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Retrospective study to analyse the factors related to the occurrence of venous thrombo-embolism in neurosurgical patients for risk stratification

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Abstract
Aims and Objective: To study the factors related to the occurrence of Venous thrombo embolism in neurosurgical patients and risk stratification.
Material and Methods: The study included all consecutive patients undergoing elective Neurosurgical intervention who developed Venous Thrombo Embolism. DVT was diagnosed when thrombus was seen, flow was absent, non-compressibility encountered and when there was no augmentation. Patients were ambulated according to a strict protocol after the surgery. The patients who developed postoperative VTE were subjected to thromboprophylaxis as per the institute protocol.
Results: Among the patients with VTE, 64.85% of the patients were between 40 to 60 yr of age. In the VTE study group both males 18(48.6%) and females 19 (51.4%) were equal. In the VTE group, Hypertension was the most common co-morbid condition 6 (16.2%) followed by thyroid disorder 3 (8.1%), diabetes 2 (5.4%). The most common blood group among the study group was O+ 15 (40.54%).
Conclusion: Venous thrombo embolism in Neurosurgical patient is a cause of increased morbidity and mortality. Patients having preop and post op motor deficit, prolonged ventilator support, age group between 40 – 60 yrs, and patients within the first 1 weeks of surgery are at a high risk of developing this complication.

Keywords: Venous thrombo embolism, craniostomy, risk factors

Introduction

The term venous thromboembolism (VTE) encompasses both DVT and its serious complication pulmonary embolism (PE). Neurosurgical patients need a special consideration with respect to the occurrence of VTE and its treatment [1].

One of the risks involved in initiating of thromboprophylaxis agents is intracranial haemorrhages. Thus neurosurgical patients are already at risk in instituting the thromboprophylaxis after a major surgical insult. A variety of factors place the neurosurgery population at increased risk for VTE; these include malignancy, duration of surgery, decreased mobilization postoperatively, postoperative paralysis, and older age. The risk of pulmonary embolism in neurosurgical patients is 5% with embolic phenomenon causing mortality ranging from 9% to 50% [2]. Venous thromboembolism affects 1-2 per 1000 people in general population which ranges from DVT to pulmonary embolism. Incidence of DVT in neurosurgical patients (cranial and spinal combined) is reported to be 29-43% without any pharmacological prophylaxis. Indians are believed to be at a lower risk of VTE due to various factors such as the inherited resistance to thrombosis formation, low BMI, lower consumption of a fat-rich diet, the warmer climatic conditions etc [3]. The reported lower incidence of VTE could also be because of the lack of awareness among the doctors and patients, and of diagnostic facilities in this part of the world. Contrary to previous belief, most of the recent studies show increasing incidence of VTE among the Indian and Asian population, and it is almost equivalent to that reported in Caucasians. Most orthopaedic studies report a similar incidence of DVT in the Indian population as compared to the Caucasians [4].

In spite of reported high morbidity and mortality, there are no clear cut guidelines for prophylaxis of VTE in neurosurgery. Many studies have not found any benefits of routine DVT prophylaxis. According to recent ACCP (American College of Chest Physicians 2012) guidelines mechanical prophylaxis is preferred over pharmacological prophylaxis in routine craniotomy patients [1]. In the present scenario, a standard guideline for providing thromboprophylaxis to patients in the Indian subcontinent is needed, which should be practical and accept table for all. There are very few Indian studies which either document the incidence of VTE or recommend any prophylaxis and there are few published Indian study to document incidence of DVT in neurosurgical patients.

Most of the neurosurgical patients are operated for long hours and have post op neurological deficit causing immobilization. Then also not every neurosurgical patient develops venous thromboembolism. Thus our study examines which factors are leading to VTE in some patient and not in others. It will help in risk stratifying patients and suggesting criteria for starting thromboprophylaxis in the same.

Most of the studies regarding stratification of patients with regard to risk factors for venous thromboembolism are based upon the orthopedic and gynaecologic patients with few studies on neurosurgical patients.

Methodology

This retrospective study included all consecutive patients undergoing elective Neurosurgical intervention who developed Venous Thrombo Embolism at SCTIMST between Jan 2013 and April 2015.

Patient Selection: All consecutive patients undergoing elective Neurosurgical intervention who developed Venous Thrombo Embolism with involvement of the pulmonary venous system at SCTIMST between Jan 2013 and April 2015 were enrolled for the present study. The patients excluded were 1) Patients who underwent Burr hole procedures, extradural procedures without intracranial pathology, simple decompressive procedures (eg Stroke, Chiari malformations 2) Patients with preoperative DVT and pulmonary embolism or those who have a known history of coagulation disorders 3) Patients undergoing surgery outside sctimst.

Records of the patients related to demographic data and clinical profile, investigation and the various risk factors and treatment history were collected. The study was approved by the Ethical Committee of the Institute. All patients participating in the study underwent baseline evaluation of routine blood investigations coagulation parameters prior to surgery. Patients with suspected venous thrombosis with confirmed Pulmonary embolism and were included in the study. In our protocol all patients with a clinical suspicion of DVT would undergo colour doppler ultrasound utilising the 5 to 10 MHz linear transducer in real time B mode. The Doppler examined bilateral common femoral (CFV), superficial femoral (SFV), popliteal, anterior tibial and posterior tibial veins in longitudinal and transverse plane. Flow, visualized thrombus, probe compressibility and augmentation were seen during the Doppler study. The results were assessed by an experienced radiologist. DVT was diagnosed when thrombus was seen, flow was absent, non-compressibility encountered and when there was no augmentation. Distal thrombus suggest thrombus involving the calf veins and proximal thrombus suggest popliteal vein or above involvement. Patients were ambulated according to a strict protocol after the surgery. The patients who developed postoperative VTE were subjected to thromboprophylaxis as per the institute protocol. Anticoagulation was initiated with Unfractionated Heparin or low molecular weight heparin with oral anticoagulants started simultaneously or a day after (as oral anticoagulants take time to act). When INR attained the therapeutic level i.e between 2- 3 heparin / LMWH were stopped. Oral anticoagulants were continued for about three to four months. Therapeutic titration was done in subsequent OPD visits after discharge.

Statistical analysis

SPSS v20.0 was used for data analysis. (SPSS v20.0 program, SPSS, Inc., Chicago, IL). The categorical data is presented as frequency distribution. The percentages were compared using the Chi square test. $P<0.05$ was considered significant. In addition, Mcnemar test was used to determine significance between chosen variables.

Results

There were a total of 1794 patients who underwent craniotomy during the study period satisfying the inclusion criteria. Of these 42 patient had venous thrombosis in the form of DVT & / PE during the hospital stay. But only 37 patients were included in the study as they demonstrate venous thrombo "embolism" and were analyzed in details.

The mean age of the 1794 who underwent craniotomy was 38.81 yr (± 18.01 SD) while the mean age of the VTE study group was 47.16 years (± 11.56 SD). All the patients in the VTE study were divided in five age groups (20- 30, 31-40, 41-50, 51-60 and > 60). The frequency of VTE was analyzed across these five age groups. VTE study group contain 4(10.81%) in 20-30 years, 5 (13.51%) in 31-40 years, 13 (35.13%) in 41- 50 years, 11 (29.72%) in 51-60 years and 4 (10.81%) in > 60 year group. Approximately less than one fourth of patients (24.32%) were < 40 years. Almost 64.85% of the patients were between 40 to 60 years of age. The incidence of DVT did not increase significantly beyond the age of 60 years. On the age distribution curve patients are seen peaking between 41 & 60 years. There was near equal proportion of males and females in both the craniotomy group and the VTE study group. In the VTE study group both males 18 (48.6%) and females 19 (51.4%) were equal.

Table 1: Incidence of Venous thrombo embolism patients

Diagnosis	No of patients	%
Pulmonary Embolism(PE) only	31	83.78
DVT+ PE	6	16.21
Total	37	100

Various co-morbidities like Hypertension, Diabetes, thyroid disorders, cardiac disorders, chronic liver disease and renal diseases were documented in VTE group. In the VTE group, Hypertension was the most common co-morbid condition 6 (16.2%) followed by thyroid disorder 3 (8.1%), diabetes 2(5.4%). Cardiac disorder, liver disease and renal disease was seen in one patient each. None of the patients in the study had other systemic malignancy. (Table 2)

Table 2: Demographic characteristics of the study population suffering from VTE

Variables	Number of patients with VTE	Percentage of total VTE patients
Sex		
Male	18	48.6
Female	19	51.4
Total	42	100
Age		
20 -30 yr	4	10.81
31-40 yr	5	13.51
41-50 yr	13	35.13
51-60 yr	11	29.72
>60 yr	4	10.81
Total	37	100
Comorbidities in VTE patients		
Hypertension	6	16.2

Diabetes Mellitus	2	5.4
Thyroid Disorder	3	8.1
Cardiac Disorder	1	2.7
Liver Disease	1	2.7
Renal Disease	1	2.7
Total	14	37.8

During the study period 1794 patient underwent craniotomy for various pathology. Mostly they were operated for glioma 423 (23.57%), aneurysm 313 (17.4%), meningioma 240 (13.37%), epilepsy 190(10.59%). The other reasons for the craniotomy were sellar suprasellar lesion 184 (10.25%), schwannomas 114 (6.35%), clival lesions 15 (0.8%), epidermoid 24 (1.33%), hematomas 37 (2.06%), tuberculomas 1 (0.05%) and trigeminal neuralgia 3 (0.16%). Venous thrombo embolism was seen in 2.06% of the total craniotomy patients. Tumours were the most common overall pathology constituting about 25 (67.56%) of the patients. Among the tumours schwannom 8 (21.62%), glioma 6 (16.21%) and the meningioma 6 (16.21%) constitute the major pathologies. The other pathologies were craniopharyngioma 2 (5.4%), pituitary adenoma 2 (5.4%), clival lesion 1 (2.7%), trigeminal neuralgia 1(2.7%), hematoma 1 (2.7%), tuberculoma 1 (2.7%). Inspite of large number of epilepsy patients being operated there was no epilepsy patient who had VTE. (Table 3)

Table 3: Distribution of patients in craniotomy group, VTE group and their proportion

Diagnosis	Total	VTE	% of Total Craniotomy Patients (1794)	% of total VTE patients (37)
Aneurysm	313	9	2.87	24.32
Craniopharyngioma	47	2	4.25	5.40
Clival lesion	15	1	6.67	2.70
Epidermoid	24	0	4.16	0
Glioma	423	6	1.41	16.21
Meningioma	240	6	2.50	16.21
Pituitary adenoma	137	2	1.45	5.40
Trigeminal neuralgia	3	1	33.33	2.7
Hematoma	37	1	2.70	2.7
Tuberculoma	1	1	100	2.7
Epilepsy	190	0	0	0
Schwannoma	114	8	7.01	21.62
Others	250	0	0	0
Total	1794	37	2.06	100

All patients included in the study underwent surgeries appropriate to their pathologies. Patient were prior admitted in the neurosurgical ward or the neurosurgical ICU as per the condition during the admission. The median interval between the admission and the surgery was 4.00 days (mean 6.11 days, SD 6.24), ranging between 0- 34 days.

After the patient underwent surgery patient were kept in neurosurgical ICU as per the postop clinical condition, intubation status, postop imaging. We generally do postop CT scan on the next day after the drain removal. But scan can be done immediately postop if required as per the intraop impression. IV cannula, central line, Foleys catheter were removed the next day as per the protocol or as needed and patient were mobilized as soon as possible. Inspite of all these measures some 37 patient develop venous thrombo embolism in the post op period. The median interval between the surgery and the development of the VTE was 8.00 days (mean 8.19 days, SD 5.38), ranging from 1 – 21 days.

In order to find out whether any association is found between the blood group of the patients and the development of the VTE, enquiry was made regarding their blood groups. The most common blood group among the study group was O+ 15 (40.54%), followed by A+ 11 (29.72%), B+ 10 (27.6%), AB + 1(2.7%). No negative blood group was found among the 37 patient who developed VTE. (Table 4)

Table 4: Association between incidence of VTE and Blood groups

Blood Group	N	%
A+	11	29.72
B+	10	27.02
O+	15	40.54
AB+	1	2.7
Total	42	100.0

Table 5: Biochemistry in VTE patients

Variables	Hb	PCV	BUN	Creatinine	Sr Na+	Sr K+	PT INR
Mean	11.39	34.62	11.24	.89	137.95	3.72	1.34
SD	2.006	5.471	6.164	.313	3.844	.451	.427
Range	7	21	36	2	19	3	2

Patient after the admission underwent routine investigation to search for any abnormality and appropriate corrections. Investigation prior to the development of VTE were considered. Specially those investigation indicating the body fluid status and coagulation were evaluated. The mean haemoglobin level in VTE patient study group was 11.39 ± 2.006 mg/dl ranging from 9- 16 mg/dl. Similarly the packed cell volume 34.62 ± 5.47 percent, BUN 11.24 ±6.164 mg/dl, Sr creatine 0.89 ±.31 mg /dl, Sr Sodium 137.95 ± 3,844 mEq/L, Sr Potassium 3.72 ±0.45 mEq/L, and PTINR was 1.34 ±0.427. These values were not grossly different from the normal range. (Table 5)

Discussion

Venous thrombo embolism is a major cause of morbidity and mortality in all surgical patients). Neurosurgical patients are considered to be under moderate risk for VTE.[1] Incidence of VTE in population based studies was found to be between 70-113 cases/100000/ year. There are multitude of factors responsible for occurrence of venous thromboembolism in the neurosurgical patients. Our study is one effort to find these factors so as to identify high risk patients to start effective prophylaxis and prevent avoidable morbidity and mortality.

In our study the proportion of patients undergoing elective neurosurgical procedures who developed VTE in the postoperative period was 2.06%. John *et al* in their study of 38058 neurosurgical cases found the incidence of VTE to be 1.7% consisting 0.6% PE and 1.3% of DVT.[5] Sahu and Nair *et al*, have reported incidence of 3.7% in 260 screened patients undergoing cranial and spinal surgery.[6]Our study reports an incidence of VTE comparable to the other Asian and western incidence though not as high as that in the western population.

The mean age of the VTE study group was 47.16 years (± 11.56 SD). Approximately less than one fourth of patients (24.32%) were < 40 years. Almost 64.85% of the patients were between 40 to 60 yr of age. The incidence of DVT did not increase significantly beyond the age of 60 years. On the age distribution curve patients are seen peaking between 41 & 60 yr. Various studies [7, 8] shows that the incidence of VTE increases exponentially with the age. It is < 5 / lakh among the childrens (<15 yr) to 450-600 / lakh in persons > 80 years [7]. However Agarwal *et al*, found no significant correlation of DVT with age and sex [9].

There was near equal proportion of males and females in both the craniotomy group and the VTE study group. In the VTE study group both males 18 (48.6%) and females 19 (51.4%) were equal. Anderson *et al* had similar incidence in both men and women [10]. Silverstein *et al*, however noted higher incidence in younger women and modest higher proportion in older men [11].

In the VTE group, Hypertension was the most common co-morbid condition 6 (16.2%) followed by thyroid disorder 3 (8.1%), diabetes 2 (5.4%). Cardiac disorder, liver disease and renal disease was seen in one patient each. None of the patients in the study had other systemic malignancy. In the literature, a twofold increased risk of developing DVT in patients with hypertension has been described [10, 12].

In our study venous thrombo embolism was seen in 2.06% of the total craniotomy patients. Tumours were the most common overall pathology constituting about 25 (67.56%) of the patients. Among the tumours schwannom 8 (21.62%), glioma 6 (16.21%) and the meningioma 6 (16.21%) constitute the major pathologies. Inspite of large number of epilepsy patients being operated there was no epilepsy patient who had VTE. Brandes *et al*, who reported an incidence of 27% in malignant gliomas [13]. Julian *et al*, in their study of 42 VTE patients, consisted glioma 15.8%, meningioma 37.2%, Schwannoma 29.7% [14].

The most common blood group among the study group was O+ 15 (40.54%), followed by A+ 11 (29.72%), B+ 10 (27.6%), AB + 1 (2.7%). No negative blood group was found among the 37 patient who developed VTE. Fatema M *et al*, has described Non O blood group as inherited risk factor for the development of VTE [15]. Further Baudouy D, *et al*, proposed that Non –O blood groups are involved in first VTE event and also in the recurrence [16]. He further added that blood group B is strongly associated with VTE recurrence and suggest long anti -coagulant therapy after first event. He noted that O blood group had 5 fold decreased risk of VTE recurrence. In our study we found blood group O as the most common entity which is exactly opposite to the present available literature.

We had considered the laboratory investigation prior to the development of the VTE. The values which are found were not grossly different from the normal range. All patients included in the study underwent surgeries appropriate to their pathologies. Patient were prior admitted in the neurosurgical ward or the neurosurgical ICU as per the condition during the admission. The median interval between the admission and the surgery was 4.00 days (mean 6.11 days, SD 6.24), ranging between 0- 34 days. During this period, we have not routinely screened the patients for any DVT. In our study all of patients in the VTE group had undergone surgery for more than 4 hours. Our findings resembled those reported by Raslan and Bharadwaj *et al* [17]. Lengths of who identified surgery> 4 hours were as possible risk factors.

Conclusion

Venous thrombo embolism in Neurosurgical patient is a cause of increased morbidity and mortality. Patients having preop and post op motor deficit, prolonged ventilator support, age group between 40-60 years, and patients within the first 1 weeks of surgery are at a high risk of developing this complication. A prospective regression study with large number of patient is required to clearly bring out the entire spectrum of risk factors.

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