
VS	1	6	
Combined Mechanism	1	5	
Acetabular fracture	0	2	
REBOA [a]	10 (43.5%)	17 (34%)	0.44
Pelvic Angioembolization	3 (13%)	2 (4%)	0.16
Number of packs placed	6.4	6.1	0.13
Repacked	2 (9%)	0 (0%)	n/a
Time to packing removal			0.24
<24 h	2	11	
24–48 h	17	35	
>48 h	4	4	
Time to VTE chemoprophylaxis or therapeutic anticoagulation initiation <48 h [b]	14/19 (74%)	33/46 (72%)	0.87
Missed doses of VTE chemoprophylaxis [b]	0.3	0.8	0.19

[a] REBOA = Resuscitative endovascular balloon occlusion of the aorta.
[b] Data only available for patients admitted after January 04, 2016.

VTE prophylaxis and treatment

VTEp was initiated in 72% of patients within 48 h of admission, and 89% missed ≤2 doses. Enoxaparin sodium, 40 mg twice daily, or heparin drip was started in 89% of patients as VTEp, VTE treatment, or as treatment of a blunt cerebrovascular injury. The remaining 11% of patients received 5,000 mg subcutaneous heparin twice daily until they could be transitioned to enoxaparin. The indication for prophylactic unfractionated heparin was intracranial hemorrhage. Neither missed doses nor late initiation (>48 h) of VTEp was associated with VTE development ($p = 0.19$, $p = 0.87$, respectively).

Of patients with VTE diagnosis, 100% were treated with therapeutic anticoagulation and 44% (10/23) also had placement of an inferior vena cava (IVC) filter. The majority of patients with a PE (6/10) were on VTEp at time of PE diagnosis. One patient was diagnosed with a PE while on therapeutic anticoagulation for an aortic injury and had therapeutic partial thromboplastin time (PTT) (>60sec) throughout the course of treatment. One patient was diagnosed with a PE while on a therapeutic heparin drip for DVT but had intermittent subtherapeutic (<60sec) PTT measurements. On chart review, the timing of PE diagnosis in relation to VTEp or anticoagulation initiation could not be determined in two patients. Two patients with PE required transcatheter embolectomies for right heart strain and one of these patients had withdrawal of treatment due to severe right heart failure and embolic cerebrovascular accident, likely secondary to a patent foramen ovale. No other deaths were attributed to VTE or its' sequelae.

Discussion

This study demonstrated a 23% incidence of DVT and an additional 8% incidence of PE in critically ill, complex pelvic fracture patients who survived greater than 48 h after undergoing PPP/EF for hemorrhage control. VTE was not associated with increased overall mortality. VTE's were diagnosed early, usually within a week of admission and 31% of screening ultrasounds were positive. There were no differences between the VTE and non-VTE group with respect to risk factors, including timing of VTEp initiation.

The rate of VTE in pelvic fracture patients is thought to be higher than that of other trauma patients, with current literature showing rates up to 17%.[15] Our study demonstrates that the VTE may be much higher in a select group of critically injured pelvic fracture patients who undergo PPP. However, it should be noted that this PPP group is a critically ill population, representing only 6% of our

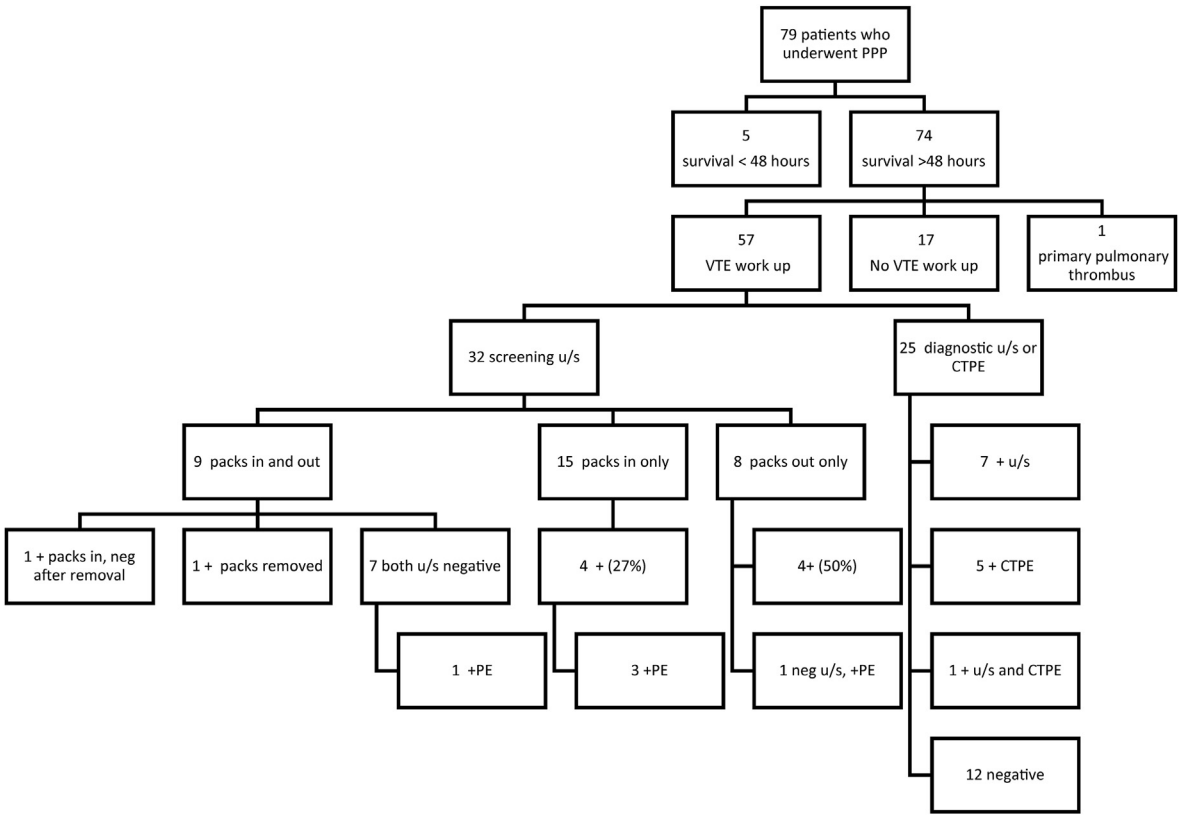

Fig. 2. Breakdown of VTE work up and diagnosis.

overall pelvic fracture population, who is likely at risk for VTE for a variety of reasons and is more severely injured based on ISS compared to most studies reported in the literature. Independent of injury mechanism, receiving four or more transfusions in the first 24 h has been associated with increased VTE risk.[15] All of our patient population, by protocol, received at least 2 units of pRBC prior to PPP/EF, and received additional blood products during and after PPP/EF. In fact, ongoing concern for bleeding and coagulopathy likely played a role in the timing of initiation of VTEp and may contribute to VTE formation. Benjamin et al. demonstrated early VTEp initiation reduces VTE, is associated with lower mortality in patients with isolated pelvic fractures, and low molecular weight heparin is the preferred VTEp over unfractionated heparin.[14] VTEp initiation earlier than 48 h may reduce VTE rates, but often, this is not possible in the multiply injured patient population, as they frequently have injuries that may be worsened by VTEp initiation, such as intracranial hemorrhage or solid organ injury. Malinoski et al. reported a 7% VTE rate in critically-ill trauma patients who could not receive VTEp.[23] Our practice is to initiate VTEp as soon as bleeding is controlled, which in this patient cohort lead to the majority of our patients being initiated on enoxaparin VTEp within 48 h with an average of <1 missed doses.

Though not statistically significant, the rate of PE was twice as high in patients who did not have a screening ultrasound (16% versus 32%, $p = 0.06$). This could be due to earlier identification of a DVT and hence initiation of therapeutic anticoagulation and subsequent prevention of PE. Van Gent et al. have reported a relatively high rate of de novo pulmonary embolism in the trauma population.[24] It is possible that this was the case in our 6 patients who had a PE without DVT. Excluding patients with PE alone, the DVT rate for our patient population was 23%, which is closer to the reported limits of DVT rates in severely injured patient populations.

While we did not identify any significant differences in the patients that developed VTE versus those that did not, it is interesting that 60% of the patients that required angioembolization in addition to PPP developed VTE.This may be simply a marker of the severity of injury in this small group of 5 patients or may indicate that this intervention increases VTE risk.

It should be noted that this cohort of patients with complex pelvic trauma undergoing PPP, there was a 15% mortality rate. This rate is half of the 2015 AAST study reporting a 32% mortality for patients presenting with pelvic fracture in shock, lower than our group's 2017 study with a mortality of 21% in patients undergoing PPP, and lower than a recent meta-analysis showing a 24% mortality for patients with open pelvic fractures.[1,6,11] So, although PPP/EF may lead to increased VTE risk, it is still a life-saving technique for this critically ill population.

This study is a single institution's experience and did not compare mortality or VTE incidence in patients who undergo pelvic angioembolization for primary hemorrhage control. There are no studies investigating VTE in patients who undergo AE primarily for hemorrhage control, the most comparable patient population, therefore, we cannot draw any conclusions regarding the role PPP has in VTE formation compared to AE. Given our increased survival, it is possible that this VTE rate may just be a reflection of the anticipated incidence in this higher risk, severely injured population. Screening duplex ultrasonography was utilized at the surgeon or surgical intensivist's discretion, and so less than half of patients received a screening ultrasound; however, over two-thirds of patients ultimately had some kind of VTE work up. Not all patients who had PE had a LE U/S, so we do not know the rate of de novo PE. No conclusions can be drawn regarding use of IVC filters, as the majority of our patients had IVC filter placed after diagnosis of PE. This study was not designed to compare VTE rates in patients who

underwent screening ultrasound versus those who did not and therefore, was not powered to demonstrate this difference.

This study brings up several questions for future research. First, if PPP is causally related to DVT, perhaps packing should be modified and pack removal done earlier. Do et al. have described using a preperitoneal balloon tamponade in swine.[25] Screening U/S captures clinically asymptomatic DVTs and facilitates early anticoagulation. Adams et al. advocates for screening ultrasound in all trauma patients at high risk for VTE, but Shackford et al. note the potential downsides and magnitude of surveillance bias.[13,26] How do we mitigate VTE risk, aside from early VTEp initiation? The role of prophylactic IVC filter placement in trauma patients remains unclear.[27] Should prophylactic IVC filters be placed in this population, especially if they have positive screening ultrasound with their packs in place and/or are unable to receive early VTEp due to other injuries? Is the VTE incidence equal in patients who undergo PPP compared to AE? VTE in pelvic fracture is complex and warrants further investigation.

PPP is an effective life-saving maneuver for hemorrhage control in pelvic fracture patients with hemorrhagic shock, but it is associated with an increased likelihood of VTE. As we continue to improve survival in this patient population, morbidity of our life-saving interventions should be considered. We recommend packing the pelvis with as few packs as is necessary to create compression and hemorrhage control (usually 6), removing the packs as soon as is feasible after the patient has stabilized, and initiating VTEp as soon as possible. We also recommend routine ultrasound surveillance on all patients who undergo PPP, optimally while packs are in place and potentially again after pack removal.

Conclusions

In summary, the results of the present study demonstrate a high incidence of VTE in complex pelvic trauma patients undergoing PPP/EF, despite appropriate VTEp initiation. No patients died from pelvic hemorrhage, so while VTE incidence may be high, PPP/EF remains an effective and life-saving method for hemorrhage control. Given the high VTE rate and relative lower rate of PE in patients undergoing screening ultrasound, we recommend screening duplex ultrasounds in this patient population so that VTE may be identified and treated in a timely-fashion.

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