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DEEP VENOUS THROMBOSIS IN ACUTE SPINAL CORD INJURY: A COMPARISON OF ^{125}I FIBRINOGEN LEG SCANNING, IMPEDANCE PLETHYSMOGRAPHY AND VENOGRAPHY

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Abstract. Twenty acute spinal cord injury patients were surveyed for deep venous thrombosis (DVT) by ^{125}I fibrinogen leg scanning, impedance plethysmography (IPG), and venography. Leg scanning was a more sensitive indicator of thrombotic events than IPG or venography. IPG was a reliable indicator of accumulated thrombosis. The incidence of DVT assessed by leg scanning alone was 100 per cent. Its occurrence as determined by either of the screening techniques was found to be considerably greater than those of previous reports.

One of the characteristic complications of acute spinal cord iujury is the thromboembolic event. The risk of fatal pulmonary embolism within two to three months of spinal cord injury is reported to be 2 to 16 per cent (Rossier & Brunner, 1964; Walsh & Tribe, 1965; Watson, 1968; Silver & Moulton, 1970). The incidence of deep venous thrombosis (DVT) of the lower extremities, the usual source of pulmonary embolism, is about 15 per cent as determined clinically (Walsh & Tribe, 1965; Watson, 1968; Silver & Moulton, 1970). Sensitive screening techniques for detection of deep venous thrombosis, ^{125}I fibrinogen leg scanning and impedance plethysmography (IPG) have become available (Flanc *et al.*, 1968; Wheeler *et al.*, 1974). This study has been conducted to (*a*) compare the qualities of these screening techniques and (*b*) to reassess the incidence of DVT in the acute spinal cord injury patient with these techniques.

Material and Methods

Subjects

Twenty patients admitted to the spinal cord injury service of the West Roxbury Veterans Administration Hospital within two months of injury were selected for survey without regard for the presence of suspected thromboembolic event. These twenty patients were surveyed for deep venous thrombosis by ^{125}I fibrinogen leg scanning and impedance plethysmography. The level of neurological injury was cervical in 12 (seven complete, five incomplete), thoracic in three (two complete, one incomplete), thoracolumbar or lumbar in five (two complete, three incomplete). The age range was 19 to 49 and the median age was 27.

Leg Scanning

Autologous fibrinogen preparations were used for leg scanning to avoid transmission of the hepatitis virus (Frisbie *et al.*, 1975). Patients received 250 mg sodium

iodide by mouth daily for the duration of leg scanning to block thyroid uptake of free radioactive iodide. Autologous ^{125}I fibrinogen in a dose of 1-2 μCi per kg body weight was injected intravenously and leg scanning conducted according to a method described by Kakkar *et al.* (1970*a*). Precordial radioactivity was measured with a ratemeter (Jasins and Sales, Wellesley, Massachusetts) and the reading on a percentage scale set at 100 per cent. Eleven marked sites following the course of the deep venous system in each lower extremity were then read in reference to the precordial blood pool. These readings are taken one hour after ^{125}I fibrinogen administration and are the baseline. Repeat leg scanning is performed at 24-48 hour intervals. When at least 20 percentage points over the baseline accumulate at any counting site for two consecutive days a leg scan is positive.

Impedance Plethysmography

Obstruction of venous outflow was measured by impedance plethysmography according to Wheeler *et al.* (1974). Two pairs of recording electrodes are placed below the knee, and the lower extremity is elevated to 20 degrees above the horizontal. A pressure cuff is placed around the thigh, inflated to 45 cm of water and rapidly deflated 45 seconds later. Venous capacitance and venous outflow rates are recorded. The ratio of outflow to capacitance is plotted on a graph on which is recorded the distribution of outflow to capacitance ratios from a normal population and from patients with proven femoral and popliteal venous thrombosis. Thrombosis of the calf veins is seldom detected by IPG (Wheeler *et al.*, 1974; Johnston *et al.*, 1974). Impedance plethysmography was performed at daily to weekly intervals.

Venography

The presence of venous thrombosis was determined by large volume ascending contrast venography (Rabinov & Paulin, 1972). The indication for venography was positive impedance plethysmography or a clinical impression of a thromboembolic event. Venograms were performed within 24 hours of leg scanning and impedance plethysmography. The venograms were interpreted by an angiographer without knowledge of the results of the screening tests. Only a constant filling defect or non-filling of the entire deep venous system were diagnosed as thrombi.

Results

Comparison of Methods

To demonstrate the difference in sensitivities of the methods used for thrombus detection, limbs rather than patients were compared. In 17 patients 32 limbs were examined on the same day by leg scanning and impedance plethysmography. As indicated in Table I there was agreement in 18 limbs (56 per cent). There were 13 limbs in which the leg scan was positive and the IPG negative and one limb leg scan negative and IPG positive.

In ten patients, 17 limbs were examined by leg scanning and venography on the same day. As indicated in Table II, there was agreement in ten limbs (59 per cent). There were six limbs in which the leg scan was positive and the venogram negative and one limb with a negative leg scan and a positive venogram.

In 14 patients 23 limbs were examined by impedance plethysmography and venography on the same day. As indicated in Table III, there was agreement

TABLE I

Leg scanning (LS) *vs.* impedance plethysmography (IPG)

LS+IPG+	7
LS−IPG−	11
LS+IPG−	13
LS−IPG+	1
Total limbs	32

TABLE II

Leg scanning (LS) *vs.* venography (VG)

LS+VG+	7
LS−VG−	3
LS+VG−	6
LS−VG+	1
Total limbs	17

TABLE III

Impedance plethysmography (IPG) *vs.* venography (VG)

IPG+VG+	11
IPG−VG−	11
IPG+VG−	0
IPG−VG+	1
Total limbs	23

in 22 (96 per cent). Of 11 limbs with a positive IPG, 11 had DVT by venography, only one of which was distal to the popliteal vein. Of 12 limbs with a negative IPG venography was negative in 11 and positive in one (DVT distal to the popliteal vein).

Incidence of Deep Venous Thrombosis

In 14 patients leg scanning was performed until a positive reading was obtained or the 60th post-injury day occurred. A positive leg scan was obtained in each of these 14 patients (100 per cent).[1] Six patients were insufficiently screened by leg scan; three patients had leg scanning only within the first three weeks post injury and three others had venography before leg scanning could be performed.[2]

In 18 patients, IPG was conducted at intervals until a thrombosis was diagnosed or the 60th post-injury day occurred. Eleven of the 18 screened patients had a positive IPG, all confirmed by venography (61 per cent). Two additional patients were insufficiently screened by IPG. One had a negative IPG at the 31st and another at the 46th post-injury days.

Risk Factors

No association between age, level of injury, or surgery and DVT could be made.

Association of muscle tone with DVT could be evaluated in 12 patients. Assuming that no venous thrombosis of the lower extremities existed prior to spinal cord injury, the onset of deep venous thrombosis—as indicated by leg scanning, IPG or venography—occurred in the acute post-traumatic period when all 12 patients were still in a flaccid state. Five of these had a lower motor neuron lesion and remained flaccid. The onset of DVT relative to muscle tone was unknown in the remaining eight patients studied.

[1] Seven of these patients (50 per cent) demonstrated fibrin uptake in the upper thigh.

[2] A high incidence of fibrin deposit by leg scanning is induced by venography (Harris *et al.*, 1975). Therefore, subsequent leg scanning is invalidated.

Pulmonary Embolism

One of several suspected pulmonary embolic events was studied and confirmed by pulmonary angiography. Of particular interest was the fact that leg scanning and impedance plethysmography were negative 12 hours preceding embolism in this patient.

Discussion

^{125}I fibrinogen leg scanning, a sensitive measure of fibrin deposit, indicates the presence of an active thrombotic process as opposed to an inactive one. The previously reported insensitivity of this technique for detection of deep venous thrombosis of the thigh (Flanc *et al.*, 1968) was not apparent in this study. Half of the positive leg scans recorded in this study indicated DVT in the thigh. Muscle atrophy occurring after spinal cord injury allows closer proximation of the detector probe to the deep venous system of the thigh and might account for increasing sensitivity of detection in this area. The greater sensitivity of the leg scanning technique relative to the IPG observed in this study has been noted in a previous direct comparison of these techniques in surgical patients (Gazzaniga *et al.*, 1974).

The size of the thrombus detectable by leg scanning is not predictable. An active thrombotic process detectable by leg scanning may not be associated with a thrombus detectable by venogram. In contrast, the size of the thrombus detectable by impedance plethysmography is predictable. A positive IPG, a measure of obstructed venous flow, indicates an accumulated thrombus, consistently verified by venography in this study.[1] Thrombi detectable by impedance plethysmography are large and located proximal to the calf veins. Deep venous thrombosis in the calf is undetectable by IPG, probably because of collateral circulation through the extensive superficial venous system of the calf. The reliability of IPG for detection of the larger thrombi of the popliteal and more proximal deep venous system as indicated in this study is similar to the experience of previous studies of non-spinal cord injury patients (Bergquist *et al.*, 1973; Wheeler *et al.*, 1974; Johnston *et al.*, 1974; Gazzaniga *et al.*, 1974).

The estimated incidence of deep venous thrombosis in the acute spinal cord injury patient using these screening techniques is high in comparison of those of previous reports. When fibrin deposit by leg scanning is the criterion for DVT, the incidence of thrombosis in general surgery patients is 30 per cent (Kakkar *et al.*, 1970*b*), in hip surgery patients 50-85 per cent (Morris *et al.*, 1974; Harris *et al.*, 1975), in stroke patients 60 per cent (Warlow *et al.*, 1972), and in acute spinal cord injury patients 100 per cent. Features which may distinguish the acute spinal cord injury patients from other patient groups with a high incidence of deep venous thrombosis are the duration of immobility, vasomotor paralysis, and hypercoagulability (Hachen, 1974; Naso, 1974).

The incidence of deep venous thrombosis as determined by IPG with confirmation by venography is 61 per cent. This incidence of confirmed DVT is a minimal one. Both the insensitivity of IPG for calf vein thrombosis and the restrictive interpretation of the venograms themselves suggest the error is one of underdiagnosis. No small thrombi were diagnosed by venography in this study. Nevertheless, the 61 per cent incidence obtained is considerably higher than the

[1] False positive IPG recordings are avoided by attention to technique and the requirement for repeatability of a positive recording.

15 per cent incidence of DVT as determined clinically (Walsh & Tribe, 1965; Watson, 1968; Silver & Moulton, 1970). It has been reported previously that clinical evaluation of DVT is a relatively crude method of detection (Flanc *et al.*, 1968; Wheeler *et al.*, 1974).

A risk factor which can be suggested is flaccidity, since the onset of all thrombotic events which could be timed occurred in this state. More experience is necessary to substantiate this observation. Age, preceding surgery and level of injury could not be implicated as risk factors from the limited data available. A survey by Watson (1968) reported no striking correlation between age, level of injury, and surgery with DVT.

Clinical evaluation of prophylactic regimens for thromboembolic complications of spinal cord injury have required a relatively large number of patients and years of follow-up (Silver & Moulton, 1970; Hachen, 1974). It is suggested that evaluation by sensitive screening techniques can reveal a prophylactic effect with fewer subjects and by more objective criteria.

Conclusion

Twenty acute spinal cord injury patients have been surveyed for deep venous thrombosis (DVT) by ^{125}I fibrinogen leg scanning, impedance plethysmography (IPG), and venography within 60 days of injury.

Leg scanning was a more sensitive indicator of thrombotic events than impedance plethysmography or venography. Of 32 limbs examined the same day by leg scanning and IPG, there was agreement in 18 (56 per cent). Of 17 limbs examined the same day by leg scanning and venography, there was agreement in ten (59 per cent).

Impedance plethysmography was a reliable indicator of accumulated thrombosis. No small thrombi were diagnosed by this method. Of 23 limbs examined the same day by IPG and venography, there was agreement in 22 (96 per cent).

The incidence of DVT assessed by leg scanning alone was 100 per cent (14 of 14 patients with a completed 60-day survey).

The incidence of DVT in acute spinal cord injury patients as determined by either of the screening techniques was found to be considerably greater than those of previous reports.

Résumé

Utilisant la scintigraphie par le fibrinogène marqué au iode ^{125}radioactif, la pléthysmographie par impédance (PGI) et la phlébographie, les auteurs se sont attachés à mettre en évidence l'incidence des thromboses veineuses profondes (TVP) chez 20 patients avec traumatisme médullaire aigu.

La scintigraphie s'est révélée être une méthode de détection plus sensible des phénomènes thrombotiques que la PGI ou la phlèbographie.

La PGI est un examen fiable qui permet de détecter la formation progressive d'une thrombose, bien que cette technique ne permette pas de diagnostiquer des thrombi de moindre importance. Sur 23 membres examinés le même jour par PGI et phlébographie, les résultats concordèrent dans 22 cas (96 pour cent).

L'incidence des thromboses veineuses profondes diagnostiquées par la seule scintigraphie a été de 100 pour cent (14 sur 14 patients au cours de la période d'investigation de 60 jours).

Quelle qu'ait été la technique de détection utilisée, les auteurs ont trouvé que la fréquence des thromboses veineuses profondes chez les patients avec un traumatisme médullaire aigu était nettement plus élevée que celle mentionnée dans des publications antérieures.

ZUSAMMENFASSUNG

Der diagnostische Wert von 125 I Fibrinogen-Bein-Skanning, Plethysmographie (IPG) und Venographie wurde bei 20 Patienten mit akuter spinaler Verletzung verglichen. Die Beinskanning Technik war ein besserer Indikator als IPG oder Venographie. IPG war ein zuverlässiger Indikator bei akkumulativer Thrombosis. Bein-skanning allein ergab ein 100 Prozent Resultat verglichen mit früheren Ergebnissen.

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Discussion

DR HACHEN (*Switzerland*). The findings of Professor Rossier clearly demonstrate how early venous thrombosis may develop and I would like to hear whether he has given low-dose heparine as we do in Geneva and what time he starts. At the same time I would like to draw attention to a paper published last week by Professor Kakkar of King's College on 4500 cases treated with low-dose heparine in orthopaedic patients and he gave very interesting data on that. I think we can now conclude that very early low dose heparine therapy is very effective and not dangerous and especially that the bleeding incidence is not larger than if you don't give anti-coagulants. We actually start low-dose heparine 24 hours after the lesion, we try 5000 units for the first two days before we increase by 10,000 units from the third day, and we have had not a single case of thrombo-embolism.

PROFESSOR A. ROSSIER (*U.S.A.*). In answer to your question, we have started on a very, I would say, irregular basis with low-dose heparine. Because of this study, we wanted to prove something and before proving it we could not interfere with low-dose heparine. I was a bit reluctant to carry out this study but I was pushed by two of my physicians who specialise in coagulation. I was a bit concerned because I knew from our previous work that the incidence was high so I was questioning the validity of submitting a patient to some type of danger. The advantage, which is why we conducted this study, is that it is conducted systematically from the very first day we have the patient. Therefore, we do the IPG's twice a week up to 60 days, and therefore we will catch the DVT and treat it.

Your second point of prophylactic low-dose heparine in Kakkar's method, we have used this, I believe, on six patients now. Two developed DVT under the treatment. They were screened before we started it. The IPG was negative, the venogram was negative, the leg scan was negative. However, they developed DVT.

DR P. DOLLFUS (*France*). How soon after injury did you get your patients? Secondly, in Colmar we now use low-dosage heparine the hour after the patient comes in, unless he has had a head injury. Thirdly, since we have tilted up the patient's legs to 15 degrees I have not seen a swollen leg, as I used to see clinically somewhere else.

PROFESSOR A. ROSSIER. May I first deal with your last point. The clinical sign is a very crude method, and you cannot rely upon it. If I take the clinical sign in these patients, we did not have even a quarter of them showing clinical signs because they are measured upon admission and every subsequent day they are measured at the same point so if there is a clinical sign we will catch it. To answer your first question, I do not have the breakdown of the patients—out of these 20 patients I think the earliest we had one was six hours after injury. Basically, most of them were within four to six days after injury. We purposely decided within two months—some of them came within six hours, one week, two weeks up to four or five weeks. The majority was within one week.

DR THOMAS (*G.B.*). Have you considered, Professor Rossier, that you may be causing a high incidence of DVT by your investigations?

PROFESSOR ROSSIER (*U.S.A.*). Which investigation?

DR THOMAS (*G.B.*). Venography in particular.

PROFESSOR ROSSIER (*U.S.A.*). Venography was only carried out when the IPG was positive, never otherwise. So, my answer is no. Otherwise it could be yes.

DR HACHEN (*Switzerland*). I think we should use low-dosage heparine 5000 units twice daily only in the very beginning when we get patients with multiple injuries. From the third day on we certainly need to increase to 5000 to 10,000 and carry on for at least three weeks to one month.

PROFESSOR ROSSIER. I cannot tell you if you are right or wrong. I do not feel I am in a position to do it. I can just tell you that I have seen one DVT developing under twice 5000 heparine and I know that he did not have DVT before as both the IPG and the leg scan was negative, becoming positive within 12 hours. So I know that it can move very fast, although being under low-dose heparine.

DR COOK (*G.B.*). In the discussion, several references have been made to giving heparine according to Kakkar. I hesitate to quote a man without having his paper immediately available, but my distinct impression is that Kakkar gives heparine preoperatively and he would consider that to give it after a paraplegia would be much too late. Kakkar has also drawn attention to the fact that giving it later may prevent incidence of deep vein thrombosis but does not prevent or affect the incidence of pulmonary embolism.

QUESTIONER (*Indian*). I would like to ask Dr Silver about the patients in whom deep vein thrombosis is suspected. Do they continually move the legs again or are the legs kept at rest and elevated?

DR SILVER. On admission to the Unit, every patient has a test to see if the deep veins are thrombosed or patent by means of the sonic aid. If we are satisfied from the sonic aid that there is not deep vein thrombosis and from the thighs method that the leg is not swollen, then they would have routine movements of the leg, and we would also start on prophylactic anticoagulants. If the sonic aid was blocked or the leg was swollen, then we would assume that there is deep vein thrombosis and we would stop all passive movements to both legs.