Is Postoperative Deep Vein Thrombosis A Problem in Neurosurgical Patients with Brain Tumours in Singapore?

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ABSTRACT

Aim: To prospectively establish the incidence of deep vein thrombosis (DVT) after cranial procedures in patients with brain tumour in Singapore.

Methodology: Over a period of one year from June 1995 to May 1996, 106 consecutive patients were recruited into the study. All patients undergoing surgery within the period of study were included. Each patient underwent a preoperative and postoperative (on postoperative Day 5 to Day 7) ultrasound examination of the lower limbs to establish the presence of DVT. Prophylaxis was limited to the peri-operative use of elastic stockings on hemiparetic limbs.

There were 56 males and 50 females aged between 22 to 86 years (median 45 years). Ethnicity was Chinese, 92% Indian, 6% and other 2%. Ninety percent of the patients were ambulant pre- and post-operatively. No patient had a prior history of DVT. The distribution by pathologic diagnosis was brain metastases, 26% meningioma, 26% glioma, 19% pituitary adenoma, 14% acoustic neuroma, 6% and 9% miscellaneous tumours.

Results: DVT was identified in 5/106 patients (4.7%), all of whom had either meningioma or glioma. All five cases occurred in supratentorial tumours. The tumour specific incidence was 7.1% for meningioma and 15% for glioma. 4/5 patients (80%) had pre-existing hemiparesis of the affected limb. No patient developed clinical pulmonary embolism.

Conclusion: The overall incidence of post-operative DVT in our population, using minimal prophylaxis, was not significantly different from the best results of prospective studies on North American or European patients employing a full regime of prophylaxis. The high-risk groups were similar. Prophylaxis using subcutaneous heparin should be used cautiously in high-risk patients.

Keywords: prospective, incidence, prophylaxis

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INTRODUCTION

The incidence of postoperative deep venous thrombosis (DVT) has been reported to be very high (from 24% to 50%) in brain tumour patients, and it is now a standard recommendation in the literature that all patients should at least receive thromboembolic deterrent (TED) stockings peri-operatively as mechanical prophylaxis against DVT and pulmonary embolism[1,2]. There is also significant support in the literature for the use of low molecular weight heparin perioperatively to provide better prophylaxis[2-6].

The current neurosurgical practice in the Singapore General Hospital and in Singapore limits the use of prophylactic TED stockings to "high risk" patients. We do not use perioperative, prophylactic low molecular weight heparin. The basis for the local practice has been the strong clinical impression that the problem of DVT is not as significant in our local population of brain tumour patients. There is, to date, no prospective study in the English literature that specifically looks at the problem of DVT in Asian brain tumour patients. This is the first of such study.

AIMS

The aim of this study was to prospectively establish the incidence of postoperative DVT in our local patients with brain tumour and allow us to compare the local incidence of DVT in this population to similar populations from North America and Europe. It would enable us to evaluate the effectiveness of our current unit protocol for postoperative DVT prophylaxis vis-a-vis recommendations in the current literature for this group of patients. The thrust of the study is the perioperative problem of DVT in brain tumour patients in Singapore, and the need for perioperative anti-coagulant prophylaxis with its attendant risk of postoperative haemorrhage.

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Table I. Details of patients with DVT.

	Diagnosis	Op Details	Pre-op DVT screen	Post-op DVT screen;
F/60y	Left parasagittal meningioma with right hemiparesis	Excision under GA five hours	DVT right calf and superficial femoral veins	No change
F/63y	Right sphenoid wing meningioma with left hemiparesis	Excision under GA five hours	Negative	Negative on 5 POD. Clinical DVT on 12 POD. Partial thrombosis of left popliteal vein on U/S.
M/44y	Right frontal glioblastoma multiforme with left hemiparesis	Excision under GA three hours	Negative	Negative on 5 POD. Clinical DVT on 27 POD. Massive left femoro-popliteal thrombosis on U/S.
M/51y	Recurrent right frontal malignant astrocytoma with left hemiplegia	Stereotactic biopsy under LA 15 minutes	DVT left calf and popliteal veins	No change
F/86y	Left frontal malignant astrocytoma presenting with change in sensorium	Stereotactic biopsy under LA 20 minutes	Negative	Positive on 5 POD with extensive left femoro-popliteal thrombosis. No clinical evidence of DVT.

Table II. Breakdown according to tumour type, location and type of anaesthesia.

	Number	U/S DVT Positive
Glioma		
- Total	20	3 (15%)
- Resection	15	1 (6.7%)
- Biopsy (1 pre-op DVT positive)	5	2 (40%)
Meningioma		
(1 pre-op DVT positive)	28	2 (7.1%)
Metastasis		0 (0%)
- Total	28	
- Resection	12	
- Biopsy	16	
Others		
(Pituitary Adenoma, Acoustic Neuroma, Misc.)	30	0 (0%)
Tumour location		
- Supratentorial (2 pre-op DVT positive)	98	5 (5%)
- Infratentorial	8	0 (0%)
Anaesthesia		
- General anaesthesia (1 pre-op DVT positive)	84	3/84 (3.6%)
- Local anaesthesia (1 pre-op DVT positive)	22	2/22 (9.6%)
Operation performed		
GA - Tumour resection (craniotomy) (1 pre-op DVT positive)	64	3/64 (4.7%)
- Others (transphenoidal resection, open biopsy, VP shunt)	20	0/20 (0%)
LA - Stereotactic biopsy (1 pre-op DVT positive)	22	2/22 (9.6%)

MATERIALS AND METHODS

All patients who underwent brain surgery in the Singapore General Hospital for brain tumour over a one-year period from June 1995 to May 1996 were recruited into this longitudinal cohort study. A total of 106 consecutive patients were recruited. All patients underwent routine preoperative screening of their hematological, coagulation and serum biochemistry parameters.

Each patient underwent a preoperative (one to two days before surgery) and postoperative (on the 5th to 7th postoperative day and clinically thereafter) ultrasound scan of the lower limbs to screen for DVT. All patients were followed up regularly post-operatively. The first visit was at one month and the second was at three months for benign tumours. For malignant tumours, there was monthly follow-up until radiotherapy was completed, All were screened for DVT. DVT prophylaxis was limited to the use of elastic stockings on the affected limb in patients with hemiparesis or hemiplegia.

The ultrasound scans were performed by a single trained and experienced technician from the hospital's cardiovascular laboratory on an Acuson 128XP5 colour duplex scanner using both 5 and 7MHz probes.

RESULTS

In our study sample, there were 56 males (53%) and 50 females (47%). Their ages ranged from 22 to 86 years, with a median age of 45 years. The ethnic composition consists of 92% Chinese, 6% Indian and 2% others. None of the patients had a prior history of DVT. All had normal coagulation parameters. Preoperatively, 95 patients (90%) were ambulant and 11 (10%) were non-ambulant.

There were 84 patients who underwent general anaesthesia for the neurosurgical procedures

and 22 patients had the procedure under local anaesthesia. Of the neurosurgical procedures, there were 64 craniotomies for tumour resection, 11 transphenoidal resections, one open biopsy, and eight ventriculoperitoneal shunts. Forty-eight procedures were completed within four hours, while 36 procedures took longer than four hours. The remaining 22 procedures were stereotactic biopsy under local anaesthesia and they were all completed within an hour.

Of the tumour histology, 28 were metastases (26%), 28 were meningiomas (26%), 20 were gliomas (19%), 15 were pituitary adenomas (14%), six were acoustic neuromas (6%) and nine were miscellaneous tumours (9%). Postoperatively, 37 patients required bed rest for less than two days, 43 patients for three to four days and 26 patients required bed rest for more than four days.

In this study, deep vein thrombosis was identified in five patients and the patients had either meningioma or glioma. The tumours were all located supratentorially. Two of the five patients were found to have deep vein thrombosis preoperatively with no evidence of progression postoperatively. Four of the five patients had pre-existing hemiparesis or hemiplegia in the limb with DVT. None of the patients with DVT suffered from any clinical evidence of pulmonary embolism. There were four deaths during the study period one from ventriculitis, one from intracranial haemorrhage, one from haemorrhagic pancreatitis and one from bronchopneumonia. None of the patients who died were found to have DVT on screening. The results are detailed in Tables I and II.

DISCUSSION

The incidence of DVT in brain tumour patients has been reported to be high. Kayser Gatchalian and Kayser[7] reported a 27.5% prevalence of DVT in an autopsy series of 334 cases of brain tumours. Ruff and Posner[8] reported a 25% incidence of venogram-proven DVT in a retrospective series of 264 unprophylaxed patients diagnosed to have glioblastoma multiforme or malignant astrocytoma up to six weeks postcraniotomy. There is no report in the English language literature relating to the incidence of DVT in Asian brain tumour patients. Physicians in Asia have long believed that the incidence of DVT and pulmonary embolism in Asians in general are less than in Caucasians. This is supported by a study by Tinckler[9] who reported a fatal postoperative pulmonary embolism rate of 0.094 per 1,000 operations in a review of 52,861 operations performed between 1962 and 1966 at a single Singapore institution compared to an incidence of 0.14% reported by DeBakey[10]. Hwang[11] reported that the fatal pulmonary thromboembolism rate in Singapore was 1.63 per 1,000 adult necropsies in a review of 36,176 necropsies performed over a 15-year period from 1952 to 1966. He contrasted this to a rate of 10% reported by Dexter et al[12] in 1960. Chau et al[13] performed 10,348 consecutive autopsies at a single institution in Hong Kong and reported that the incidence of significant pulmonary embolism at autopsy varied from 0.58% to 2.15% over three consecutive five-year periods from 1975 to 1989. They compared their findings to similar retrospective studies by Bergzvist and Lindblad[14] who reported a 12.8% rate from Sweden and Bismuke and Wagner[15] who reported a 3.8% to 9.3% rate in North America.

In this study, the results suggest that the incidence of postoperative DVT in our local patients with brain tumour is lower than the rates reported in populations in North America and Europe. However, much of the literature is retrospective or based on the clinical diagnosis of DVT[1,16,17]. In looking at the controlled prospective trials on the incidence and prophylaxis of DVT in neurosurgery, direct comparison with the results of this study is complicated by different study aims, study protocols and statistical presentation, heterogeneous study populations with unspecified proportions of the various tumours, different techniques used to detect DVT and different scanning protocols[2-5,18-22]. The studies with the most accessible data included two that used ultrasound scanning for DVT detection and the only prospective study on brain tumours (which used ^{125}I-fibrinogen leg scans for DVT surveillance) are presented in Tables III, IV and V.

Nurmohamed et al[3] conducted a prospective randomised double blind trial comparing low molecular weight (LMW) Heparin and TED stockings versus placebo and TED stockings in craniotomies, most of which were for brain tumours (including metastases, but histology otherwise unspecified). In this study, no preoperative studies were done, only postoperative ultrasonic scanning (on the 6th, 8th, 10th postoperative day and clinical thereafter) for DVT surveillance with venographic confirmation were used.

Table III. Comparision between Nurmohamed et al and present series.

	LMWH & TED	Singapore series**
Craniotomy for brain tumour	193	64
DVT positive post-op	18.7%	3/64 (4.7%)

** All three cases of DVT in the local study were used for the analysis as the study by Nurmohamed et al only used postoperative surveillance.

Even with the use of LWMH and TED in the study by Nurmohamed et al, the incidence of DVT is significantly lower in the SGH series. (Chi-square test p=0.01 vs the LWMH & TED group and p=0.008 versus the placebo & TED group). The prospective surveillance programme by Flinn et al[18] consists of 361 general neurosurgical procedures of which 78 were craniotomies for intracranial malignancies (histology unspecified). Flinn et al used pre and postoperative (on the 3rd and 7th postoperative day and weekly thereafter if hospitalised) ultrasonic scanning for monitoring.

All patients received elastic stockings and intermittent mechanical calf compression.

Table IV. Comparison between Flinn et al and present series.

	Flinn et al	Singapore series**
Craniotomy for Intracranial malignancies	78	27
DVT positive (%)	9 (12%)	3 (11.1%)

** 15 gliomas and 12 metastases resected via craniotomy were included for analysis.

The biopsies were excluded. Only patients with hemiparesis/ hemiplegia were given elastic stockings for the affected limb.

There is no significant difference in the incidence of DVT between the two series using the Chi-square test (p=0.21).

Sawaya et al[19] in a prospective perioperative study involving 46 patients undergoing craniotomy for brain tumours, used ^{125}I-fibrinogen leg scans to detect postoperative venous thrombosis.

Table V. Comparison between Sawaya et al and present series.

	Sawaya et al		Singapore series	
	No.	DVT positive	No.	DVT positive
Glioblastoma multiforme	15	60%	15	15%
Meningioma	11	72%	28	7. 1%
Metastases	20	20%	12	0%

Note that the above studies used different modalities for DVT detection. Colour doppler, as shown by several studies, has been proven prospectively to have sensitivity of 95%, specificity of 99-100% with accuracy of 97.5% in detecting proximal vein lesions (femoral and popliteal), but for calf vein lesions this may drop slightly due to limitations (such as edematous leg, obesity, varicoses, etc)[23,24]. This is superior to that achieved with ^{125}I-fibrinogen[25,26]. ^{125}I-fibrinogen uptake test is based on the concept that the radioactive tracer is incorporated into actively forming thrombi. This technique is therefore not sensitive in detecting thrombi that are not actively forming[27].

Despite using colour doppler in our series, which is more sensitive and specific in detecting deep vein thrombosis, the incidence in Sawaya et al's series is significantly higher for all three tumour types as compared with our local series. This is statistically shown by the Chi-square test (p=0.006 for glioblastoma, p=0.0001 for meningioma, p=0.02 for metastases).

The risk factors for DVT are well defined. They include older age, obesity, varicose veins, estrogen therapy, previous DVT or pulmonary embolism, deficiency of antithrombin III, protein C or S, trauma, heart failure and infection. Other factors specific to neurosurgical patients include intracranial malignancy, weakness or paralysis, craniotomy, surgery lasting longer than four hours and early postoperative period[1]. In addition, patients with supratentorial tumours, suprasellar tumours, meningiomas and malignant gliomas have been suggested to be at increased risk[16,19]. From the results of this study, we found that the type of anaesthetic, extent of surgery and location of the tumour do not alter the incidence of deep vein thrombosis. The statistically significant factor (p<0.0001) is the presence of pre-existing neurological deficit.

Gallus et al[28] looked into and provided the estimates of the expected incidence of thromboembolic events in unprophylaxed patients. They used age (>40 years) and duration of operation (>60 min) to define patients at moderate risk with expected incidences of calf (distal) DVT of 10%-40%, proximal DVT of 2%-8%, symptomatic pulmonary emboli of 1%-8% and fatal pulmonary emboli of 0.1%-0.4%. Patients, who in addition had previous DVT, PE or stroke, were at high risk with expected incidences of distal DVT of 40%-80%, proximal DVT of 10%-20%, symptomatic PE of 5%-10% and fatal PE of 1%-5%. Older age, obesity, prolonged bed rest, varicose veins and estrogen treatment, increased these risks. Patients with brain tumours are acknowledged to be in the high-risk group[1].

Patients less than 40 years of age and duration of operation less than 60 mins were at low risk, with expected incidences of distal DVT of 2%, proximal DVT of 0.4%, symptomatic pulmonary embolism of 0.2% and fatal PE of 0.002%[26]. In our study, none of the patients suffered from pulmonary embolism.

CONCLUSIONS

The data from this study support the clinical impression that the incidence of deep vein thrombosis, especially in the first postoperative week, is lower in our

population of patients with brain tumour as compared to patients in North America and Europe.

From this prospective study, we have also established that the incidence of perioperative deep vein thrombosis is highest in our local patients with gliomas and meningiomas with respective incidences of 15% and 7.1%. This information, with regard to our local population, was not available prior to this study. Deep vein thrombosis was not detected in patients with other tumour histology. This study is too small to address the significance of this finding.

The incidence of DVT, is not influenced by the following:

- type of anaesthetic used i.e. general anaesthesia or local anaesthesia;
- extent of surgery, i.e. resection or biopsy; and
- location of the tumour i.e. supratentorial or infratentorial.

The presence of pre-existing neurological deficit in the form of hemiplegia or hemiparesis appears to have a strong association with DVT. Eighty percent of the patients found to have DVT had a pre-existing neurological deficit. This is further shown to be statistically significant by the Chi-square test with ($p<0.0001$). This may suggest that a prospective surveillance programme for deep vein thrombosis may be useful for patients with brain tumours with major motor neurological deficit. Two patients in the study, both of whom had hemiplegia, were found to have clinical DVT outside of the surveillance period, which was up to the 7th postoperative day. This raises the possibility that there could have been a higher incidence of asymptomatic DVT if the period of surveillance was extended. The clinical relevance of this needs to be evaluated further (as most ambulant patients will have been discharged home by this time).

With regard to prophylaxis against deep vein thrombosis in our local context, the study shows that the incidence of postoperative DVT in our population using current management protocols is similar to or less than the incidence of DVT in Caucasian populations using full mechanical and pharmacological prophylactic measures. However, it is possible that the use of TED stockings in all our patients could lower the incidence of post-operative DVT even further. LMW heparin in an environment of low incidence of DVT should be cautiously used due to the known risk of post-operative intracranial haemorrhage. The risk and benefit evaluation of these prophylactic measures will need to be studied further.

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