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Venous thromboembolism in burn patients is not prevented by chemoprophylaxis

Sheena Sikora, Anthony Papp *

BC Professional Firefighters' Burn Unit, Division of Plastic Surgery, Vancouver General Hospital, 899 W 12th Ave., Vancouver, BC V5Z1 M9, Canada

ABSTRACT

Background: Venous thromboembolisms (VTE) including deep venous thrombosis and pulmonary embolism are serious complications following burn trauma. There are inconsistencies in the literature regarding thromboembolic prevention strategies and data suggests that complications occur despite chemoprophylaxis.

Objective: To determine the prevalence of deep venous thromboembolism and pulmonary embolism in burn patients who are actively being treated with VTE prophylaxis and to determine factors that help predict which anti-coagulated patients are at risk for VTE and may benefit from further treatment.

Materials and methods: Retrospective analysis of burn data registry and patient Charts 1980–2012.

Results: Out of 1549 burn patients in the registry fifty patients (3.2%) had a VTE but charts were only available for 26 of these for further analysis. Of these, 12 patients (46%) had a VTE while on chemoprophylaxis and 14 (54%) without chemoprophylaxis. There were no differences between groups, but 90% of DVT complications occurred to Caucasian patients and none to Asians. The VTE group had significantly higher rate of inhalation injury, higher TBSA, longer hospital stay and ICU stay than matched controls.

Conclusions: Chemoprophylaxis does not prevent VTEs. Burn severity predisposes to venous thromboembolic complications.

1. Background and rationale

Prevention of venous thromboembolism (VTE), including deep venous thrombosis (DVT) and pulmonary embolism (PE), has been increasingly studied in burn patients over the last five years. According to the American College of Chest Physicians (ACCP), burn patients are placed in the highest-risk category for VTE, along with major trauma, due to the presence of a profound systemic hypercoagulable state, prolonged bed rest, performance of repeated surgical procedures, femoral venous catheter insertion and recurrent bouts of sepsis [1]. A recent systematic review of the economic burden of VTE found an annual median total healthcare cost for patients with an isolated DVT or PE in the US to be $15.843 [2].

Overall reported incidence of thrombotic complications in burn patients ranges from 0.25% to 7.0% in retrospective studies [1,3]. When undertaking universal diagnostic ultrasound to screen burn patients the risk is reported as high as 23% [1,4]. The incidence of VTE in US burn patients is reported as 0.6%. This incidence increases to 1.2% when patients undergo management in the intensive care unit (ICU) or have a total body surface area (TBSA) burn greater than 10%. TBSA burns reaching 50% or greater had the highest incidence of VTE at 2.4% [5]. According to a study using the American Burn Association's National Burn Repository, independent risk factors for VTE in burn patients included TBSA burned, number of days spent in ICU, number of operations, central venous access, increased age, obesity, burn wound infection, and transfusion of more than 4 units of packed red blood cells [6]. These complications result in significant morbidity and mortality for burn patients with the majority of PE deaths occurring within hours of diagnosis; many as a result of

* *Corresponding author.*
E-mail addresses: sheenasikora@gmail.com (S. Sikora), anthony.papp@gmail.com (A. Papp).
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unrecognized DVT [6]. Despite the availability and use of preventative agents, many patients continue to acquire these complications.

In addition to exhibiting all components of Virchowagents, many patients continue to acquire these complications. The occurring central venous catheters further aggravating endothelial damage, and activation of both fibrinolytic and thrombotic pathways [7]. The ACCP determined the following summarized list of potential risk factors for VTE in burn patients taking into account both burn and physical trauma associated with burn patients: advanced age, morbid obesity, extensive or lower extremity burns, concomitant lower extremity trauma, use of CVCs, presence of wound infections and prolonged immobility [1].

There has been some recommendation for screening asymptomatic high-risk patients for DVT using diagnostic ultrasound (DUS) after prospective studies found a DVT rate of 6–27% [1]. Unfortunately, the low sensitivity of DUS for detecting asymptomatic DVT as well as its unlikely prevention of PE have made it impractical. Additionally, at least 25% of trauma patients have suboptimal scans due to local injuries, dressings, casts, pain and poor patient cooperation. Other diagnostic modalities such as CT and MRI have high false-positive rates for DVT [1]. Lastly, preventive inferior vena cava filter (IVCF) insertion is extremely expensive and PEe to local injuries, dressi shown to occur despite them; thus these continue to be recommended only in patients with proven proximal DVT and either an absolute contraindication to full-dose anticoagulation therapy or planned major surgery [1].

DVT prophylaxis in trauma patients was first recommended 60 years ago but few randomized controlled trials have been executed and none specifically for burn trauma [1].

A systematic review of heparin to treat burn found only 9 studies with appropriate data to be included, and of these, many of the studies were of poor methodological quality (inadequate definitions of treatment and outcomes and no control for confounding factors) [8]. A survey done Canada showed no consistent prophylaxis or treatment algorithm between burn centers [7]. Also, approximately half of burn centers routinely administered either UH or LMWH for thromboprophylaxis to all admitted burn patients regardless of their risk factors. These medications are then continued until discharge [7]. Some centers administered VTE prophylaxis only if additional risk factors existed and only until patients began mobilizing [7].

In addition to limited research on effectiveness, there is also limited research on complications from these medications. The most commonly used anticoagulants are unfractionated (UH) and low molecular weight heparin (LMWH). Among a prospective trial of 625 burn patients treated with heparin, the incidence of Heparin-Induced Thrombocytopenia (HIT) was 2.3% [4].

Multiple risk assessment tools, including the Well' multiple risk assessment tools, including the Welltional risk factors existed which patients received prophylaxis and by which method [10]. Unfortunately, their applicability in burn care is unknown, and specific recommendations as to what type of prophylaxis is beneficial is lacking.

There are currently no universal guidelines for VTE prophylaxis in burn patients and limited research on the complications of medications given. Additionally, despite VTE chemoprophylaxis it has been noted that some burn patients continue to acquire a DVT or PE. A literature search using Meshed headings and keywords about the incidence and factors associated with VTE in patients being actively treated with thromboprophylaxis revealed no results. The number of burn patients who are being actively treated with VTE prophylaxis and acquire a VTE may be significant. Thus, this retrospective study will help to find which patients are at risk of VTE despite prophylaxis and what additional measures may be of benefit to prevent these complications.

1.1. *Objectives*

1. Determine the prevalence of DVT and PE in burn patients who are actively being treated with VTE prophylaxis in a Provincial Burn Center.
2. Determine factors that help predict which anti-coagulated patients are at risk for VTE and may benefit from further treatment.

2. Methods

Patients with VTE complications were drawn from the Provincial Burn Registry between 1980-2012. Fifty patients were identified but only 26 charts were available for analysis due to hospital records policy on destruction of old chart. These charts were separated into groups based on the presence of chemoprophylaxis at the time of VTE. A control group of patients on chemoprophylaxis without VTE complications was drawn randomly from the registry. Thirty-three patients were selected from this group, matched for age, gender and comorbidities.

Analysis involved 2 groups. First, patients who had a VTE while on prophylaxis were compared to those who had a VTE without prophylaxis (Part I). Secondly, those who had a VTE while on prophylaxis where compared to the control group of patients who were on prophylaxis and did not acquire a VTE (Part II).

Data collected included demographics, burn etiology, burn surface area, presence of inhalation injury, length of hospitalization including ICU days and number of operative procedures, other risk factors such as smoking, alcohol use and drug use, type of VTE, type of prophylaxis, and treatment response.

Statistical analysis is quantitative with basic statistics used where appropriate (e.g. mean, standard deviation and confidence intervals).

3. Results

Most VTE complications occurred in men (>70%). For patients who had a VTE occurrence while not on prophylaxis, 5 had inhalational injuries, and 13 had infection (including 5 wound infections, 3 pneumonias, and 4 urinary tract infections). The group on prophylaxis had similar factors including 6 patients with inhalational injuries and 14 patients contracting infections (6 wound infections, 3 pneumonias, 2 urinary tract infections, and 3 with sepsis unspecified).

Table 1 – Patient demographics.

	All patients (26)	Without DVT prophylaxis (14)	With DVT prophylaxis (12)	p-Value
Mean age (years)	41.7	41.4	42	0.92
Gender (% male)	77%	79%	75%	0.83
Ethnicity	23 Caucasians, 3 East Indians	13 Caucasians, 1 East Indians	10 Caucasians, 2 East Indians	0.58

Table 2 – Burn etiology.

	All patients (N=26)	Without DVT prophylaxis (N=14)	With DVT prophylaxis (N=12)	p-Value
Flash/flame	21 (81%)	11 (79%)	10 (83%)	0.83
Scald	1 (3.8%)	1 (7.1%)	0 (0%)	
Electrical	2 (7.7%)	1 (7.1%)	1 (8.3%	
Grease	2 (7.7%)	1 (7.1%)	1 (8.3%)	

VTE was diagnosed by Doppler ultrasound in 15 patients, VQ scan in 3 patients, CT chest for pulmonary embolism in 6 patients, pulmonary angiography in 1 patient and clinical exam in 1 patient. Twenty-four patients had associated injuries including 4 fractures, 2 eye injuries, 2 lacerations and 1 ligamentous injury. All patients had full thickness burns except five which were partial thickness. One patient died secondary to pneumonia and subsequent respiratory failure.

3.1. *Part I*

Part one of the study compared patients who acquired a VTE complication while in hospital with or without chemoprophylaxis. Fifty patients (3.2%) were identified as having a VTE complication during the study period. Twenty-six had charts available for review. Of these, 12 patients (46%) were on chemoprophylaxis at the time of their VTE and 14 (54%) were not. There were no significant differences between groups with regards to demographics (Table 1), burn etiology (Table 2), inhalation injury and substance abuse (Table 3). Interestingly, 89% of DVD complications occurred to Caucasian patients and none to Asian patients (Table 1).

Eleven (92%) patients on prophylaxis received Heparin 5000 Units, subcutaneously, twice daily. Only 1 patient received Dalteparin 5000 Units, subcutaneously daily. No other anticoagulants were used. There were no differences in incidence of pulmonary embolism whether patients were on or off chemoprophylaxis. (Table 4). There were no differences in mean total body surface area burned and length of hospital stay between groups (Table 5).

3.2. *Part II*

Part two of the study compared patients who acquired a VTE complication while on prophylaxis to a matched control group of patients who where on chemoprophylaxis and did not acquire a VTE complication.

Flash and flame injuries were most common in both groups, with an equal distribution of other etiologies. There was no difference in alcohol or drug use between groups. There was, however a significantly higher rate of inhalation injury in the VTE group. Interestingly, there was a higher proportion of smokers in the control group who did not acquire a VTE. The VTE group had higher TBSA, longer hospital stay and ICU stay and more OR visits (Table 6).

Table 3 – Substance abuse and inhalational injury.

	All patients (N=26)	Without DVT prophylaxis (N=14)	With DVT prophylaxis (N=12)	p-Value
Alcohol use	5 (19%)	3 (21%)	2 (17%)	0.76
Drug use	2 (7.7%)	0 (0%)	2 (16.7%)	0.11
Smoking	1 (3.9%)	0 (0%)	1 (8.3%)	0.27
Inhalation injury	11 (42.3%)	5 (35.7%)	6 (50%)	0.46

Table 4 – Incidence of thromboembolic complications.

	All patients (N=26)	Without DVT prophylaxis (N=14)	With DVT prophylaxis (N=12)	p-Value
DVT	15 (58%)	7 (50%)	8 (67%)	0.28
PE	10 (38%)	7 (50%)	3 (25%)	
Both DVT and PE	1 (4%)	0 (0%)	1 (8%)	
Total of all (%)	1.7%	0.9%	0.8%	

Table 5 – TBSA and length of stay in hospital.

	All patients (N=26)	Without DVT prophylaxis (N=14)	With DVT prophylaxis (N=12)	p-Value
Mean TBSA (%)	25.1	22.9	27.6	0.55
Mean hospital stay (days)	76.7	45.6	113	0.13
Mean ICU stay (days)	19.3	19.2	19.4	0.13

Table 6 – Burn etiology, substance abuse, presence of inhalation, TBSA, length of stay in hospital in ICU and number of operating room visits.

		DVT (N=12)	No DVT (N=33)	p-Value
Etiology	Flash/flame	10 (83%)	20 (60%)	0.08
	Scald	0 (0%)	9 (27%)	
	Electrical	1 (8.3%)	1 (3.0%)	
	Grease	1 (8.3%)	0 (0%)	
	Contact with hot object	0 (0%)	3 (1.9%)	
	Alcohol use	2 (17%)	11 (33%)	0.28
	Drug use	2 (17%)	8 (24%)	0.59
	Smoking	1 (8%)	17 (52%)	<0.01
	Inhalation injury	6 (50%)	5 (15%)	0.02
	Mean TBSA (%)	27.6	8.4	<0.01
	Mean hospital stay (days)	113	13.9	<0.01
	Mean ICU stay (days)	19.4	3	<0.01
	Total OR visits (N)	4	1	<0.01

4. Discussion

Burn predisposes to thromboembolic complications. Despite the fact that this has been know for decades there are no consensus guidelines for thrombosis prophylaxis and protocols between burn center vary greatly. Also, it is known that thromboembolic complications occur while on prophylaxis.

The first part of our study looked at burn patients who acquired a VTE comparing patients who were on chemoprophylaxis with those who were not. There was no significant difference in the incidence of VTE between patients with and without chemoprophylaxis suggesting that the prophylactic dose being used is likely not enough to prevent VTE in burn patients. The same has been found in patients undergoing total hip arthroplasty, where the incidence of pulmonary embolisms has remained constant despite prophylaxis [11]. It has been suggested that prophylaxis dosage using enoxaparin is not adequate [12] and it should be based on both patients' weight and burn size [13].

Part two of our study looked at burn patients who acquired a VTE while on chemoprophylaxis against a matched control group of patients who were on chemoprophylaxis and did not get a VTE. Patients who acquire a VTE while on prophylaxis have a higher TBSA burn, higher incidence of inhalation injury, and longer hospital and ICU stay than the control group. This confirms the suggestion that the severity of the injury in general is a risk factor for obtaining a thromboembolic complication.

We found that most thromboembolic complications happened to men. This is supported by previous findings where men had more VTEs than women having a relative risk of 2.05 [14]. Same study found that age older than 50 years resulted in a higher risk with smaller TBSA to develop a VTE. Being of male gender, a smoker, an alcoholic, high-age group, high % TBSA, use of central line, increased number of surgeries, and increased number of blood transfusions are identified as possible predisposing factors for DVTs [14]. Surprisingly, our study showed no increased risk with people who smoked, used alcohol or drugs or had an inhalational injury.

The incidence of VTE's in the literature vary greatly. This is partly due to most VTE's being silent and asymptomatic [15]. A large retrospective study showed that about 6% of burn patients develop a DVT and of these 26% had DVT at multiple sites. All these patients had a routine ultrasound screening to detect this. The total VTE's in our study population was only 1.7% being 0.9% without and 0.8% with DVT prophylaxis. These numbers suggest that there actually is no benefit in giving prophylaxis as there are no differences between groups.

The limitations of this study include its design. Longitudinal retrospective study makes conclusions about current standard of care difficult and it has the inability to control for all clinical factors that may influence results. Additionally, treatment paradigms have changed over the study period. As the incidence of acquiring a VTE while on chemoprophylaxis is rare, it is difficult to obtain a significant number of patients that would allow regression analysis. Longitudinal multicenter trials are indicated to determine which patients are at high risk for the development of VTE and optimal therapies. Lastly, there are some asymptomatic patients with VTE who are not diagnosed.

Conflicts of interest

None.

REFERENCES

[1] Guyatt G, Akl E, Crowther M, Gutterman D, Schuunemann J. Antithrombotic therapy and prevention of thrombosis, 9th ed: American College of Chest Physicians evidence-based clinical practice guidelines. Chest 2012;141(Suppl. 2):7S–47S, doi: http://dx.doi.org/10.1378/chest.1412S3.

[2] Prandoni P. Healthcare burden associated with the post-thrombotic syndrome and potential impact of the new oral anticoagulants. Eur J Hematol 2012;88(3):185–94.

[3] Galanis T, Kraft W, Merli G. Prophylaxis for deep vein thrombosis and pulmonary embolism in the surgical patient. Adv Surg 2011;45:361–90.

[4] Scott J, Klein M, Gernsheimer T, Honari S, Gibbons J, Gibran N. Arterial and venous complications of heparin-induced thrombocytopenia in burn patients. J Burn Care Res 2007;28 (1):71–4.

[5] Pannucci C, Osborne N, Wahl W. Venous thromboembolism in thermally injured patients: analysis of the National Burn Repository. J Burn Care Res 2011;32(1):6–12.

[6] Bushwitz J, LeClaire A, He J, Mozingo D. Clinically significant venous thromboembolic complications in burn patients receiving unfractionated heparin or enoxaparin as prophylaxis. J Burn Care Res 2011;32:578–82.

[7] Abedi N, Papp A. A survey of current practice patterns in prophylaxis against venous thromboembolism (vte) and gastrointestinal (gi) ulceration among Canadian burn centers. Burns 2011;37:1182–6.

[8] Oremus M, Hanson M, Whitlock R, Young E, Archer C, Dal Cin A, et al. Systematic review of heparin to treat burn injury. J Burn Care Res 2007;28(6):794–804.

[10] Moheimani F, Jackson D. Venous thromboembolism: classification, risk factors, diagnosis, and management. International Scholarly Research Network. ISRN) Hematol 2011;2011:1–7 Article ID 124610.

[11] Shahi A, Chen A, Tan T, Maltehfort M, Kucukdurmaz F, Parvizi J. The incidence and economic burden of in-hospital venous thromboembolism in the United States. J Arthroplasty 2016 (October), doi:http://dx.doi.org/10.1016/j.arth.2016.10.020 pii: S0883-5403(16)30747-1. [Epub ahead of print].

[12] Brown A, Faraklas I, Ghanem M, Cochran A. Enoxaparin and antifactor Xa levels in pediatric acute burn patients. J Burn Care Res 2013;34(November–December (6)):628–32.

[13] Faraklas I, Ghanem M, Brown A, Cochran A. Evaluation of an enoxaparin dosing calculator using burn size and weight. J Burn Care Res 2013;34(November–December (6)):621–7.

[14] Mullins F, Mian M, Jenkins D, Brandigi C, Shaveer J, Friedman B, et al. Thromboembolic complications in burn patients and associated risk factors. J Burn Care Res 2013;34(May–June (3)):355–60.

[15] Boersma RS, Jie KS, Verbon A, van Pampus EC, Schouten HC. Thrombotic and infectious complications of central venous catheters in patients with hematological malignancies. Ann Oncol 2008;19:433–42.