Venous Thrombosis Incidence in Burn Patients

Preliminary Results of a Prospective Study

W.L. Wahl, MD, M.M. Brandt, MD, K.S. Ahrns, CCRN,
P.J. Zajkowski, BS, M.C. Proctor, MS, T.W. Wakefield, MD, L.J. Greenfield, MD
Ann Arbor, Michigan

There are few prospective data on the incidence of deep venous thrombosis (DVT) in burn patients. In an on-going prospective study, hospitalized burn patients 18 years or older with an expected hospital length of stay more than 72 hours were imaged with baseline venous duplex ultrasound of all extremities within the first 48 hours after admission and weekly until discharge. Patient demographics and clinical risk factors for DVT were assessed. At the time of submission, 40 patients met screening criteria, and 30 were enrolled. Ultrasound diagnosed seven patients with 11 acute DVT for an incidence of 23%. One pulmonary embolism was documented. DVT patients had a mean age of 49 ± 23 years with an average TBSA burn of 15 ± 4% compared with those without thrombosis with a mean age of 44 ± 17 years (P = NS) and TBSA burn of 18 ± 25% (P = NS). There were no statistically significant differences for DVT patients in terms of age, number of central line days, hospital length of stay, or TBSA burned. Given the preliminary findings of this small study, we believe that all hospitalized burn patients are at risk for DVT. On-going investigation will be helpful in defining level of risk and improved prevention strategies for thromboembolic complications in burn patients. (J Burn Care Rehabil 2002;23:97–102)

Deep venous thrombosis (DVT) and pulmonary embolism (PE) remain common complications in traumatized patients, with the level of risk varying with the degree and site of injury.[1,2] Despite the published "high risk" of DVT for the multiply injured, many retrospective studies report incidences of thromboembolic complications in burn patients as low as 0.9% for symptomatic DVT[3] and 0 to 0.4% for symptomatic PE.[3–5] We recently reviewed our hospitalized burn patient registry for the diagnosis of symptomatic DVT and found an incidence of 2.4%.[6] In addition to this finding, burn patient autopsies reveal the presence of PE in as many as 30% of burn deaths.[7,8] These findings prompted us to determine prospectively the incidence of DVT in our burn population and to examine which medical and burn-associated factors may be associated with thromboembolic complications.

From the University of Michigan Health System, Ann Arbor, Michigan.
Reprint Requests: Wendy L. Wahl, MD, Trauma Burn Center, University of Michigan Health System, 1500 E. Medical Center Drive, Ann Arbor, Michigan 48109-0033.

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PATIENTS AND METHODS

All adult burn patients admitted to the University of Michigan Health System between July 12, 2000, and July 12, 2001, were screened for enrollment into the study. Study inclusion criteria included age 18 years or older, an acute burn injury without accompanying blunt or penetrating trauma, an estimated hospital length of stay (LOS) of more than 72 hours, and ability to obtain informed consent. Patient demographic information concerning age, weight, height, burn site, size and mechanism, LOS, and past medical history were abstracted from the patient chart. Data on complications, ventilator days, central venous catheter (CVC) days, DVT prophylaxis, length of immobility, number of operative procedures, and time to DVT or PE diagnosis were tracked prospectively. Patients diagnosed with necrotizing fasciitis or exfoliative skin disorders were excluded.

All patients enrolled in the study underwent venous duplex ultrasound (USN) of all four extremities at the bedside within 48 hours of admission and weekly until discharge. If the patient was discharged before the second USN, the second USN was performed at the first clinic visit. Acute DVT was diagnosed by the established

criteria of vein noncompressibility, venous dilation, and decreased echogenicity.[9,10] Imaged veins in the lower extremities included the external iliac, common femoral, superficial femoral, popliteal, anterior tibial, peroneal, posterior tibial, and gastrocnemius. The imaged upper extremity veins were the internal jugular, subclavian, axillary, brachial, radial, and ulnar. Adequacy of each scan was noted, and the reasons for an incomplete exam were documented. All studies were performed by a trained vascular technician and reviewed by the Diagnostic Vascular Unit attending physician. Recent certification confirmed a sensitivity of 96% and specificity of 90% for USN diagnosis of DVT in our Diagnostic Vascular Unit. Patients who became symptomatic for DVT, either in the study or off-study, underwent USN of the symptomatic extremity only. Patients with symptoms or signs suggestive of PE underwent helical chest computerized tomography (CT) to diagnose or to exclude PE.

All patients who were nonambulatory from their burns or illness were treated with DVT prophylaxis per our unit protocol. All patients received enoxaparin 40 units s.q. q.d. unless contraindicated because of allergy, excessive bleeding, or unexplained thrombocytopenia. Sequential compression devices (SCD) were used where possible in those not receiving low-molecular-weight heparin (LMWH).

All patients received occupational and/or physical therapy consultations for range of motion and to assess splinting needs. Range of motion of a grafted extremity was held for 48 hours after skin grafting or if the patient was hemodynamically unstable. Prolonged immobility was defined as those patients who exceeded the standard postoperative time period for decreased mobility.

Medical risk factors which were examined as risk factors for DVT included previous history of DVT or PE, family history of thromboembolism, congestive heart failure and coronary artery disease, history of pelvic or extremity trauma, history of malignancy, current use of hormonal supplements or oral contraceptives, and obesity.[11,12] Body-mass indices (BMIs) were calculated to assess for degree of obesity, where BMI = (weight in kg)/(height in meters^2).[13] Normal BMI was measured as 21 to 25 kg/m^2, with overweight defined as 25 to 30 kg/m^2, and obesity as more than 30 kg/m^2.

Potential burn-related risk factors for DVT, including TBSA burn, CVC days, site of CVC compared with site of DVT, ventilator days, excess time of immobility, number of operative procedures, and presence of a burn wound infection and burn on the DVT extremity, were tracked prospectively. Burn wound infection was defined as a quantitative tissue biopsy with $\geq 10^5$ organisms per gram of tissue.[14,15]

Approval for human subject research was obtained through the Hospital Institutional Review Board. Statistical comparisons between groups were performed with Student's *t*-tests for continuous variables and χ^2 analyses for dichotomous variables, where $P \leq 0.05$ was significant.

RESULTS

One hundred seven adult patients completed their hospitalizations for burn injury between July 12, 2000, and July 12, 2001. Of these, 41 patients were not expected to have a LOS greater than 72 hours, with six patients admitted for comfort care only. Another 19 patients were excluded because their burn injuries were more than 48 hours old. Five patients had a combination of blunt trauma with a burn injury. Four patients met more than one exclusion criterion.

Forty patients met all inclusion criteria. Ten patients were not enrolled because of patient refusal (n = 4), inability to obtain consent (n = 3), and inability to obtain the first USN within 48 hours of admission (n = 3). The remaining 30 patients form the study group. In this group there were 8 women and 22 men with a mean age of 45 ± 18 years and mean TBSA of 17 ± 23% (Table 1). The majority of burns were a flash or flame mechanism (n = 25), with nine patients diagnosed with inhalational injury by bronchoscopy.

In the study group 11 DVT were diagnosed in seven patients (Table 2). There were four patients with lower extremity DVT, one with upper extremity DVT, and two with both upper and lower extremity DVT. There was an average of 2.8 USN done per patient, with the diagnosis of acute DVT made on the

Table 1. Demographics of study participants

Group	n	Age (yr)	TBSA (%)	Gender (% Male)	LOS (days)	Mortality (%)
All	30	45 ± 18	17 ± 23	73	16 ± 18	17
DVT/PE	7	49 ± 23	15 ± 4	71	23 ± 18	14
No DVT	23	44 ± 17	18 ± 25	74	16 ± 15	17

DVT, deep venous thrombosis; *PE*, pulmonary embolism.

Table 2. Site of thrombosis

	Lower Extremity DVT			Upper Extremity DVT					
DVT Patient	Below Knee	Femoral	External Iliac	Subclavian	Internal Jugular	Deep Brachial	SVT Cephalic/Basilic	PE	Prophylaxis
1	0	0	1	0	0	0	0	0	LMWH
2	0	1	1	0	1	0	0	0	SCD
3	0	1	0	0	0	0	0	0	LMWH
4	2	0	0	0	0	0	1	1	LMWH
5	0	0	0	0	0	1	1	0	none
6	1	0	0	0	0	0	0	0	SCD
7	2	0	0	0	1	0	1	0	SCD and LMWH

SVT, superficial venous thrombosis; *LMWH*, low-molecular-weight heparin; *SCD*, sequential compression device.

first scan in three of the seven patients diagnosed with DVT. The average time to DVT diagnosis was 6.7 days. Five patients had persistence of the DVT for multiple scans, one patient had DVT present on only one scan, and one patient died after DVT diagnosis and had no follow-up USN. Seventy-five percent of scans were considered technically complete, with all segments adequately visualized. The most common reason cited for a technically inadequate USN was edema in the infrapopliteal region.

One of the lower extremity DVT patients, who had bilateral gastrocnemius DVT, was diagnosed with PE at autopsy after an unexpected cardiac arrest. The patient with an upper extremity DVT also had a questionable subsegmental PE on helical chest CT. Six of the seven DVT patients received DVT prophylaxis with either LMWH or SCD or both. The one patient who developed deep brachial vein thrombus and possible subsegmental PE was considered ambulatory with hand burns and a flank burn, and did not receive prophylaxis (Table 2). All survivors were treated with therapeutic heparin or therapeutic low-molecular-weight heparin followed by conversion to oral warfarin therapy for treatment of DVT.

Comparison between the DVT group and the no-DVT group showed no significant differences for age, TBSA burn, LOS, or mortality (Table 1). Presence of medical risk factors for DVT, including history of malignancy, obesity, history of previous DVT or PE, history of previous extremity or pelvic trauma, congestive heart failure or coronary artery disease, and hormonal supplementation or oral contraceptives, are listed in Table 3. There were no differences between the DVT and no-DVT groups for any of these conditions.

Other potential risk factors for DVT related to the burn injury, including number of CVC days, presence of CVC in a DVT extremity, number of ventilator days, number of surgical procedures, presence of a burn wound infection, and presence of a burn on the DVT extremity, are listed in Table 4. DVT formation in a burned extremity was statistically significant at $P = 0.012$.

The overall incidence of DVT in the study group was 23.3%, with a 3.3% incidence of PE (6.7% including the questionable PE). There were an additional six patients who developed superficial venous thrombosis of the upper extremity, for an overall incidence of 43% for any thrombotic complication (Table 2). The one documented PE was found at autopsy in a patient with healed burns and continued pulmonary insufficiency after an electrical injury, who died on hospital day 12 from an acute cardiac arrest. Postmortem examination was indeterminate as to the cause of death, but did reveal evidence of a lobar PE. The three additional deaths in the study group with no-

Table 3. Medical risk factors for DVT

Group	n	Malignancy	Obesity	DVT/PE	Trauma	CAD/CHF	Hormonal Supplements
All	30	3 (10)	11 (37)	1 (3)	8 (27)	2 (7)	1 (3)
DVT/PE	7	2 (29)	4 (57)	1 (14)	2 (29)	2 (29)	0
No DVT	23	1 (4)	7 (30)	0	6 (26)	0	1 (4)

DVT, deep venous thrombosis; *PE*, pulmonary embolism; *CAD*, coronary artery disease; *CHF*, congestive heart failure.
Figures are number and (percentage).

Table 4. Possible burn-associated risk factors for DVT

Group	n	TBSA burn %	CVC (days)	CVC in DVT Extremity, No. (%)	Ventilator (days)	Immobility, No. (%)	OR (n)	Wound Infection, No. (%)	DVT in Burn Extremity, No. (%)
All	30	17 ± 23	10 ± 7.9	4 (13%)	6 ± 11	17 (57%)	2 ± 2.3	7 (23%)	4 (13%)
DVT/PE	7	15 ± 4	7 ± 7.4	4 (57%)	9 ± 18	3 (43%)	2.3 ± 2.1	2 (29%)	4 (57%)*
No DVT	23	18 ± 25	10 ± 21	0	5.4 ± 9	14 (61%)	2 ± 2.4	5 (22%)	0

*$p < 0.05$.

CVC, central venous catheter; *DVT*, deep venous thrombosis; *OR*, operating room; *PE*, pulmonary embolism.

DVT were in patients where the family withdrew support, and there was no gross evidence of DVT or PE before death.

In addition to the study group who underwent USN on a weekly basis, seven patients who became symptomatic with worsened extremity pain, swelling, or erythema suggestive of DVT underwent USN of the symptomatic extremity. Symptoms or signs of desaturation, tachypnea, or pleuritic chest pain were evaluated with helical chest CT. Two patients were diagnosed with thrombotic complications outside of the study group, one with a DVT and one with a PE. These patients had been excluded from the original study group because of a pelvic fracture in the DVT patient and a 2-week-old burn in the PE patient. If we regroup all patients admitted during the study period by the presence or absence of DVT/PE, there was a total of 9 patients diagnosed with DVT or PE (total DVT/PE), and 98 patients with no documented thromboembolic events. There was no difference in the age, TBSA burn, or mortality for the total DVT/PE group. The medical risk factors for the total DVT/PE group were not different from the total no-DVT group. For burn-associated risk factors, CVC days were higher in the total DVT/PE group, 6.9 ± 5.8 days, vs 3.7 ± 11.6 days for the total no-DVT group. The overall incidence for the study group combined with the symptomatic nonstudy patients was 8.4% for DVT and for 1.9% for PE (2.8% including the questionable PE).

DISCUSSION

Despite vast improvements in the management and survival of thermal injuries over the last century, there has been little study of thromboembolic complications in burn patients. The association between thromboembolism and burns has been well described in autopsy data from more than 30 years ago.[7,8,16] Clinically symptomatic DVT incidence has been reported at 0.9 and 7%,[3,4] with PE diagnosed clinically in only a fraction of cases (0 to 0.4%).[3–5] Many studies do not include autopsy data to exclude PE as the cause of death, and most studies look at the incidence of symptomatic DVT or PE. When Wait and colleagues[4] performed routine USN to assess the incidence of DVT associated with CVC in burn patients, he reported a much higher incidence of DVT, with 7% symptomatic DVT and 12.6% asymptomatic DVT.

Using radiolabeled ^{125}I fibrinogen studies, Mayou et al[17] found that as many as 60% of burn patients had positive studies for acute DVT. Most recently, Harrington and colleagues[18] from the U.S. Army Institute of Surgical Research found a symptomatic DVT incidence of 1.77 and 0.77% for PE. They conclude that a prospective screening trial that assesses all risk factors for DVT and PE should be performed before routine prophylaxis is used.

The same reports that highlight low incidences of DVT support the suggestion that older age[5,18] and larger TBSA burns[3,5,18] may be risk factors for DVT, which may benefit from DVT prophylaxis. All of these studies were retrospective and reported only the symptomatic incidence of DVT, which may be difficult to discern in a burn patient who may have a burned extremity with pain, swelling, and/or erythema that masks a possible underlying DVT.

In this small, prospective study we did not find that older age, TBSA burn, or obesity were associated with thromboembolic complications, although because of the sample size a type II error cannot be excluded. Burned extremities, however, were statistically more likely to develop a DVT. Presence of a CVC was not a significant contributor to DVT in this study. In a previous retrospective report we found a high association between burn wound infection and DVT diagnosis in the extremity with a burn wound infection.[6] This association did not prove to be significant in this small study.

In the nonstudy patients we diagnosed one DVT and one PE in two patients. If we combine all patients who had thrombotic complications (study patients and nonstudy patients), there is a statistically significant difference for the number of CVC days and hos-

pital LOS. We would expect that the hospital LOS would be longer in the study group compared with the patients who were not enrolled, because 44 of 77 unenrolled patients had expected LOS of 72 hours or less. We would also expect the number of CVC days to be lower for the nonstudy patients with shorter LOS. There were seven patients in the nonstudy group who underwent USN for clinical suspicion of DVT, with one documented DVT. Despite the fact that only 7 of the 77 nonstudy patients had an USN looking for DVT, the DVT incidence of all the adult burn inpatients (those in the study plus those who were symptomatic) revealed an incidence of 8.4%, which is higher than any published retrospective studies.

One of the concerns about thromboembolic complications in burn patients is the risk of prophylaxis. High rates of complications have been reported from the past use of subcutaneous heparin injection, with reported bleeding risks as high as 4% with LMWH in more recent studies.[2] If these agents cannot be employed because of bleeding, allergy, or antiplatelet antibodies, SCD often cannot be placed on a burned extremity. Because bleeding complication rates with LMWH are thought to be higher than the assumed low incidence of DVT, the risk-benefit ratio for DVT prophylaxis with LMWH has been considered unjustified.

In light of our findings of a high incidence of DVT and the inability to predict which "asymptomatic" DVT will become symptomatic, we support the recommendation that DVT prophylaxis should be routine. Approximately 20% of calf vein thromboses will propagate proximally, with an associated PE rate of 40 to 50%.[19] Calf thrombi are also associated with a 25% incidence of chronic venous insufficiency.[19] In this study with an incidence of DVT of at least 9.3%, and maybe as high as 23%, the risks of DVT prophylaxis seem justified.

The best modality for prophylaxis, however, remains questionable. In this study all but one DVT patient received prophylaxis. There were treatment failures with both SCDs and LMWH. We estimate that approximately 150 patients randomly assigned to two different treatment arms would be needed to determine whether one or another prophylactic modality would be most beneficial.

When one considers that burn patients often fulfill all of Virchow's triad of stasis, local injury, and hypercoagulability, it does not seem unreasonable that burn patients may be at risk for DVT and PE. Curreri et al[20] described multiple coagulation derangements in burn patients, including elevated platelets, fibrinogen, factor V, and factor VIII, which could contribute to a procoagulable state. As survival rates for burn injury have significantly improved, the focus of what causes morbidity and mortality may need to change. With better nutritional support, wound care, and ICU management, patients are more likely to survive the burn itself. More invasive intravenous access and longer hospital stays for patients who survive outside of the initial resuscitation phase may contribute to the increased incidence of DVT in recent studies. It may also be that the technology of venous duplex USN has improved from the past when venography and radiolabeled fibrinogen studies were the tests of choice. The ability to make a DVT diagnosis is now simpler. The body of literature surrounding DVT and PE in any hospitalized patient is now prolific, heightening the clinician's awareness of the potential problem.

CONCLUSION

Although this is a small, preliminary study, it is prospective and calls into question which factors are truly associated with thromboembolic complications in burn patients. We believe it is important to report the incidence of DVT as much higher than previously published. This higher incidence of DVT occurred despite the use of DVT prophylaxis in our patient population. Further study of more patients will allow for multivariate analysis to define the true risk factors for DVT and PE and how we might better provide prophylaxis against these complications.

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