Original article

Is pre-operative assessment of coagulation profile with Thrombelastography (TEG) useful in predicting venous thromboembolism (VTE) following orthopaedic surgery?

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ABSTRACT

Introduction: Epidemiologic data on the incidence of venous thromboembolism (VTE) in Indian population vary widely. Most studies show that the incidence of VTE is lower in Asian patients than in Western population. Screening tools to identify high-risk patients should enable us to reduce this complication. **Methods:** The incidence of VTE in 101 patients who underwent knee or hip arthroplasty, or surgery for hip fractures, without chemoprophylaxis for deep vein thrombosis (DVT) was documented. Diagnosis of DVT was made with Duplex ultrasonography. We also assessed the usefulness of pre-operative assessment of the hypercoagulable status of the patient in predicting the occurrence of VTE, using the Thrombelastography (TEG) test.

Results: The incidence of DVT in the study population was 7%. Six of the 7 patients who developed DVT had surgery for hip fractures, while one had knee replacement. The thrombus was above the knee joint level in 6 of the 7 patients. Pre-operative TEG was positive in only one of the 7 patients, but was positive in 37 of the remaining 94 patients.

Conclusion: Incidence of DVT in the study population is sufficiently high to recommend some form of prophylaxis to prevent VTE following hip and knee surgery. Pre-operative assessment of the patients' coagulation status with Thrombelastography does not predict the risk of VTE. The use of other lab parameters that could help in selective chemoprophylaxis needs to be explored.

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1. Introduction

Epidemiological data on the incidence of venous thromboembolism (VTE) in Asian populations vary significantly.^{1–9} While many studies have shown that the incidence of deep vein thrombosis (DVT) is lower in Asian patients than the Western population,^{1,3,4,9} some of the recent studies from China and south east Asia have shown significant incidence of DVT in high-risk orthopaedic patients.^{2,5–7}

In India, there are conflicting reports on the incidence of VTE.^{1–4} While Bagaria⁴ and Jain et al.³ reported a low incidence of DVT, Agarwala et al.² and Dhillon⁵ showed an incidence of around 60% in patients who did not have prophylaxis peri-operatively. In view of the conflicting data available, we found it necessary to have a

prospective study on the incidence of VTE in high-risk orthopaedic surgery patients who were not on chemoprophylaxis at our institution.

Acknowledging the risks associated with routine anticoagulation, we wanted to explore the use of laboratory tests to aid identify subjects who are at high-risk of developing VTE. Thrombelastography (TEG) is a laboratory test that has been very useful in predicting individuals who are hypercoagulable, and therefore more likely to develop VTE.^{10,11} It has also been shown to be useful in predicting which patients would develop DVT despite standard anticoagulation.¹¹ In this study, we aimed to assess the usefulness of pre-operative TEG in predicting the incidence of DVT in the study population.

2. Methods

All consecutive patients who presented with a fracture around the hip or with arthritis, requiring an arthroplasty of the hip or

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Fig. 1. Normal TEG curve. *R*, time taken for clot formation to begin; *K*, time period between initiation of clot formation and the time when an amplitude of 20 mm is attained; α angle, angle subtended on the graph by the tangent drawn to the curve starting from the initiation of coagulation, over the baseline; MA, maximum amplitude (highest amplitude) attained on the curve.

knee were included in the study. At admission, the patients were screened for DVT clinically and a coagulation workup including Prothrombin time (PT), activated partial thromboplastin time (APTT) and platelet count was done. Blood was also collected pre-operatively for the TEG analysis that was done using the Classical Thrombelastography technique (TEG, Haemoscope, Skokie, IL, USA), details of which are described later. While analyzing the TEG results, the *R* and *K* values as well as the alpha angle and maximum amplitude were assessed (Fig. 1). Risk factors for DVT were assessed – history of cancer, inflammatory bowel disease or autoimmune disorders, varicose veins, smoking, use of oral contraceptive pills, or hormone replacement therapy and diabetes. We excluded patients taking anti-platelet agents and oral anticoagulant treatment prior to surgery, patients who had been bedridden prior to admission and those who required ICU treatment post-operatively. All patients included in the study did not receive any form of chemoprophylaxis, which was the standard practice in the unit at the time of the study. All patients were mobilized early and had mechanical prophylaxis in the form of hourly mobilization of the ankle by the patient himself or by his relatives. Patients who requested anticoagulant prophylaxis as part of their treatment when the study proposal was explained to them, were also excluded from the study. The study was cleared by the institutional ethics board.

Post-operatively, all patients were examined clinically for symptoms and signs of VTE on a daily basis and with Duplex ultrasonography of both lower limbs 2 weeks after surgery, or earlier if there was any clinical evidence of DVT. Clinically, DVT was suspected if there was increased pain with leg swelling and a tense, tender calf compartment and a positive Homans' test. The patients were also examined clinically for DVT at 6 months and at 2 years after the surgery. A history of inappropriate leg swelling or pain in the legs was sought at the time of review. Duplex ultrasonography was done in patients suspected to have had DVT at the time of review.

3. Results

We studied 101 patients who underwent major orthopaedic surgery – 23 patients had fixation of fractures around the hip, 54 had arthroplasty of the hip for trauma or hip arthritis, and 24 had total knee replacement surgery. Of the 78 patients who underwent arthroplasty, 36 patients had degenerative arthritis,

26 had inflammatory arthritis, and 16 had post-traumatic sequel. The average age of the patients was 53.8 years (range 24–86), with 52 male and 49 female patients. All 101 patients were followed up at 6 months, but the details of only 45 patients were available at 2 years.

Seven patients developed clinical evidence of DVT at a median of 11 days from surgery (range 4–20 days). This was confirmed with Duplex ultrasonography. Six patients had thrombosis above the knee and one had a symptomatic DVT below the knee. None of the other patients developed either clinical or ultrasonographic evidence of DVT or clinical signs of pulmonary embolism. Of the remaining 94 patients, none developed DVT after discharge, though one died of unknown aetiology, a year after the surgery. Of the 7 patients who developed DVT, 2 patients died 18 months after the surgery – one of myocardial infarction and the other following a cerebrovascular event. The patient who had below knee thrombosis was the one who died of the cerebrovascular event.

Six of the 7 patients developed DVT following surgery for fracture of the hip (5 had trochanteric fracture fixation and one had hemiarthroplasty for a fracture neck of femur), and one developed DVT following knee arthroplasty for rheumatoid arthritis. On assessing the risk factors, 47 of the 101 patients had risk factors, but only 4 of the 7 patients who developed DVT had one or more of the risk factors (Table 1).

While there were 4 patients who had a platelet count of more than 450,000 and one patient with an APTT <23 s, none of these patients with abnormal coagulation parameters developed DVT.

Table 1
Risk factors for VTE.

Risk Factors	In the total population (N = 101)	In those who developed DVT (N = 7)
Smoking	14	2
H/o cancer	3	–
Varicose veins	3	–
H/o hormone replacement therapy (HRT)	1	–
H/o oral contraceptive pills (OCP) intake	2	–
Inflammatory bowel disorder	1	–
Autoimmune disorder	15	1
Diabetes	15	2

All patients who developed DVT had a normal APTT, PT, and platelet count.

On analyzing the pre-operative Thrombelastography (TEG) studies, 37 of the 101 patients were found to have abnormal values. 12 had sustained trauma, 8 had arthroplasty for degenerative arthritis, and 17 had arthroplasty for an inflammatory pathology. Two patients had a low *R* value on TEG (normal: 3–8 min); 8 had a low *K* value (normal: 1–3 min); 4 had a high alpha angle (normal: 57–78°); and 24 had a high maximal amplitude (normal: 51–69 mm).

Only one of the seven patients who developed DVT had an abnormal TEG value pre-operatively. This patient, who underwent a total knee replacement, had abnormal maximum amplitude on the TEG (70.7 mm).

4. Discussion

There are varying reports on the incidence of deep venous thrombosis in the Indian population, many of which suggest that the rates of occurrence of thrombo embolic events is lesser as compared to those documented in Western literature. However, there are conflicting reports as shown in Table 2.^{1,12–24} Bagaria et al. reported an incidence of 6.12% of VTE in a population of 147 patients who had major hip and knee surgeries without prophylaxis.⁴ Jain et al. reported only 2 episodes of DVT in 71 patients (106 major surgeries of the hip and knee) who did not have anticoagulant prophylaxis peri-operatively.³ Goyal et al. reported an incidence of DVT of 6% in the group of patients without any form of prophylaxis, and 2% in the group who had peroperative calf muscle electrostimulation.¹² Agarwala et al., on the other hand showed an incidence of 60% in 50 patients who did not have prophylaxis peri-operatively using venography as the end point.²

In our series, the incidence of DVT was 7%. Most other authors^{1,3,4,9,12,19,20,22–24} who have reported a similar incidence had also used Colour Doppler as the end point, rather than venography. Venography may pick up a lot of asymptomatic DVTs,^{2,5,7} which may not be clinically relevant. However, an incidence of DVT of 7% is sufficient to cause any clinician to modify their clinical practice, so as to reduce this potential morbidity. It therefore seems logical to start all patients undergoing major lower limb orthopaedic surgery on anticoagulation to prevent such mishaps.

However, anticoagulation has its own share of problems, including bleeding from surgical wound, wound infection, cutaneous bleeds, major organ bleeds and occasionally death.²⁵ The American Academy of Orthopaedic Surgeons (AAOS) sought to reduce the problems associated with anticoagulation by introducing a protocol that differed from the American College of Chest Physicians (ACCP).²⁵ They categorized patients based on the risk of bleeding and the risk of coagulation, and initiated prophylaxis using a combination of mechanical prophylaxis, aspirin and low molecular weight heparin. Several of these concepts were incorporated in the ACCP Clinical Practice Guidelines that was revised in 2012.²⁶ More studies are required to assess the efficacy of this programme.

In the AAOS guidelines, the categorization for anticoagulation is based on the risk factors for bleeding and clotting. As an addendum to this clinical screening, we looked at the use of lab parameters that have been used in the past to predict a hypercoagulable state. Thrombelastography (TEG), a global hemostasis assay like thrombin generation test, has been used to predict a hypercoagulable state in many clinical situations.¹¹

TEG is based on the study of the viscoelastic changes that occur in an in vitro sample of whole blood. It aids in step-by-step

Table 2

Incidence of DVT in various Indian studies involving orthopaedic surgeries.

Year	Author	Study design	Prophylaxis used	Total Number	Number of DVT cases	Test used
1999	Nagi ¹³	Prospective (THR, TKR, lower limb fracture surgery)	None	50	4 (8%)	Compression ultrasonography
2002	Sharma ¹⁴	Prospective (Hip fracture surgery)	None	112	22 (19.6%)	Colour Doppler
2003	Agarwala ²	Prospective (THR, TKR & hip fracture fixation)	Dalteparin	44	19 (43.2%)	Venography
			None	50	30 (60%)	Venography
2003	Rajagopalan ¹⁵	Prospective (THR, TKR & femur fracture fixation)	Dalteparin	102	8 (7.8%)	Colour Doppler
2004	Bhan ¹⁶	Prospective (THR, TKR, spinal fusion, lower limb fracture surgery)	Mechanical	100	0	Colour Doppler
			None	30	7 (23.3%)	Colour Doppler
2004	Jain ¹	Prospective (THR)	Enoxaparin	25	0	Colour Doppler
			None	25	0	Colour Doppler
2004	Jain ³	Prospective (THR, TKR)	None	106	2 (1.9%)	Colour Doppler
2005	Agarwala ¹⁷	Prospective (THR, TKR & hip fracture fixation)	Dalteparin	90	31 (34.4%)	Colour Doppler
2006	Maini ¹⁸	Retrospective (bipolar hemiarthroplasty)	None (1994–98)	271	25(9%)	Not mentioned
			LMWH (1999–2003)			
2006	Bagaria ⁴	Prospective (THR, TKR & hip fracture fixation)	None	147	9(6.2%)	Colour Doppler
2007	Mavalankar ¹⁹	Prospective (THR, TKR, lower limb fracture surgery)	None	125	9 (7.2%)	Colour Doppler
2011	Sen ²⁰	Prospective (Pelvi-acetabular fracture fixation)	None	56	12 (21.4%)	Colour Doppler
2011	Sen ²¹	Systematic review (Hip fracture surgery)	LMWH or Mechanical	115	10 (11.5%)	Colour Doppler or venography
			None	276	40 (14.5%)	Colour Doppler or venography
2012	Goyal ¹²	Prospective (Hip fracture surgery)	Peroperative calf muscle electrostimulation	100	2 (2%)	Colour Doppler
			None	100	6 (6%)	Colour Doppler
2013	Nair ²²	Prospective arm (THR, TKR)	Enoxaparin–4 weeks + mechanical	197	0	Colour Doppler + D-dimer
		Retrospective arm (THR, TKR)	Enoxaparin–7–11 days + mechanical	795	6 (0.8%)	Colour Doppler + D-dimer
2013	Chandak ²³	Prospective (THR, TKR)	None	135	5 (3.7%)	Colour Doppler
2016	Patidar ²⁴	Prospective (THR, Hip fracture surgery)	None	102	1 (0.98%)	Colour Doppler
	CMC	Prospective (THR, TKR, Hip fracture surgery)	None	101	7%	Colour Doppler

* Stands for current study.

Fig. 2. TEG curves generated in the test. (a) Example of a normal TEG curve. (b) Example of a hypercoagulable state.

assessment of clot formation and stabilization, and helps to assess clot strength. In the classical method, a whole blood sample is collected and incubated in a cuvette (cup) at 37 °C. The cuvette is rotated slowly in a small arc, to mimic sluggish blood flow. A stationary pin is suspended through a torsion wire in the centre of the container. Once the coagulation cascade gets initiated, a stable clot starts to form. The speed and the strength of clot formation in the cup is transmitted to a sensor through the torsion wire as the needle gets held by the clot formation and the same is documented electronically. All the different stages of clot formation and the final clot stability are reflected in the graphs obtained, which can be used for qualitative analysis of the patient's coagulation process. Rotational Thromboelastometry (ROTEM) is a variation of this process in which the sensor shaft rather than the cup rotates.^{27,28}

For this study, we used the used classical method of TEG testing.

Four parameters are of significance in the TEG curve (Fig. 1). R (reaction time) refers to the time taken for clot formation to begin, starting from the time the test is initialized. K value is a measure of the time period between the initiation of clot formation and the time when amplitude of 20 mm is attained. Alpha angle is the angle subtended on the graph by the tangent drawn to the curve starting from the initiation of coagulation, over the baseline. MA (maximum amplitude) is a direct measurement of the highest amplitude attained on the curve and is a reflection of clot strength. The reference ranges obtained on 330 healthy blood donors are: R (3–8 min), K (1–3 min), alpha angle (55–78°) and MA (51–69 mm). A short K and R time or a high alpha angle indicates a hypercoagulable state. (Fig. 2)

TEG identifies individuals who have a hypercoagulable state and has been shown to be useful in predicting which patients could potentially develop DVT despite standard anticoagulation.¹¹ In this study, we attempted to assess its usefulness in predicting the occurrence of DVT in patients, who did not receive chemoprophylaxis. We found that pre-operative TEG was not an efficient tool to help identify patients, who develop post-operative DVT. Among the 6 patients who developed post-operative DVT, only one had abnormal pre-operative TEG values. This study however cannot claim that TEG is not useful in predicting a hypercoagulable state. It is possible that surgery, especially following trauma, may change and influence the coagulation status of an individual. This could potentially lead to a situation that predisposes the individual to DVT. This change in the coagulation status following surgery has been looked at in a few studies.^{29,30} The changes in coagulability that occur following trauma, especially after surgery, need to be explored in more detail.

5. Conclusion

The 7% incidence of DVT in the study population is sufficiently high to suggest initiation of some mode of prophylaxis to prevent this complication following hip fracture surgery and lower limb arthroplasty. Whether routine chemoprophylaxis in all patients or selective chemoprophylaxis in high-risk patients is more beneficial – needs to be evaluated with more studies. As a screening tool, pre-operative thromboelastography does not seem to predict the occurrence of VTE sufficiently well. The use of other lab parameters

that could help in selective chemoprophylaxis needs to be explored.

Conflicts of interest

The authors have none to declare.

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