ORIGINAL ARTICLE

Incidence and risk factors for development of venous thromboembolism in Indian patients undergoing major orthopaedic surgery: results of a prospective study

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Introduction: The incidence of venous thromboembolism (VTE) in Western populations undergoing major orthopaedic surgery without any thromboprophylaxis has been reported to range from 32% to 88%. There is however limited information on incidence of VTE in Indian patients and most of the Indian patients undergoing these surgeries do not receive any form of prophylaxis regardless of their risk profile.

Methods: A prospective study was performed on 147 patients undergoing major orthopaedic surgery for total knee replacement (TKR), total hip replacement (THR), and proximal femur fracture fixation (PFF) without any prophylaxis. These patients were profiled for presence of the known risk factors responsible for development of VTE. A duplex ultrasound on both lower limbs was done 6 to 10 days after surgery. Twenty three patients underwent THR, 22 patients underwent TKR, and 102 underwent surgery for PFF. The patients were assessed clinically for any signs of deep venous thrombosis (DVT) and pulmonary embolism (PE). A helical CT scan was done in case of suspicion of PE and a duplex ultrasound was done in case of clinical suspicion of DVT irrespective of the stage of study.

Results: The overall incidence of VTE was 6.12% and that of PE was 0.6%. The risk factors that were found to be significantly responsible for development of VTE ($p < 0.05$) were: immobility greater than 72 hours, malignancy, obesity, surgery lasting more than two hours.

Conclusion: The study reconfirms the belief that DVT has a lower incidence in Indian patients as compared with other ethnic groups.

Venous thromboembolic disease is a term used to denote deep venous thrombosis (DVT) and pulmonary embolism (PE). The incidence of venous thromboembolic disease in patients who underwent total hip or total knee arthroplasties and in patients who have sustained a fracture of the proximal end of the femur has ranged from 32% to 88% in the Western population.^{1–4} The use of routine thromboprophylaxis has shown to decrease the incidence to 15%–30%.^{3, 5–10} There are various factors that have been shown to be associated with high incidence of venous thromboembolism (VTE) (see box).

The incidence of VTE in Asian patients were traditionally considered to be lower than the Western population.^{16–22} However, a recent study has shown the incidence of postoperative VTE in a so called traditionally “low risk” Chinese population undergoing total hip and knee replacement to be 27.5%.²³ There are a lack of data on the incidence of DVT and the risk factors associated with it in an Indian population. We conducted a prospective study to determine the incidence of VTE and the risk factors associated with development of VTE in a cohort of Indian patients who underwent surgeries for total hip or knee replacement and for fractures of the proximal femur.

METHODS

Study design

The study is an observational study of cohort of consecutive Indian patients undergoing orthopaedic surgery at a tertiary Indian hospital. The patients were recruited over a period of two years and followed up one month after surgery. Required approvals from ethics committee as per the institutional policy was obtained before the start of the study.

Case selection

All consecutive patients under going total hip (THR) or knee replacement (TKR) and hip fracture surgeries were considered as eligible for enrolment in the study. These patients were then screened against inclusion criteria; the data on excluded patients were also recorded including the reason for exclusion. Informed consent was obtained from all patients.

Inclusion

Indian patients of both sexes who were admitted for THR, TKR, or proximal femoral fracture (PFF) surgery were included in the study. The following patient and procedural characteristics were recorded at inclusion and after the surgery: age greater than 60 years, female sex, smoker, history of cancer, history of VTE, family history of VTE, varicose veins, obesity (body mass index (BMI) greater than 30), whether receiving hormonal replacement therapy, history of thrombophilia, chronic renal failure, congestive cardiac failure, time of admission more than seven days before surgery, tourniquet use, use of regional anaesthesia, surgery lasting more than two hours, postoperative immobilisation greater than 72 hours.

Exclusion criteria

Occasional patient planned to receive during their hospital stay preoperative or postoperative pharmacological prophylaxis using unfractionated heparin, LMWH, heparinoids, oral anticoagulation therapy, hirudin, antiplatelet agents, or dextran. Patients having received any antiplatelet agent or

Abbreviations: DVT, deep vein thrombosis; PE, pulmonary embolism; VTE, venous thromboembolism; THR, total hip replacement; TKR, total knee replacement; PFF, proximal femur fracture fixation

Risk factors for VTE^{11–15}

- Malignancy
- Obesity (body mass index >30)
- History of VTE in patient or in family.
- Hormonal replacement therapy
- Oral contraceptive use
- Congestive heart failure
- Varicose veins
- Prolonged immobilisation
- Haematological disorders
- Chronic renal failure

oral anticoagulation therapy in the week preceding inclusion were also excluded.

Treatment of confirmed cases

The confirmed cases of VTE (both DVT and PE) were treated with intravenous infusion of heparin followed by a course of oral warfarin for a period of three months. The therapeutic level monitoring for heparin was done using activated partial thromboplastin time and of warfarin by international normalised ratio.²⁴

Ultrasound examination

An experienced radiologist using 7.5 or 10 MHz linear transducer probes performed duplex ultrasonography. Both the surgical and contralateral lower limbs were scanned between the sixth and tenth days from calf to groin region. Posterior and anterior tibial, peroneal, popliteal, superficial, and common femoral veins were visualised. Non-compressibility or visualisation of an intraluminal thrombus was considered as evidence of DVT.

An experienced orthopaedic surgeon assessed the patients twice daily during their hospital stay for any clinical signs or symptoms that may show the presence of underlying VTE—such as, fever, calf swelling, pain, or tenderness of calf. If there was suspicion of presence of underlying VTE the ultrasound examination was carried out within four hours irrespective of the day of study.

Helical CT scan

If the patient had any clinical signs or symptoms suggestive of PE—that is, pleuritic chest pain, angina-like pain,

hemoptysis, dyspnea, palpitations, pleural rub, wheezing, cough, tachypnea, diaphoresis, wheezes, or cyanosis—they had a helical CT scan to record the pulmonary thrombus.

Statistical analysis

The incidence of reported DVT, PE, and VTE was calculated. Relative risk and 95% confidence intervals for each of the factors was assessed and significant risk factors ($p < 0.005$) were recorded.

RESULTS

The average age of patients undergoing THR, TKR, and hip surgeries was 64.2 years, male to female ratio was 71/67 or 1.05. THR was performed in 23 of 147 patients (15.6%); TKR in 22 of 147 patients (14.9%), and PFF surgeries was carried out in 102 patients (69.38 %). Overall incidence of VTE disease in the entire study group was 6.12% (9 of 147 patients). The incidence of VTE was 8.6% (2 of 23 patients) in THR surgery patients, 6.8% (7 of 102) in hip fracture surgery group, and 0% (0 of 29) in the TKR group. Of the total of nine patients that had VTE, three had proximal venous thrombosis (33%), five had distal venous thrombosis (55.5%), and one had PE confirmed on necropsy (11.1%). There were seven cases of ipsilateral DVT (77.1%) and one case of contralateral DVT (11.2%). There was no case of bilateral DVT.

The risk factors that were found significant ($p < 0.05$) were: immobility >72 hours (relative risk (RR) = 11.364, $p = 0.0001$), malignancy (RR = 10.214, $p = 0.008$), obesity (RR = 6.909, $p = 0.005$), surgery lasting more than two hours (RR = 4.318, $p = 0.041$) (table 1).

DISCUSSION

This study provides information on incidence and risk factors for VTE in an Indian population undergoing major orthopaedic surgery. An accurate assessment of the incidence and the risk factors in this ethnic group will probably help clinicians in making important decisions about thromboprophylaxis in the perioperative period. An additional advantage of studies that provide data on ethnic disparity is that they can highlight risk factor differences in two groups and lead to public health measures that control the additional risk factors that are present in the groups with high prevalence.²⁵

Epidemiological data on the incidence of VTE in Asian populations is ambiguous. While most studies have shown that the incidence of DVT is lower in Asian patients than the Western population,^{7 18–21 26} some of the recent studies from China and Paacific island have shown significant incidence of DVT in the high risk orthopaedic patients.^{16 17 23 27 28} In view

Table 1 Univariate analysis of patient and procedural characteristics

Characteristic	Total patients	VTE patients	Relative risk
Age > 60	50	1	4.25
Female	67	7	3.453
Smoker	25	2	1.270
Malignancy	2	2	10.24
History of VTE	1	0	NS
Family VTE	0	0	NS
Varicose veins	0	0	NS
Obesity (BMI >30)	27	6	6.909
Hormone therapy	2	0	NS
Thrombophilia	0	0	NS
Chronic renal failure	4	0	NS
Congestive cardiac failure	9	2	3.532
Time of ADM >7 days	32	4	2.467
Tourniquet use	22	0	NS
Regional anaesthesia	138	8	NS
Surgery >2 hours	28	5	4.318
Immobilisation >72 hours	16	6	11.364

NS, cannot be calculated because at least one variable is 0.

of conflicting data from other countries in Asia it was necessary to have a prospective study on the incidence of VTE in high risk orthopaedic surgery patients from India. A previous study by Jain *et al* on Indian patients that studied the incidence of DVT found a low incidence of DVT.¹⁷ Only two of their 71 patients developed DVT. The results of our study are consistent with this previously published result and reconfirm that incidence of VTE in Indian patients is significantly lower than the Western population. This study not only determined the incidence of DVT but also the PE that along with the DVT constitute VTE disease. As both DVT and PE constitute VTE and are important causes of post-operative morbidity and are managed on similar lines, comprehensive data on the incidence of VTE will probably help in formulating guidelines for this group of patients of Indian origin.

The differential incidence of occurrence of a particular disease in various ethnic groups is often attributed to presence or absence of multiple acquired and genetic traits. The genetic traits that may be possible explanations for this reduced incidence of VTE in Asian population include activated protein C resistance, decreased prevalence of homocystinaemia, and a lesser prevalence of mutation known as factor V Leiden that is more common in Western population.^{29–33a} Acquired traits that are thought to be risk factors for development of VTE and have been found to be less prevalent in Asians include obesity and heart failure.³⁵

Determining the risk factors for development of VTE is important as this may help clinicians identify the at risk patients and give them prophylaxis appropriately. There have been various studies to determine the risk factors for VTE in high risk orthopaedic surgery patients in the West.^{12 28 36–42} Based on the findings from these studies we evaluated 17 factors for their role in causation or association with occurrence of VTE. In this study immobility >72 hours, malignancy, obesity, surgery lasting more than two hours were found to be the significant risk factors.

Immobility and malignancy were found as significant risk factors in most of the previous studies that were conducted to determine the risk factors for VTE. Obesity was not found to be significant risk factor in some of these studies^{36 38 40} but many studies including this particular study found it to be a significant risk factor.^{12 37 39 41 42} This may be an important variable that accounts for ethnic differences, as the overall incidence of obesity is lower in Indian patients as compared with the Western population.⁴³ The incidence of the obesity in this study was higher than that reported in the general population, which may have been secondary to increased incidence of hip fracture in this population.⁴⁴ We could not find any data that suggested significant positive correlation between the incidence of VTE and duration of surgery, this study showed that surgery lasting for more than two hours was associated with significant risk of development of VTE. This may be important as prolonged surgery may thus be considered an indication of postoperative thromboprophylaxis.

An apparent shortcoming of this study is the presence of small numbers, which may warrant caution especially while interpreting the findings with respect to determination of risk factors. These numbers although statistically small are clinically not insignificant, particularly in view of obtaining this large a group of non-prophylaxised patients. There is an increasing trend towards use of routine thromboprophylaxis in orthopaedic surgery in India based on the data obtained from Western populations. The finding of this study may thus emphasise the need of a multicentre prospective randomised trial to validate the use of the thromboprophylaxis before it is universally adopted for the Indian population.

The use of appropriate investigative modality in screening of DVT is important to ensure valid and comparable data. Ultrasound examination has been shown to be a useful tool with a high sensitivity and specificity for detection of DVT.^{1 45–50} Brothers *et al* in their meta analysis of 10 reports have shown a high combined specificity of 0.96.⁴⁵ The technique however is operator dependent, and as a single operator did not perform the test in all patients there is probability of an interobserver differences.

PE in most postoperative cases occurs subsequent to DVT in the veins proximal to and including the popliteal veins. Helical (spiral) computed tomography has been shown to be a reasonably specific and sensitive non-invasive modality for detection of PE.^{51–53} In this study only those patients that had symptoms suggestive of PE had helical computed tomography so we might have missed some asymptomatic cases of PE.

In conclusion we find that in this large prospective study of an Indian population undergoing high risk orthopaedic surgery, the incidence of the VTE is significantly lower than the Western population and thus as a corollary it may be prudent not to apply the Western criteria of universal thromboprophylaxis in this ethnic group and limit the use of thromboprophylaxis to those with significant risk factors found in this study.

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