



S **D**
DTIC
ELECTE
AUG 30 1993
A

93-19799



93 8 24 128

Thromboembolic Complications in Thermally Injured Patients

Loring W. Rue III, M.D., William G. Cioffi, Jr., M.D., Robert Rush, M.D., William F. McManus, M.D., and Basil A. Pruitt, Jr., M.D.

United States Army Institute of Surgical Research, Fort Sam Houston, San Antonio, Texas, U.S.A.

The frequency of thromboembolic complications in burn patients has been estimated to range from 0.4% to 7%. The clinical significance of these events is often debated and has prompted some centers to adopt the routine prophylactic use of low dose heparin prophylaxis. A 10 year review of 2,103 burn patients treated at this institution was undertaken. Twenty-five (1.2%) patients, with a mean age of 40.0 years and an average burn size of 49.3% total body surface area (TBSA), were identified as having significant pulmonary thromboembolism (PTE). In only 3 (0.14%) patients was the thromboembolism considered to be a cause of death. Nineteen (0.9%) patients, with an average age of 36.7 years and a mean burn size of 48.3% TBSA, developed clinically evident deep venous thrombosis (DVT); however, in only 1 (0.05%) patient did the disease progress to fatal PTE.

A review of the literature reveals a 0.6% to 5% incidence of complications related to low dose heparin therapy which includes bleeding, thrombocytopenia, and arterial thrombosis. We feel that the infrequency of clinically significant PTE and DVT in burn patients and the comparable or greater rate of complications associated with heparin prophylaxis mitigate against the routine use of low dose heparin therapy except in patients at high risk for these events.

Estimates of the frequency of thromboembolic complications following thermal injury range from 0.4% to 7%. Mechanical and pharmacologic methods of prophylaxis have been employed in attempts to reduce the incidence of this complication. Mechanical measures have included early mobilization, elastic wrapping, or application of pneumatic compression devices to the lower extremities. In addition, elevation of the foot of the bed and avoidance of inadvertent pressure on the lower extremity during surgery and in the postoperative period have been suggested. Recommended preventive pharmacologic measures have included low dose heparin, warfarin, aspirin, and various dextran solutions [1].

Characteristic physiologic alterations which occur in thermally injured patients would appear to place them at significantly greater risk for the development of thromboembolic complications than the typical general surgical or trauma patient. All elements of Virchow's triad are met by the hypercoagulable state induced by thermal injury, the prolonged immo-

bilization and frequent operative procedures necessary to achieve wound closure, and the potential for vascular damage secondary to multiple venous line insertions.

The clinical significance of this complication is often debated. Some burn centers routinely administer low dose heparin prophylaxis to all thermally injured patients. Other centers reserve prophylactic heparin therapy for use in those patients with additional major risk factors for thromboembolism. These include advanced age, previous history of venous thrombosis, obesity, lower extremity trauma, and malignancy. These investigators contend that the risk associated with prophylactic heparin therapy exceeds the risk of the disease process itself. The purpose of this study is to determine the incidence and clinical significance of thromboembolic complications in a population of thermally injured patients.

Methods and Materials

The charts of all thermally injured patients admitted to the U.S. Army Institute of Surgical Research during the period from January 1, 1980 to December 31, 1989 were reviewed for evidence of thromboembolic complications. The patient age, burn size, and the presence of established risk factors were recorded. The incidence of deep venous thrombosis (DVT) and pulmonary thromboembolism (PTE) was segregated by age and burn size by use of a multiway table. Log linear analysis was performed to identify associations between incidence, age, and burn size. The signs and symptoms of thromboembolism as well as the method of documentation were recorded. Pulmonary embolism was diagnosed by either ventilation/perfusion scan or pulmonary angiogram. Deep venous thrombosis was diagnosed by Doppler flow studies or venogram. Patients in whom the diagnosis of thromboembolism was made postmortem had autopsy documentation of their disease.

All central venous access lines and sites were changed every 3 days to minimize the occurrence of suppurative thrombophlebitis. To reduce disuse atrophy and optimize functional recovery, all patients received passive range of motion exercises and active mobilization when their clinical condition permitted. Low dose subcutaneous heparin therapy was employed in presumed high risk patients at the discretion of the clinician.

Presented at the Société Internationale de Chirurgie in Stockholm, Sweden, August, 1991.

Reprint requests: Library Branch, U.S. Army Institute of Surgical Research, Bldg. 2653, Fort Sam Houston, Texas, 78234-5012, U.S.A.

This document has been approved
 for public release and sale; its
 distribution is unlimited.



World Journal
 of Surgery

© 1992 by the Société
 Internationale de Chirurgie

Reprinted by the publisher
 No further reproduction allowed

Table 1. Incidence of deep venous thrombosis in thermally injured patients.

Burn size (% TBSA)	Age (yrs)			
	<20	21-40	41-60	>60
<20%	0/408	0/398	1/135	1/87
21-40%	1/145	3/234	1/86	1/69
41-60%	1/81	5/147	0/60	1/33
61-80%	1/27	1/61	2/33	0/12
>81%	0/12	0/43	0/21	0/11

TBSA: Total body surface area; Patients with deep venous thrombosis/total number of patients.

Results

During the 10 year period of this study, 2,103 patients were admitted including 336 children. The mean burn size of all patients admitted during this time was 27.8% of the total body surface area (TBSA) and the mean age was 29.6 years. Three hundred sixty-nine patients died, for a mortality of 17.5%.

Nineteen (0.9%) patients, including 2 patients with both DVT and PTE, developed clinically significant deep venous thrombosis during their hospitalization. The mean age of the patients who developed significant DVT was 36.7 years (range 1-81 years) and the mean burn size was 48.3% TBSA (range 14-89 TBSA). The segregation of the occurrence of DVT by age and burn size is shown in Table 1. Log linear analysis revealed a weak association between burn size and the incidence of DVT, but not between age and DVT. The average time of diagnosis was on postburn day 40. Twelve (63.2%) patients had sustained inhalation injury requiring mechanical ventilatory support with positive end expiratory pressure (PEEP). Thirteen (68.4%) patients had burns of the lower extremity requiring excision, grafting, and postoperative immobilization. Five (26.3%) patients were considered to be obese as determined by the subjective assessment of the admitting physician. No patient had a prior history of myocardial infarction. Six (31.6%) patients had femoral venous access lines inserted prior to diagnosis.

Twelve of 19 patients had clinical evidence of lower extremity swelling, and 9 patients complained of calf and/or inner thigh pain, or had erythema or increased calf calor. Venography was employed in 9 patients and Doppler flow studies were utilized for diagnosis in 3 patients. In 7 patients, including 2 children, DVT was diagnosed only at autopsy.

Only 1 patient had received prophylactic low dose intermittent heparin therapy prior to diagnosis. All patients in whom a diagnosis of DVT was made antemortem were anticoagulated with continuous intravenous heparin for 5 to 10 days. Surviving patients were discharged on oral warfarin.

Twenty-five (1.2%) patients, including 2 children, were diagnosed as having clinically significant pulmonary embolism. One patient developed recurrent pulmonary emboli during hospitalization. The mean age of the patients who were diagnosed with pulmonary embolic events was 40.0 years (range 1.5 to 84 years) and the mean TBSA burned was 49.3% (range 12.5 to 84%). Segregation of patients with pulmonary embolism by age and burn size is depicted in Table 2. Log linear analysis revealed a weak association between burn size and incidence of pulmonary embolism, but not age and incidence. The average

Table 2. Incidence of pulmonary embolus in thermally injured patients.

Burn size (% TBSA)	Age (yrs)			
	<20	21-40	41-60	>60
<20%	0/408	0/398	3/135	3/87
21-40%	0/145	1/234	0/86	0/69
41-60%	1/81	6/147	2/60	0/33
61-80%	1/27	0/61	1/33	1/12
>81%	2/12	3/43	1/21	0/11



Fig. 1. Photograph demonstrating fatal pulmonary embolus in a morbidly obese burn patient. The arrows indicate thrombus within the pulmonary vessel.

postburn day of presentation was 31. Sixteen (69.5%) patients had inhalation injury requiring mechanical ventilation and PEEP. Twelve (52.2%) patients had burn injuries of the lower extremities requiring excision, grafting, and postoperative immobilization. Eight (34.8%) patients were considered to be obese by the examining physician. No patient had a past medical history of DVT, malignancy, or pulmonary embolus. Two patients, however, had a previous history of myocardial infarction. Thirteen (56.5%) patients had femoral venous access lines inserted during hospitalization.

Presenting signs and symptoms included chest pain in 7 patients, dyspnea in 5 patients, tachypnea in 6 patients, and hemoptysis in 3 patients. Three patients sustained cardiopulmonary arrest as a result of their embolic event (Fig. 1). Ventilation/perfusion scintigraphy was the method utilized to establish the presence of PTE in the 8 patients in whom an antemortem diagnosis was made. Three of these patients subsequently underwent pulmonary angiography to confirm the diagnosis. Significant pulmonary emboli were found in 15 patients at autopsy only; however, in only 3 (0.14%) patients was pulmonary embolism thought to be directly responsible for death. Only 2 patients were noted to have had concomitant clinically evident DVT during hospitalization. One was diagnosed antemortem by a Doppler flow study and the other patient, a child, was found to have a significant ileo-femoral thrombosis at autopsy.

Table 3. Incidence of pulmonary embolism in thermally injured patients.

Author, yr, [ref]	Pulmonary embolism
Sevitt and Gallagher, 1961, [4]	5.5%
Pruitt <i>et al</i> , 1970, [6]	0.55%
McDowall, 1973, [7]	0.49%
Purdue and Hunt, 1988, [8]	0.4%

Four patients with PTE had received low dose heparin prophylaxis. Three of the 4 patients died during their hospitalization, but in only 1 of these patients was the PTE considered to be the cause of death. Neither of the 2 patients with evidence of both DVT and PTE was managed with low dose heparin. All patients in whom an antemortem diagnosis of pulmonary embolus was made received continuous intravenous heparin therapy for a period of 3 to 30 days following diagnosis. All surviving patients were discharged on oral warfarin. The 1 patient with recurrent pulmonary emboli during hospitalization was inadequately anticoagulated as defined by laboratory coagulation indices.

Discussion

On the basis of Virchow's triad for the development of venous thrombosis, the thermally injured patient appears to be at considerable risk for the development of clinically significant thromboembolic complications. Curreri and coworkers [2] reported dramatic elevations in platelet counts, fibrinogen, and factors V and VIII in the recovering burn patients. A recent investigation has also demonstrated a decrease in the levels of antithrombin III and protein C during the early post injury period [3]. These factors, particularly if dehydration develops following thermal injury, may promote a hypercoagulable state. Immobility, as a consequence of prolonged ventilatory support, lower extremity thermal injury, and frequent operative intervention, predisposes to venous stasis. Finally, the frequent utilization of central venous access catheters, particularly those inserted in the femoral vein, is associated with vascular trauma.

The risk of thromboembolism in trauma patients is thought to be increased. Sevitt and Gallagher [4] reported a 16% incidence of pulmonary embolism and a 65% incidence of deep venous thrombosis in an autopsy series of injured patients. The same authors, however, reported a lower overall incidence in autopsied thermally injured patients (5.5%) (Table 3). Warden and colleagues [5] reported that pulmonary emboli are common postmortem findings in burn patients, occurring in as many as 30% of patients autopsied. The diagnosis of antemortem embolic events is much less common. Pruitt and associates [6] reported a 0.55% incidence of pulmonary emboli in a cohort of 1,086 burned patients. In only 1 (0.09%) patient was the embolus considered to be the cause of death. McDowall [7] reported a 0.49% incidence of fatal pulmonary emboli in a series of 2,250 burned patients, with a 0.3% incidence of nonfatal emboli. Most recently, Purdue and Hunt [8] reported a 0.4% incidence of pulmonary embolus in a five year review of thermally injured patients.

The frequency of deep venous thrombosis in thermally in-

jured patients is less well established. McDowall [7] reported only 2 patients with clinically evident deep venous thrombosis in a series of 1,000 consecutive admissions.

The use of low-dose heparin as prophylaxis for thromboembolic events is based upon the multicenter study of Kakkar and coworkers [9] which reviewed the safety and efficacy of such prophylaxis in postoperative surgical patients. A 1.2% incidence of clinically significant pulmonary emboli was reduced to 0.4% with low-dose heparin therapy. This same study reported clinically evident deep venous thrombosis in 4% of postoperative surgical patients, which was reduced to 1.9% with the use of low-dose heparin therapy.

Low-dose heparin therapy is not without complications. Pachter and Riles [10] reported a 27% incidence of bleeding and wound complications in surgical patients treated with low-dose heparin immediately prior to operation and for 5 days following the operation in contrast to a 7.5% incidence of similar complication in patients receiving only postoperative heparin therapy. Patients not receiving heparin had a 1.4% incidence of those complications. Heparin induced thrombocytopenia is a commonly reported event. Comerota and White [11] have reported that the incidence of this complication is between 0.6-5% when patients are treated with low-dose heparin prophylaxis. Green and colleagues [12] attribute such thrombocytopenia to the development of an antibody directed against a heparin-platelet complex antigen. Kapsch and Silver [13] reported that heparin induced thrombocytopenia is not dependent on the route of administration, dosage, or source. Consequently, all patients receiving heparin are at risk for development of this complication which may progress to paradoxical intravascular thrombosis. These authors estimated that the incidence of this complication in patients receiving heparin therapy is 0.6%.

The present series of 2,103 patients had a low frequency of clinically significant thromboembolic complications. In view of the comparable or increased frequency of complications associated with heparin therapy, routine heparin prophylaxis applied to all patients appears unwarranted in thermally injured patients. Heparin prophylaxis should be reserved for those patients with a previous history of pulmonary embolism or deep venous thrombosis or the morbidly obese, particularly with concomitant lower extremity burn injuries that will require excision, grafting, and postoperative immobilization. Our recent review [14] revealed a significant risk of pulmonary embolus in the morbidly obese burn patient. Seven patients were identified as meeting the strict criteria of morbid obesity, 100 pounds over ideal body weight or 100% excess in body weight, and 4 (57.1%) of these patients suffered pulmonary embolism during their hospital stay. Our data indicate a relationship between the incidence of thromboembolic complication and burn size, but not age. In addition, a significant percentage of our afflicted patients had deep lower extremity burns, a common finding in patients with large burns. This, in conjunction with our earlier review [14], would suggest a potential benefit of heparin prophylaxis in a select group of patients with large burns that include the lower extremity as well as the morbidly obese burn patient.

It is likely that the most effective preventive measure in this patient population, as with most surgical patients, is early mobilization and the regular rotation of venous access line sites so as to avoid unnecessary venous trauma. Routine pharmaco-

logic intervention in all burned patients appears to be largely unwarranted and perhaps hazardous.

Résumé

La fréquence de complications thromboemboliques chez le brûlé varie entre 0.4% et 7%. La signification clinique de ces événements est souvent discutée mais a incité plusieurs équipes à utiliser de façon systématique et prophylactique de l'héparine à bas poids moléculaire (HBPM). D'après une revue de 2,103 dossiers de brûlés soignés dans notre centre, 25 patients (1.2%), d'âge moyen de 40.0 ans, et ayant une surface corporelle totale brûlée moyenne de 49.3%, ont eu une embolie pulmonaire avec retentissement clinique. Pour trois d'entre eux (0.14%), l'embolie a été considérée comme la cause du décès. Dix-neuf patients (0.9%) d'âge moyen de 36.7 ans et ayant une surface corporelle totale brûlée moyenne de 48.3%, ont développé des signes de thrombose veineuse profonde. Seul un de ces patients (0.05%) a eu par la suite un embolie fatale. Selon une revue de la littérature, l'incidence de complications en rapport avec l'utilisation d'HBPM, comprenant l'hémorragie, la thrombocytopenie et la thrombose artérielle, oscille entre 0.6% et 5%. Nous pensons que la relative basse fréquence de thromboembolie pulmonaire associée à un taux non négligeable de complications en rapport avec l'emploi d'HBPM vont contre son utilisation systématique chez le brûlé sauf chez les patients à haut risque de thromboembolie.

Resumen

La incidencia de complicaciones tromboembólicas en pacientes quemados ha sido estimada entre 0.4% y 7%. La significación clínica de estos fenómenos es frecuentemente discutida y ha hecho que algunos centros adopten rutinariamente la profilaxis con heparina de baja dosificación. Se emprendió la revisión de 2103 pacientes quemados tratados en esta institución en el curso de 10 años. Veinticinco pacientes (1.2%) con una edad media de 40.0 años y un promedio de área corporal quemada de 49.3%, fueron identificados como casos de tromboembolismo pulmonar significativo. En sólo tres pacientes (0.14%) se consideró que el tromboembolismo fue la causa de muerte. Diecinueve pacientes (0.9%), con una edad promedio de 36.7 años y un área de quemadura de 48.3% de la superficie corporal total, desarrollaron trombosis venosa profunda clínicamente evidente; sin embargo, sólo en un paciente (0.05%) la enfermedad avanzó hasta el tromboembolismo pulmonar fatal.

Una revisión de la literatura reveló una incidencia de com-

plicaciones relacionadas con la heparina de baja dosificación de 0.6-5%; tales complicaciones incluyen sangrado, trombocitopenia y trombosis arterial. Creemos que la rareza del tromboembolismo pulmonar y la trombosis venosa profunda clínicamente significativos en los pacientes quemados y el riesgo, comparable o mayor, de complicaciones asociadas con la profilaxis con heparina, militan en contra de su uso rutinario, excepto en pacientes con alto riesgo de desarrollar tales fenómenos.

Acknowledgments

The views of the authors do not purport to reflect the positions of the Department of the Army and the Department of Defense.

References

- Hull, M.B., Rascob, G.E., Hirsh, J.: Prophylaxis of venous thromboembolism: An overview. *Chest* 89:3745, 1986
- Curreri, P.W., Katz, A.J., Gotin, L.N., Pruitt, B.A.: Coagulation abnormalities in the thermally injured patient. *Curr. Top. Surg. Res.* 2:401, 1970
- Pratt, S.M., Allen, R.C., Smith, A.A., Berkland, M., McManus, W.F., Mason, A.D. Jr., Pruitt, B.A. Jr.: Antithrombin III deficiency in thermally injured patients. U.S. Army Institute of Surgical Research Annual Research Progress Report for Fiscal Year, 1986, pp. 50-57
- Sevitt, S., Gallagher, N.: Venous thrombosis and pulmonary embolism: A clinico-pathological study in injured and burned patients. *Br. J. Surg.* 48:475, 1961
- Warden, G.D., Wilmore, D.W., Pruitt, B.A.: Central venous thrombosis: A hazard of medical progress. *J. Trauma* 13:620, 1973
- Pruitt, B.A. Jr., DiVincenti, F.C., Mason, A.D., Foley, F.D., Flemma, R.J.: The occurrence and significance of pneumonia and other pulmonary complications in burned patients: Comparison of conventional and topical treatments. *J. Trauma* 10:519, 1970
- McDowell, R.A.W.: Pulmonary embolism and deep venous thrombosis in burned patients. *Br. J. Plast. Surg.* 26:176, 1973
- Purdue, G.F., Hunt, J.L.: Pulmonary emboli in burned patients. *J. Trauma* 28:218, 1988
- Kakkar, V.V., Corrigan, T.P., Fossard, D.P.: Prevention of fatal postoperative pulmonary embolism by low doses of heparin. *Lancet* 2:45, 1975
- Pachter, H.L., Riles, T.S.: Low dose heparin: Bleeding and wound complications in the surgical patient. *Ann. Surg.* 186:669, 1977
- Comerota, A.J., White, W.V.: The use of dihydroergotamine and heparin in the prophylaxis of deep venous thrombosis. *Chest* 89:389S, 1986
- Green, D., Harris, K., Reynolds, N.: Heparin immune thrombocytopenia: Evidence for a heparin-platelet complex as the antigenic determinant. *J. Lab. Clin. Med.* 91:167, 1978
- Kapsch, D., Silver, D.: Heparin-induced thrombocytopenia with thrombosis and hemorrhage. *Arch. Surg.* 116:1423, 1981
- Sheridan, R.L., Rue, L.W., McManus, W.F., Pruitt, B.A. Jr.: Burns in the morbidly obese. *J. Trauma* (in press)

Invited Commentary

Cleon W. Goodwin, M.D.

Department of Surgery, Cornell University Medical College, New York, New York, U.S.A.

The role of anticoagulation in the prevention of thromboembolism in burned patients currently is unknown, as it is more generally for non-burn trauma. Patients with acute spinal cord injury and hip fractures are the major groups that benefit from prophylactic regimens of anticoagulation [1]. Whether or not to use anticoagulation in burned patients presents significant medical-legal problems, especially when interpreted by expert consultants with no experience in the treatment of patients with severe injury. The use of prophylactic heparinization in burned patients is problematical because of the increased risk of thrombocytopenia and of bleeding, particularly under newly placed skin grafts. Heparin itself may cause thrombosis, and often accentuates the coagulation abnormalities associated with the presence of large inflammatory wound surfaces and sepsis.

In a previous study, the present authors describe a series of 210 patients with large burns [2]. Ninety-three patients died, three quarters from infection. In this burn center with a universal autopsy rate, only 1 patient was found to have pulmonary embolism. Overall, the morbidity and mortality in this series was related to age, burn size, and the presence or absence of inhalation injury.

What is impressive about the present paper is the exceedingly small number of patients developing thromboembolic phenomena. In 2,103 patients consecutively studied over 10 years, there was a 1.2% incidence of pulmonary embolism and in only 3 (0.14%) patients was this complication judged to be the cause of death. Further, 19 (0.9%) patients developed deep venous thrombosis, and only 1 of these developed fatal pulmonary embolism. The authors report a very weak association between burn size and thromboembolic phenomena but this relationship is not supported by their previous study [2]. Our experience at

the Burn Center of the New York Hospital-Cornell Medical Center suggests that patients with smaller burns appear more susceptible to venous thrombosis.

Who should receive anticoagulation and can these rare burned patients who are likely to develop thromboembolic disease be identified and treated? Burn size is a poor predictor at best and probably should not be used as a treatment criterion. Otherwise, the authors' recommendations for low dose prophylactic heparinization appear reasonable. Grossly obese patients and those with small lower extremity burns treated with splints and dressings should receive low dose heparin if prolonged mobilization is anticipated. Early physical therapy and ambulation is a major preventative measure in these patients and may obviate the need for low dose heparinization.

Lower extremity swelling, especially if the patient has leg burns, is very common in burned patients and should be evaluated with noninvasive venous studies; however, most such studies indicate the absence of deep vein thrombosis. If deep vein thrombosis is identified, these patients should be fully anticoagulated, first with heparin and later with coumadin. In addition, patients with proven (by ventilation-perfusion scan and/or pulmonary angiogram) pulmonary embolism also should be fully heparinized.

The incidence of thromboembolism in burned patients is so low, at least with burn care as practiced by the United States Army Institute of Surgical Research and its clinical descendants, that controlled clinical trials probably are impossible to carry out. As such, the need for the various forms of anticoagulation must be individualized for each patient, realizing that the treatment in some cases may be as hazardous as no treatment.

References

1. Prevention of Venous Thrombosis and Pulmonary Embolism. National Institutes of Health Consensus Development Conference Statement, vol. 6, p. 6
2. McManus, W.F., Mason, A.D. Jr., Pruitt, B.A. Jr.: Excision of the burn wound in patients with large burns. *Arch. Surg.* 124:718, 1989

Accession For		
NTIS	CRA&I	<input checked="" type="checkbox"/>
DTIC	TAB	<input type="checkbox"/>
	U.announced	<input type="checkbox"/>
Justification		
By		
Distribution /		
Availability Codes		
Dist	Avail and/or Special	
A-1	20	