

➤ **Original Article** ➤

RAVS Study: One Indian Single Center Analysis of Patients with VTE

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Objective: Venous thromboembolism (VTE) includes deep vein thrombosis (DVT) and pulmonary embolism (PE). VTE affects all races, age groups, and genders. The objective of this registry was to analyze the patient characteristics, clinical outcomes, management strategies, and temporal trends in VTE at a single center.


Materials and Methods: Consecutive medical records of inpatients between January 2007 and March 2018, meeting the inclusion criteria (confirmed diagnosis of DVT by Doppler ultrasound scan and/or PE by chest computed tomography) were identified and collected. A total of 1,024 patients were reviewed.

Results: Eight hundred and twelve patients with VTE were enrolled into the study; 37.4% were referrals from outside hospitals, 33.1% of the total patients had no risk factors, hence classified as unprovoked VTE and the rest of the patients had single or multiple risk factors which may have provoked the VTE, 68.8% presented with swelling and pain, and 88.5% had proximal DVT.

Conclusion: VTE is no longer a rare phenomenon in the Indian population, as believed earlier. The knowledge of VTE, prophylaxis, and treatment strategies is minimal among small institutes, nursing homes, and among general practitioners who are not affiliated with teaching institutes.

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Therefore, educating primary care physicians/surgeons on VTE is paramount, as this would reduce the incidence of VTE in India as well as associated morbidity and mortality rates.

Keywords: venous thromboembolism, deep vein thrombosis, retrospective registry, anticoagulants

Introduction

Venous thromboembolism (VTE) includes deep vein thrombosis (DVT) and pulmonary embolism (PE). DVT is seen in nearly two-thirds of patients with symptomatic VTE, while PE is seen in one third of the patients.¹⁾ Venous thromboembolism affects all races, age groups, and both genders. According to the global burden of diseases, injuries and risk factors study, VTE associated with hospitalization was the leading cause of disability-adjusted life years lost in low-income and middle-income countries and the second most common cause in high income countries.²⁾ The global incidence of VTE is 0.75–2.69 per 1,000 population and 2–7 per 1,000 in the elderly.³⁾ Hospital-associated VTE is a major and serious public health concern with increasing prevalence.

The ENDORSE and other studies have shown high VTE associated mortality risk and underutilization of prophylactic techniques in Indian hospitals; only 19.1% of the medical and 16.3% of the surgical patients at risk of developing VTE received the American College of Chest Physicians (ACCP)-recommended prophylaxis.⁴⁾ Hospital-associated VTE is a major concern with increasing prevalence and the need for adoption of thromboprophylaxis as a routine practice was corroborated by an autopsy-based study conducted at Chandigarh, India, which showed an overall incidence of PE in adults being 15.9% with PE as a cause of mortality in 80% of the patients.⁵⁾

Hospital-associated VTE is commonly seen in prolonged hospital stays with up to 10%–15% fatality rates

despite being one of the most common preventable causes of hospital death. Patients are prone to complications such as post-thrombotic syndrome (30%–50%), recurrent VTE after stopping anticoagulation therapy (>20%), and chronic thromboembolic pulmonary hypertension (4%).^{6,7)}

This registry was created with the intention of analyzing retrospectively the data pertaining to patient characteristics, clinical outcomes, predictors of mortality, especially in acute DVT, management strategies as well as temporal trends in VTE in a single center.

Methods

This is a retrospective single center study carried out at the Department of Vascular and Endovascular Surgery, Ramaiah Medical College, Bangalore, India.

For the study, consecutive medical records were analyzed of inpatients from January 2007 to March 2018. Patients had to meet the inclusion criteria, i.e., a confirmed diagnosis of acute or acute-on-chronic DVT by Doppler ultrasound scan and/or PE by chest computed tomography (CT), based on the International Classification of Diseases code.

No formal sample sizing calculations were made as the primary analyses were purely descriptive in nature.

Data collection

Patients with symptomatic, acute or acute-on-chronic DVT or PE confirmed by objective testing and meeting the inclusion criteria were enrolled into the study. Outpatients were excluded. The diagnosis and site of DVT was confirmed using duplex ultrasonography, based on the presence of thrombus seen on B-mode imaging, compressibility of veins, and augmentation response. PE was diagnosed using a combination of CT pulmonary angiogram, ventilation–perfusion scan, and D-Dimer. Selected investigations as per requirement of each cases clinically were performed.

Results

A total of 1,024 medical records were reviewed and analyzed. Data from 812 (79%) medical records were analyzed and the remaining 212 (21%) were excluded as they did not meet the inclusion criteria or lacked sufficient data to support the diagnosis. Data from 812 medical records with diagnosis of acute or acute-on-chronic DVT by Doppler ultrasound scan and/or PE by CT pulmonary angiogram, were analyzed.

A total of 33 (4.06%) patients had bilateral lower limb DVT and 742 (91%) had unilateral limb DVT, of which 100 (13.4%) patients had DVT with PE. Twenty-nine

Table 1 Demography of patients referred from broad specialties

General physician	135 (16.6%)
Cardiologist	48 (5.9%)
Orthopedic surgeon	36 (4.43%)
Nephrologist	57 (7.02%)
General surgeon	41 (5.05%)
Oncologist	21 (2.58%)
Neurologist	23 (2.83%)
Gynecologist	18 (2.22%)
Pediatrician	14 (1.72%)
Gastroenterologist	28 (3.44%)
Others*	391 (48.15%)

*Others include referrals from outside hospitals, neurosurgeon, pediatric surgeon, gastroenterologist, and specialty not specified.

Table 2 Predisposing factors for venous thromboembolism

Predisposing factor	VTE patients (n)
Surgery**	206
Malignancy	137
Tobacco use	87
Trauma	90
Immobilization for >3 days	71
Immobilization+multiple factors	132
Hormonal therapy	7
Indwelling central venous catheter	30
Denovo	269
Ventilator support	9
Hypercoagulable states	8
Post-transplant	27
Stroke	25

Thirty-three percents of the patients had one risk factor, 22.9% of the patients had two risk factors, 11% of the patients had multiple risk factors, and 33.1% of the patients had unprovoked VTE. **Surgeries include orthopedic surgery—total hip replacement, total knee replacement and other orthopedic interventions, general surgical procedures, gastrointestinal, obstetrics/gynecological procedures, genito-urinary, neurosurgery, oncology, and bariatric surgery. ^{||}Malignancy includes gastrointestinal, genito-urinary, lung, breast, blood/lymphatic cancers.

VTE: venous thromboembolism

(3.5%) patients had upper limb DVT.

The demography of patients referred from other broad specialties is described in **Table 1**. A total of 304(37.4%) patients were either referred from outside hospitals with diagnosed VTE or presented to Vascular Surgery Out Patient Department with symptoms of VTE.

The cause of DVT was idiopathic in 269 (33.12%) patients. The major predisposing factor for DVT was found to be undergoing major surgery—which included major orthopedic procedures, major abdominal surgeries, and other major surgeries. Other predisposing factors are de-

Table 3 Symptoms in venous thromboembolism patients

Symptom	VTE patient n (%)
Limb swelling	96 (11.8%)
Pain	54 (6.6%)
Swelling+pain	559 (68.8%)
Discoloration of limb	74 (9%)
Breathlessness	6 (0.7%)
Others*	25 (3%)

*Others: erythema of the limb, chest pain, cough, syncope, fever
VTE: venous thromboembolism

Table 4 Level of DVT

Level of DVT	n (%)
Proximal DVT	719 (88.5%)
Distal DVT	62 (7.6%)
IVC thrombosis	2 (0.2%)
Upper limb DVT	29 (3.57%)

DVT: deep vein thrombosis; IVC: inferior vena cava

scribed in Table 2.

Clinical presentation of VTE

The most common symptom among patients diagnosed with VTE was swelling with pain, which was seen in 559 (68.8%) of the patients. Swelling alone was seen in 96 patients (11.8%) with VTE (Table 3). Proximal DVT was found in 719 (88.5%) patients and distal DVT in 62 (7.6%) (Table 4).

Management strategies

Duplex ultrasonography was used for the diagnosis and the site of DVT. Diagnosis of PE was done using a combination of CT pulmonary angiogram, ventilation-perfusion scan and D-Dimer. It must be noted that not all of these investigations were performed in each patient.

Anticoagulants formed the mainstay of treatment. Patients with a confirmed case of proximal DVT or PE were started on either Low Molecular Weight Heparin (LMWH) or fondaparinux considering comorbidities and contraindications. LMWH, fondaparinux, or unfractionated heparin was given for at least 5 days along with an oral anticoagulant, until the international normalized ratio was in the range of 2–2.5. The oral anticoagulant was given to the patients with confirmed proximal DVT or PE within 24h of diagnosis and was continued for 3 months. Either a vitamin K antagonist (e.g., acitrom, warfarin) or the non-vitamin K antagonist oral anticoagulant novel oral anticoagulants (NOACS) (e.g., rivaroxaban, dabigatran, or apixaban) was given. Patients with unprovoked proximal DVT, with no additional risk of major bleeding, and probable high risk of recurrence

were assessed and anticoagulation was continued beyond 3 months in these patients. Major bleeding was defined as any bleeding requiring intervention such as blood transfusion. Minor bleeding was defined as any bleeding treated just with stoppage of anticoagulation therapy. Major bleeding was seen in 2% of the patients on anticoagulation therapy and minor bleeding in 17% of the patients. Treatment of bleeding included cessation of anticoagulation therapy and reversal of anticoagulation effects using available specific reversal agents along with specific blood products.

One hundred and thirty-seven patients underwent systemic thrombolysis with urokinase or recombinant tissue plasminogen activator. None of them had undergone thrombectomy/catheter-directed thrombolysis. In 36 patients with absolute contraindications to anticoagulation, an inferior vena cava filter was placed.

The average duration of hospital stay in patients diagnosed with VTE was 5.2 days. Among surgical patients with VTE, the average duration of hospital stay was increased by 6.2 days (over and above the regular stay of surgical patients).

Discussion

To the best of our knowledge, the present retrospective study involving patients with VTE is the largest single-center study of its kind in India.

VTE is a common and potentially life-threatening condition. Due to increased awareness and early diagnosis, the incidence of VTE is rising contrary to the earlier belief that it is low in Asian countries⁸⁾ as compared to that in Western population. A large prospective epidemiological study involving 19 centers in Asia showed that DVT occurred in 41% of the patients undergoing major joint surgery without thromboprophylaxis.⁹⁾ In a multinational cross-sectional study across 32 countries in 358 hospitals, 52% (64% surgical and 42% medical patients) of 68,183 inpatients (45% surgical and 55% medical inpatients) were found to be at risk for developing VTE.¹⁰⁾ India contributed with 2,058 patients, where 54% (61% surgical and 45% medical) of the inpatients had the same risk factors for VTE as the rest of the world. There is a greater awareness regarding VTE among orthopedic and general surgeons at our institute resulting in lower incidence of VTE in our institution. The incidence of VTE post-orthopedic interventions is 4.43% and that post-general surgical procedures is around 5.05%. However, when all postoperative patients were considered from various broad specialities, the incidence was 25.3%. With our increasing efforts over the past 18 years to raise the awareness of VTE among hospitalized patients and need of prophylaxis, the incidence of postoperative DVT is de-

clining; however, the referrals from outside hospitals with diagnosed VTE are rising. Referrals include patients who have undergone treatment from ayurvedic, homeopathic, and other alternative medicine treatments, postoperative patients referred from small clinics, hospitals and 'Google doctors'—who chose to treat themselves rather than visit a physician.

An autopsy study on 1,000 medical patients at the Postgraduate Institute of Medical Education and Research, Chandigarh, India revealed that PE was present in 159 (16%) of the 1,000 patients who died in the hospital—36 patients suffered from a fatal embolus, which was a major contributor to the death in 90 patients; in 30 patients, the embolus was an incidental finding at autopsy as death occurred due to some other cause. A clinical (pre-mortem) suspicion of PE was recorded in 30% of the patients and a diagnosis of PE could be made in <10%. More than 80% of the 159 patients with PE were young (<50 years).⁵⁾ In our institution, 42 patients diagnosed with VTE died during the course of hospital stay, of which 28.5% were diagnosed with PE. VTE as the cause of death could not be quantified. The incidence of PE in our hospital was 12.89% as compared to the 45.1% reported in the International Cooperative Pulmonary Embolism Registry.¹¹⁾

The overall incidence of VTE in our institution was 14.2 VTE patients per 100,000 admissions, as compared to the study conducted at Christian Medical College Vellore, which showed an incidence of 17.46 VTE patients per 100,000 admissions. The general surgical postoperative status of the patients had a relatively higher incidence of 5.05% as compared to their orthopedic postoperative status, which constituted around 4.4% of the study population. The incidence of VTE showed a male preponderance, with 59.3% being males in our study. The incidence of proximal DVT was 88.5%, distal DVT was 7.6%, and upper limb DVT was 3.57% as compared to a study conducted by Ng et al., in which the incidence of proximal DVT was 60.7% and that of distal DVT 38.2%.⁸⁾ The majority of the patients presented with swelling and pain (68.8%), the second most common symptom being only limb swelling (11.8%). In our study, the cause of DVT was idiopathic in 269 (33.12%) patients. The incidence of DVT in postoperative patients—which underwent major orthopedic procedures, major abdominal surgeries, and other major surgeries—was 25.36%, as compared to data from other pooled studies, which showed an average incidence of 25%–29%.¹²⁾ There is a decline in the incidence of DVT in our hospital due to increased awareness, regular investigations, and early referral to a vascular surgeon for suspected DVT.

Anticoagulants formed the mainstay of treatment. As mentioned earlier, patients with confirmed proximal DVT or PE were given LMWH or fondaparinux considering

comorbidities and contraindications along with oral anticoagulation. The use of NOACS has increased over the past year and no case of bleeding with NOACS have been reported in our institution.

This retrospective study is limited by the lack of crucial data such as referral trends from outside hospitals, cause of mortality in patients diagnosed with VTE, follow-up of patients beyond 6 months, recurrence rates, incidence of post-thrombotic syndromes, and type of malignancy associated with VTE.

Conclusion

VTE is prevalent in India and is no longer a rare phenomenon among the Indian population as believed earlier. There is increased awareness of VTE among large institutions in South India; however, the knowledge of VTE, prophylaxis, and treatment strategies is minimal among small institutes, nursing homes, and general practitioners who are not affiliated with teaching institutes. The majority of the population in South India primarily seek treatment at local clinics who provide ayurvedic treatment, homeopathic treatment, and from people who are unaware of VTE. The need of the hour is educating the primary care physicians/surgeons about VTE, as this would reduce the incidence of VTE in India as well as associated morbidity and mortality rates.

Disclosure Statement

None declared.

Author Contributions

Study conception: RPB, VVJP

Data collection: VVJP

Analysis: VVJP

Writing: VVJP, ANG

Critical review and revision: all authors

Final approval of the article: all authors

Accountability for all aspects of the work: all authors

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