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ANALYSIS OF D-DIMER VALUES IN POST-OPERATIVE PATIENTS OF MAJOR HIP AND KNEE SURGERY

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Abstract

Background: Measurement of D-dimer has been established as an effective indirect indicator of thrombotic activity. Many studies have indicated role of D-dimer values in post-operative patients for early diagnosis of Deep Vein Thrombosis. In our study we obtained and evaluated D dimer values in Indian patients and compared it with existing literatures. **Methods:** Total 50 patients were selected who were planned for major hip and knee surgeries. D-dimer values were obtained one day prior to surgery, post-operative days 1, 3, 5, 7 and 14th day. B Mode ultrasound and color Doppler was done in all patients for the exclusion of DVT on post-operative day 7. **Results:** The D-dimer values were found to be sharply elevated and peaked at the post-operative day one, then gradually decreased to near baseline level by 7th day and continued to be in the same range till 14th day. Our study did not show a second peak in D-dimer values. No confirmed case of DVT was reported based on venous Doppler ultrasound. **Conclusion:** The first peak of D-dimer on post-operative day 1 could be attributed to the tissue injury due to surgical trauma. The second peak which comes around day 7 is more likely to corroborate with impending DVT. We concluded in our study that Indian patients undergoing major hip and knee surgeries tend to have a low risk of DVT, as compared to western studies.

Keywords: Deep Venous Thrombosis; D-Dimer; Arthroplasty; Major Hip and Knee Surgery.

Abbreviations

- DVT Deep Vein Thrombosis
- VTE Venous Thrombo Embolism
- PE Pulmonary Embolism
- TKA Total Knee Arthroplasty
- THA Total Hip Arthroplasty
- PFN Proximal Femoral Nailing
- LMWH Low Molecular Weight Heparin

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INTRODUCTION

Various studies have confirmed that patients undergoing major orthopaedic procedures involving hip, knee arthroplasty and major hip fracture fixation surgery constitute the highest risk group for the development of post-operative venous thromboembolism, manifested as deep vein thrombosis or pulmonary embolism.[1] Although the occurrence of symptomatic DVT and PE is low, asymptomatic DVT which is confirmed with imaging varies from 42% to 57% post-THA and from 41% to 85% post-TKA.[2]Asymptomatic DVT rarely progresses to symptomatic PE and most of asymptomatic cases are usually detected by venography.[3] However, estimates indicate that 40-50% of untreated symptomatic DVT patients will develop PE within 3 months and 10% of symptomatic PE cases will die within 1 hour of onset.[3] Therefore, rapid and accurate diagnosis of DVT in the acute postoperative period is essential to prevent devastating complications.

Venographic study is considered to be the gold standard in the diagnosis of DVT of the lower extremity. However, it is an invasive procedure that can incur certain risks and is expensive. Ultrasonography is a reasonable alternative, but the sensitivity of ultrasound in detecting DVT is inferior to venography.[4]

Measurement of D-dimer, a fibrin clot breakdown product has previously been established as an effective indirect indicator of thrombotic activity.[5]It is simple, fast, convenient and inexpensive having the economic potential of reducing the use of more complex and expensive tests such as venography and ultrasonography. However, the interpretation of the D-dimer test in cases with DVT after major orthopaedic surgeries is still controversial.[4,5] A combined assessment of the clinical probability of DVT and the measurement of the plasma D-dimer concentration are currently recommended as initial diagnostic approach for patients presenting with suspected lower extremity DVT followed by venous doppler ultrasonography.[6]Some studies have shown that baseline value of D-dimer below 500 ng/ml, makes it possible to exclude DVT.[1] However, whether an elevated level which could have a strong co-relation with DVT, is not established by the existing literature. So we sought to evaluate the following:

A. Whether there is any racial difference in the trends of D-dimer values in the Indian patients as per the existing literature in western population.

B. Whether there is any significance of D-dimer values to diagnose or rule out DVT.

MATERIALS AND METHODS

This study was an observational cross sectional study conducted at our institution between September 2018 and March 2020. This study was approved by the Institutional Ethics Committee (IEC) with certificate number F. No.17/IEC/MAMC/2018/07. Informed written consent for the publication of clinical details, according to the declaration of Helsinki was taken from the patients. Total 50 patients of either gender were considered for this study who underwent major hip and knee surgeries like THA, TKA, Bipolar Hemi-arthroplasty, and PFN. Patients with current diagnosis or a documented history of VTE on anticoagulation therapy,

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known history of bleeding diathesis, with prolonged prothrombin time, thrombocytopenia and any other pre-operative co-morbidities with high risk of VTE and all patients who were not willing to participate in the study were kept under exclusion criteria. The patient demographics for the study cohort are displayed in Table 1.

Table 1: Demographics of patients

	Total (n=50)	TKA (n=17)	THA (n=19)	Bipolar-Hemi (n=12)	PFN (n=2)
Age (years)	55.94 ± 17.56	63.41	38.21	72.33	62.5
Sex	22M/28F	2M/15F	14M/5F	7M/5F	1M/1F
BMI	28.34	30.29	27.21	27	30.5
WELL'S SCORE	0.5	0.29	0.10	1.25	1.5
Pre-op D-dimer (ng/mL)	564.34 ± 494.79	292.06 ± 65.22	290.26 ± 113.56	1278 ± 435.54	1199

All patients were assessed using WELL'S scoring system, designed to predict clinical probability of DVT for each patient prior to scheduled surgery. The peri-operative period was defined in this study as the period from the 1st day preceding the surgery until 1 week post-operatively. The D-dimer values were obtained on the day prior to surgery and post-operative days 1, 3, 5, 7 and also day 14 if values were continuing to rise. We used automated latex enhanced immunoassay for the quantitative determination of D-dimer. All patients had undergone B Mode ultrasound and colour venous Doppler in bilateral lower limb for the exclusion of DVT on post-operative day 7.

We did not use any prophylaxis in pre-operative period. In post-operative period we followed our institution's protocol to start early ambulation at post-operative day 1, used compression stockings and also started tablet Aspirin 75 mg once a day from post-operative day 1. Data was analysed and statistically evaluated using SPSS-PC-25 software version.

Quantitative data was expressed in mean ± standard deviation and difference between two comparable groups were tested by student's t-test (unpaired) or Mann Whitney "U" test. Spearman correlation coefficient was used to see the correlation between quantitative variables. 'P' value less than 0.05 was considered statistically significant.

RESULTS

The range of D-dimer in study subjects was from 112 ng/ml to 5000 ng/ml. The D-dimer values were sharply elevated (mean±SD 2481.88±1391) and peaked at the post-operative day 1 (peak value 5000 ng/ml) which is statistically significant (P value <0.001) (Figure 1). The D-dimer level decreased on the post-operative day 3 (mean±SD 1724.84±1011) as compared to post-operative day 1 which was also statistically significant (P value <0.01). However, this value on post-operative day 3 was also around 3 times higher than the baseline value, which was also significant (P value <0.001). The baseline D-dimer level exceeded the reference value of 500 ng/ml in 15 out of 50 study subjects. Out of these 15 cases, 14 were acute cases of fracture around the hip, so such excess may be attributed to the traumatic event.

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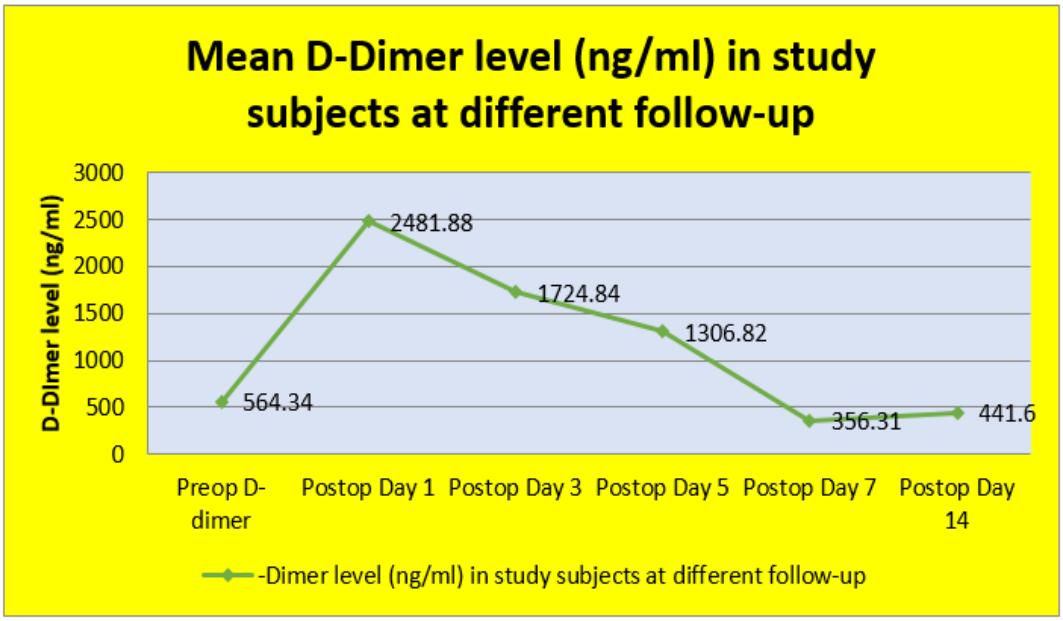
Figure 1: Mean D-dimer level at different follow-up



For evaluation, D-dimer values at the scheduled time were compared between patients who underwent TKA, THA, Bipolar hemi-arthroplasty and PFN (Table 2). The mean D-dimer value in TKA group on post-operative days 1, 3 and 5 were higher than THA group which was statistically significant (day 1 P value 0.01, day 3 P value < 0.01, day 5 P value 0.03) (Figure 2).

Table 2: D-dimer level in different study groups

D-dimer(ng/ml)	Total (n=50)	TKA (n=17)	THA (n=19)	Bipolar Hemi(n=12)	PFN (n=2)
Pre-op	564.34±494	292.06±65	290.26±113	1278.25±435	1199
Post-op day 1	2481.88±1391	3206.35±1533	1874.58±1135	2359.33±1248	2828.50±730
Post-op day 3	1724.24±1011	2244.06±1232	1319.74±758	1637.58±811	1683.50±634
Post-op day 5	1306.82±946	1723.59±981	1137.0±938	990.08±804	1278.0±875
Post-op day 7	356.31±200	284.25±231	351.95±160	473.67±191	270±72
Post-op day 14	441.60±213	509.73±228	369.07±149	465.0±263	333±140

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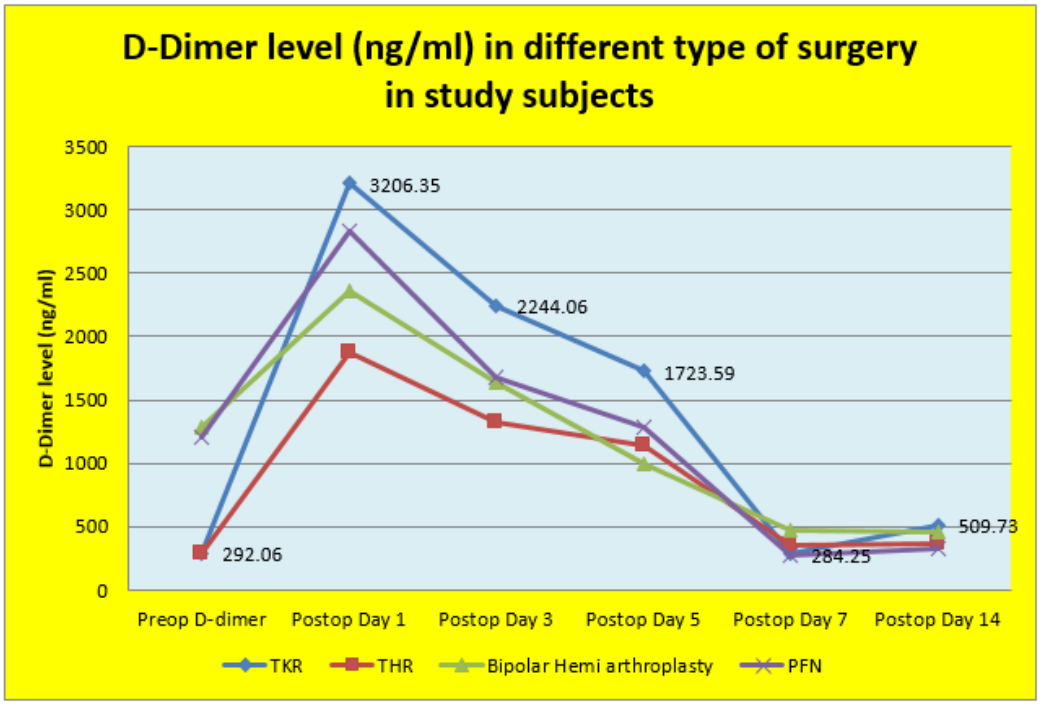
Figure 2: D-dimer level in different study groups



The mean D-dimer value in Bipolar hemi-arthroplasty group on days 1 and 3 were higher than THA group but it was not significant (day 1 P value 0.33, day 3 P value 0.25) (Table 3). Also, on post-operative days 1 and 3 the values of D-dimer were higher for cemented surgeries which were statistically significant (day 1 P value 0.03, day 3 P value 0.02) (Figure 3).

Table 3: "P" value in different groups:

D-dimer	P value in total patients with pre-op value	P value between TKA and THA groups	P value between THA and Bipolar Hemi groups	P value between cemented and un-cemented surgeries
Day 1	**<0.001**	**0.01**	**0.33**	**0.03**
Day 3	**<0.001**	**<0.01**	**0.25**	**0.02**
Day 5	**<0.001**	**0.03**	**0.68**	**0.24**
Day 7	**0.01**	**0.06**	**0.06**	**0.82**
Day 14	**0.57**	**0.08**	**0.44**	**0.12**

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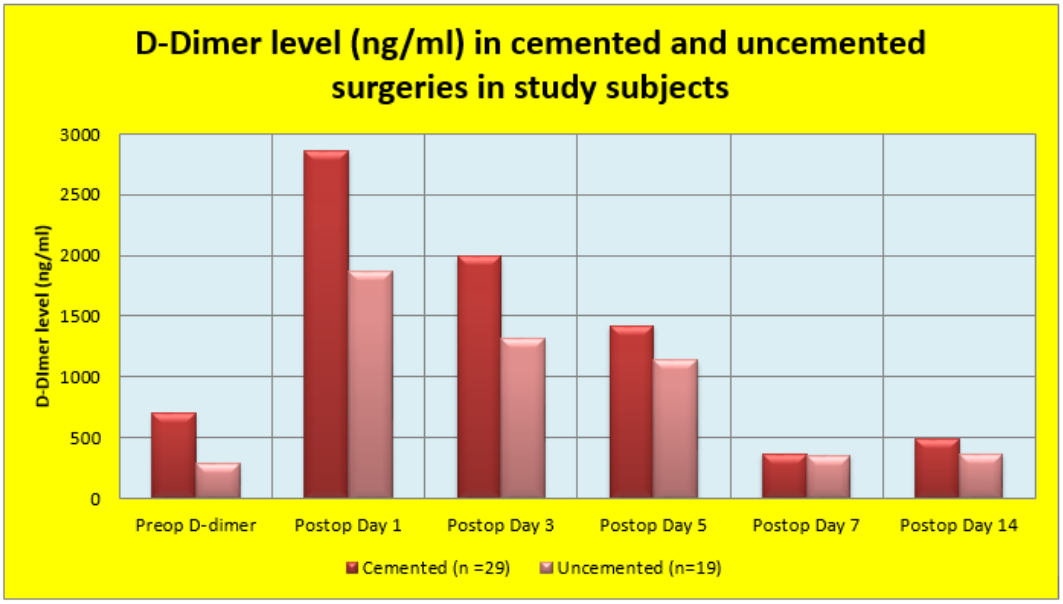
Figure 3: Mean D-dimer level in cemented and uncemented surgeries



Superficial wound infection was seen in one patient of TKA three weeks after surgery, which responded well to oral and topical antibiotics only. No case of confirmed DVT was diagnosed based on B Mode ultrasound color venous Doppler.

DISCUSSION

Post-operative DVT is a well-recognised complication following major hip and knee surgeries and can be difficult to diagnose clinically due to the presence of lower limb swelling and pain as a result of the surgery. Prompt diagnosis and treatment is essential to avoid clot propagation and pulmonary embolism.

There is paucity of data establishing the correlation of d-dimer values with risk of DVT in Indian literatures. In our study we tried to analyse the trend of D-dimer values with associated risk of DVT in Indian population. We felt that knowledge of this new "Trend" would aid in determining whether the test has a role in diagnosis or to rule out DVT.

The principal finding of our study was that D-dimer values were sharply elevated and peaked at the post-operative day 1 then it gradually decreased to the near baseline level by day 7 and continued to be in the same range till day 14. The study by Young Seuk Lee et al.[8] concluded that D-dimer level peaked at post-operative day 1 and then decreased to near baseline at day 2. After that, it slowly elevated again and reached its second peak at post-operative week 2. However, they did not explain this sudden decrease on day 2.

Yuying Cheng et al.[9] demonstrated that D-dimer values sharply increased on post-operative day 1, decreased on day 3 and again increased on day 6 in both VTE and non-VTE group. Our study in contrast, showed only one peak at day 1 and second peak was not observed.

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McLauchlan et al. [10] showed the highest levels were on days 1 and 7.Shiota et al.[5] found double peaked distribution with peaks at day 1 and day 7 post-operatively. Wu et al.[11] found a high peak value of D-dimer concentration at 4 hour after surgery and decreased gradually on post-op day 1 and day 4 in both DVT(+) and DVT(-) groups. They also demonstrated that the D-dimer values were higher in DVT(+) group than DVT(-) group at post-operative day 4. In our study, D-dimer values were raised from post-operative day 1 in almost all cases which could be attributed to the tissue injury due to surgical trauma. As the second peak was not observed in our cases compared to many other studies, it indirectly means very low chance of having DVT in our subjects. Second peak which comes around day 7 is more likely to corroborate with impending DVT.

The second finding of our study was that, although the pattern of rise in post-operative levels were same in all the study groups, the mean D-dimer values in TKA group on post-op days 1, 3 and 5 were higher than THA group which were statistically significant. The results of our study supported by McLauchlan et al.[10] which concluded that, the TKA group showed significantly higher mean D-dimer levels on days 3, 5 and 7 as compared to THA group. Shiota et al.[5] found the D-dimer response was more robust for TKA than THA but only on day 1 post-operatively. Schoenecker et al.[12] also found that the measured D-dimer was higher for TKA group compared to THA group for all time points in the study. Bytniewski et al.[1] found similar results and showed higher level of D-dimer in TKA group than cemented and cementless THA in all study points. Wu et al.[11] concluded that patients undergoing TKA sustained a higher incidence of post-operative DVT as compared with THA owing to the use of tourniquet. A meta-analysis study also demonstrated that TKA patients managed with a tourniquet had higher risk of thromboembolic complications. Inadequate exsanguinations of the blood in the limb, stasis and ischemia contribute to the thrombosis formation. Circulatory indices of thrombosis such as D-dimer values significantly increases immediately following deflation of the tourniquet after TKA. It may decreases by 1 to 3 days post-operatively.[11]

Another important finding of our study was that the pre-operative D-dimer level in acute trauma group was higher than non-acute trauma or atraumatic group. Our study was supported by many pre-existing studies including Li-Dan Zhang et al.[13] reported that the level of D-dimer was significantly higher in the acute trauma group than in the non-acute trauma group. Huang et al.[14] reported that D-dimer became higher in the hip fracture group in elderly patients, before and after surgery. Chen Liu et al.[20] concluded that D-dimer levels at different site of fracture are different with higher in femoral fracture. Elevation of serum D-dimer in the acute post-operative period is due to both intravascular and extra-vascular coagulation and fibrinolysis. After surgical trauma, both intravascular and extra-vascular fibrin deposition have an important role in haemostasis and compartmentalization of injury. Subsequent fibrinolysis in both the domain, leads to fibrin breakdown and D-dimer formation. The quantitative D-dimer test is unable to differentiate between physiological extra-vascular and pathologic intravascular fibrin degradation, which suggest that both contribute to the acute D-dimer elevation post-operatively.[12] In our study we performed venous colour Doppler in all 50 study subjects but we did not diagnose any case of confirmed DVT. Zhang et al.[15] concluded that USG could be a useful tool for diagnosis of DVT, but it has a lower positive rate and a higher

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false negative rate. The rate of missed diagnosis of lower limb DVT by USG amounts to 50% or so in the patients without symptoms of DVT. The negative results do not preclude the possibility of DVT. Bytniewski et al.[1] concluded that higher level of D-dimer in post-operative period in the research group of patients does not relate to higher risk of thromboembolic disease. Wu et al.[11] demonstrated that DVT was identified by bilateral ascending venography in 29 of 200 TKA patients but no fatal PE or VTE related complications occurred. They concluded that because all the DVTs occurred in the leg veins, decreased thrombus volume and size might result in poor accuracy of D-dimer test in prediction or diagnosis of post-operative DVT.

Asian patients have been reported to have a lower prevalence of DVT and PE after major hip and knee surgeries compared with western patients. In the report by Klatsky et al.[19] showed that Chinese, Japanese, Filipinos, and other Asian each had lower VTE risk than both Whites and South Asians, mostly Asian Indians, had risk similar to each other. A study by Jain et al.[16] concluded that incidence of DVT in Indian patients is very low and is not comparable with American and European populations. In our study we used the combined approach to effectively prevent the DVT which comprised of early ambulation on post-operative day 1, use of compression stockings and Tablet Aspirin 75 mg once a day from post-operative day 1. In 2019, a study by Timothy L. Tan et al.[17] concluded that aspirin administered to high risk patients seems to be as effective as potent anticoagulant LMWH and more effective than warfarin. In 2019, an another study by Alexander J. et al.[18] demonstrated an association between the use of aspirin as prophylaxis against VTE and a reduced risk of mortality following Total Joint Arthroplasty. We had some limitations while doing the study. D-dimer at our institution was measured using automated latex enhanced immunoassay instead in western countries they were measured using Enzyme Linked Immunoassay (ELISA). In this study, we only monitor D-dimer and Doppler examination during patient hospitalization although VTE may occur within the first 3 months after major hip and knee surgery. We could enrol only 50 subjects because of limited time availability. Thus, the next step of our research is to recruit more patients and follow up these patients for a longer duration in order to establish a complete prospective model of VTE in patients undergoing major hip and knee surgeries.

CONCLUSION

In our study, we did not diagnose any case of confirmed DVT based on venous Doppler ultrasound and none of the patient developed any symptomatic DVT or PE. So the question of correlation with D-dimer does not arise in our study. In our study, D-dimer values were raised from post-operative day 1 in almost all cases which could be attributed to the tissue injury due to surgical trauma. As the second peak was not observed in our cases compared to many other studies, it indirectly means very low chance of having DVT in our cases. Second peak which comes around day 7 is more likely to corroborate with impending DVT. We concluded in our study that Indian patients undergoing major hip and knee surgeries tend to have a low risk of DVT, as compared to western studies.

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Declarations

Funding: This study was not supported by any funding.

Conflict of Interest/Competing interest: on behalf of all authors, the corresponding author states that there is no conflict of interest/competing interest.

Availability of data and materials: All the data will be available upon motivated request to the corresponding author of the present paper.

Ethical standard statement: The study was approved by the institutional ethics committee (IEC) board of Maulana Azad Medical College and associated Lok Nayak Hospital with certificate number F. No.17/IEC/MAMC/2018/07.

Informed Consent in Studies with human subjects: All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation and with the Helsinki Declaration of 1975, as revised in 2008. Informed consent was obtained from all patients for being included in the study.

Animal Studies: This article does not contain any studies with animal subjects.

Consent for Publication: Written informed consent was obtained from each patient to authorize the publication of their data.

Author's Contribution: VK Gautam conceived the idea for the study. Kamal Kishor collected the related data and performed the statistical analyses. Dibyendu Biswas drafting the article and BC Koner revised it for critically important intellectual content. VK Gautam gave final approval of the version to be published.

References

1) Bytniewski P, Machała W, Romanowski L, Wiśniewski W, Kosowski K. (2014) The dynamics of D-dimer level fluctuation in patients after the cemented and cementless total hip and total knee replacement. J Orthop Surg Res. 9:89. doi: 10.1186/s13018-014-0089-0. PMID: 25304935; PMCID: PMC4198732.

2) Lee S, Hwang JI, Kim Y, Yoon PW, Ahn J, Yoo JJ. (2016) Venous Thromboembolism Following Hip and Knee Replacement Arthroplasty in Korea: A Nationwide Study Based on Claims Registry. J Korean Med Sci. 31(1):80-8. doi: 10.3346/jkms.2016.31.1.80. Epub 2015 Dec 24. PMID: 26770042; PMCID: PMC4712584.

3) Kearon C. (2003) Natural history of venous thromboembolism. Circulation. 107(23 Suppl 1):I22-30. doi: 10.1161/01.CIR.0000078464.82671.78. PMID: 12814982.

4) Chen CJ, Wang CJ, Huang CC. (2008) The value of D-dimer in the detection of early deep-vein thrombosis after total knee arthroplasty in Asian patients: a cohort study. Thromb J. 6:5. doi: 10.1186/1477-9560-6-5. PMID: 18505594; PMCID: PMC2426673.

5) Shiota N, Sato T, Nishida K, Matsuo M, Takahara Y, Mitani S, Murakami T, Inoue H. (2002) Changes in LPIA D-dimer levels after total hip or knee arthroplasty relevant to deep-vein thrombosis diagnosed by bilateral ascending venography. J Orthop Sci. 7(4):444-50. doi: 10.1007/s007760200077. PMID: 12181657.

6) Bates SM, Jaeschke R, Stevens SM, Goodacre S, Wells PS, Stevenson MD, Kearon C, Schunemann HJ, Crowther M, Pauker SG, Makdissi R, Guyatt GH. (2012) Diagnosis of DVT: Antithrombotic Therapy and Prevention of Thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. Chest. 141(2 Suppl):e351S-e418S. doi: 10.1378/chest.11-2299. PMID: 22315267; PMCID: PMC3278048.

7) Falck-Ytter Y, Francis CW, Johanson NA, Curley C, Dahl OE, Schulman S, Ortel TL, Pauker SG, Colwell CW Jr. (2012) Prevention of VTE in orthopedic surgery patients: Antithrombotic Therapy and Prevention of Thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines.

The Seybold Report
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DOI: 10.5281/zenodo.10153033

Chest. 141(2 Suppl):e278S-e325S. doi: 10.1378/chest.11-2404. PMID: 22315265; PMCID: PMC3278063.

8) Lee YS, Lee YK, Han SB, Nam CH, Parvizi J, Koo KH. (2018) Natural progress of D-dimer following total joint arthroplasty: a baseline for the diagnosis of the early postoperative infection. J Orthop Surg Res. 13(1):36. doi: 10.1186/s13018-018-0730-4. PMID: 29439725; PMCID: PMC5811971.

9) Cheng Y, Liu J, Su Y, Zhao H, Zhao Y, Wen M, Lu S, Zhang W, Wu J. (2019) Clinical Impact of Coagulation and Fibrinolysis Markers for Predicting Postoperative Venous Thromboembolism in Total Joint Arthroplasty Patients. Clin Appl Thromb Hemost. 25:1076029619877458. doi: 10.1177/1076029619877458. PMID: 31608652; PMCID: PMC6900621.

10) Rafee A, Herlikar D, Gilbert R, Stockwell RC, McLauchlan GJ. (2008) D-Dimer in the diagnosis of deep vein thrombosis following total hip and knee replacement: a prospective study. Ann R Coll Surg Engl. 90(2):123-6. doi: 10.1308/003588408X261627. PMID: 18325211; PMCID: PMC2443306.

11) Wu CT, Chen B, Wang JW, Yen SH, Huang CC. (2018) Plasma D-dimer is not useful in the prediction of deep vein thrombosis after total knee arthroplasty in patients using rivaroxaban for thromboprophylaxis. J Orthop Surg Res. 13(1):173. doi: 10.1186/s13018-018-0883-1. PMID: 29996862; PMCID: PMC6042345.

12) An TJ, Engstrom SM, Oelsner WK, Benvenuti MA, Polkowski GG, Schoenecker JG. (2016) Elevated d-Dimer Is Not Predictive of Symptomatic Deep Venous Thrombosis After Total Joint Arthroplasty. J Arthroplasty. 31(10):2269-72. doi: 10.1016/j.arth.2016.02.059. Epub 2016 Mar 10. PMID: 27062350.

13) Zhang LD, Liu HB, Li YN, Ma HM, Liu YB, Wang MY. (2012) Correlation analysis between plasma D-dimer levels and orthopedic trauma severity. Chin Med J (Engl). 125(17):3133-6. PMID: 22932194.

14) Huang W, Xu LY, Shao SY, Yao L, Wang TB. (2013) Impact of hip fracture on coagulation function in elderly patients. Beijing Da Xue Xue Bao Yi Xue Ban. 45(5):742-4. Chinese. PMID: 24136270.

15) Zhang Y, Xia H, Wang Y, Chen L, Li S, Hussein IA, Wu Y, Shang Y, Yao S, Du R. (2019) The rate of missed diagnosis of lower-limb DVT by ultrasound amounts to 50% or so in patients without symptoms of DVT: A meta-analysis. Medicine (Baltimore). 98(37):e17103. doi: 10.1097/MD.0000000000017103. Erratum in: Medicine (Baltimore). 98(49):e18469. PMID: 31517841; PMCID: PMC6750306.

16) Jain V, Dhaon BK, Jaiswal A, Nigam V, Singla J. (2004) Deep vein thrombosis after total hip and knee arthroplasty in Indian patients. Postgrad Med J. 80(950):729-31. doi: 10.1136/pgmj.2003.018127. PMID: 15579615; PMCID: PMC1743161.

17) Tan TL, Foltz C, Huang R, Chen AF, Higuera C, Siqueira M, Hansen EN, Sing DC, Parvizi J. (2019) Potent Anticoagulation Does Not Reduce Venous Thromboembolism in High-Risk Patients. J Bone Joint Surg Am. 101(7):589-599. doi: 10.2106/JBJS.18.00335. PMID: 30946192.

18) Rondon AJ, Shohat N, Tan TL, Goswami K, Huang RC, Parvizi J. (2019) The Use of Aspirin for Prophylaxis Against Venous Thromboembolism Decreases Mortality Following Primary Total Joint Arthroplasty. J Bone Joint Surg Am. 101(6):504-513. doi: 10.2106/JBJS.18.00143. Erratum in: J Bone Joint Surg Am. 102(9):e42. PMID: 30893231.

19) Nicole Tran H, Klatsky AL. (2019) Lower risk of venous thromboembolism in multiple Asian ethnic groups. Prev Med Rep. 13:268-269. doi: 10.1016/j.pmedr.2019.01.006. PMID: 30723661; PMCID: PMC6351426.

20) Liu C, Song Y, Zhao J, Xu Q, Liu N, Zhao L, Lu S, Wang H. (2016) Elevated D-dimer and fibrinogen levels in serum of preoperative bone fracture patients. Springerplus. 5:161. doi: 10.1186/s40064-016-1817-1. PMID: 27026858; PMCID: PMC4766159.