



Distribution of Predisposing Factors for Venous Thromboembolism in a Teaching Hospital

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Abstract

Background: Venous thromboembolism (VTE) includes both Deep Venous thrombosis (DVT) and Pulmonary Embolism (PE). This study aimed to utilize the causes of VTE and show the demographic data of the patients and effectiveness of treatment of anticoagulant in a teaching hospital in Saudi Arabia.

Methods: A retrospective cross sectional study was conducted among KAUH hematology department. This study was approved by the Unit of biomedical ethics of medicine at King Abdulaziz University Hospital (KAUH). Target sample included children, adolescent, young adults, adults and geriatrics. Both genders, who diagnosed with VTE. To assess the distribution of predisposing factors.

Result: A total of 84 patients diagnosed with VTE, the mean age was 52.73 ± 20.29 years.

Female patient constituted of total patients 58.3% (49 cases) were male 41.7% (34 cases) majority of cases were cancer related. Other predisposing factors were hematological malignancies followed by cardiovascular diseases, postoperative patients and immobilization. Half of the sample showed improvement 42 (50%), the most frequently used therapeutic anticoagulation drugs in VTE patients were Warfarin, Enoxaparin and UFH, while the frequency rates were 73, 55 and 41, respectively.

Conclusions: In summary, female and geriatrics are at significant risk for VTE more than the others. Majority of the study participants were diagnosed with cancer. The main types were colon cancer, breast, liver and lung cancer. The mortality rate was higher for patients with cancer associated DVT, on the other hand, about half of the patients showed an improvement and full recovery.

Keywords: Venous thromboembolism, Deep Venous thrombosis, Pulmonary Embolism, Anticoagulants, malignancies

Background

Venous thromboembolism (VTE) includes both Deep Venous thrombosis (DVT) and Pulmonary Embolism (PE). DVT means presence of blood clots in veins commonly in deep veins and less extent in superficial veins at any site of body. Most likely to occur in deep veins of lower extremity than in upper extremity. PE is medical condition described the travel of blood clots from its formation site and go through blood circulation to place in pulmonary artery or one of its branches and causing a blockage. Its cause variable complication according to its anatomical site and symptoms ^[1]. VTE could be fatal in some patients or cause poor quality of life ^[2].

There are several factors leading to thrombosis, it classified into personal factor (e.g. age, gender, race, obesity, pregnancy, immobilization, genetics factors and low physical activity) environmental factors (e.g. long distance travel, air pollution and trauma), related to certain disease (e.g. cancer, heart disease, respiratory failure, thrombophilia, acute infection and fracture), related to treatment (hospitalization, recent surgery, patients admitted to intensive care unit, catheterization, hormonal therapy use, oral contraceptive use and corticosteroid use). The incidence of DVT is increase in Cancer patient and in orthopedic patient too particularly in lower limb as in hip or knee surgeries ^[1,3-6]. Additionally, The rate of VTE recurrence is increased approximately 30% within first 10 years after the diagnosis of VTE ^[7].

Anticoagulants drugs are classified into two main groups parenteral and oral drugs which are they Parenteral anticoagulant drugs include: low-molecular-weight heparins (LMWHs) and Unfractionated heparin (UFH), oral anticoagulant drugs include: warfarin [8]. While the standard therapy for VTE is LMWH [9-11]. Therefore, according to National Comprehensive Cancer Network (NCCN) guidelines anticoagulation should be used as prophylaxis for all hospitalized and surgical cancer patients [12].

Recent studies in 2018, confirmed that the LMWH and Warfarin have similar incidences rate for VTE recurrence, while patients who received Rivaroxaban drug have lower risk of recurrence by 26% - 28% when compared with warfarin and LMWH in the order already mentioned [13].

In young adult life until approximately middle age, VTE occurs at a low rate of 0.5 to 1 event per 1,000 person-years. This rate is higher in midlife and by age 80, VTE incidence is substantially higher, occurring at a rate of approximately 5 to 7 VTE events per 1,000 person-years [11].

We have designed a retrospective study, aimed to explain the predisposing factors of VTE and show the demographic data of the patient and effective of treatment with anticoagulant in king Abdulaziz university hospital of daily practice.

Method

A Cross sectional, medical record review study in was conducting among 84 VTE diagnosed Patients between 2010 to 2019 at KAUH hematology department, This study was approved by the Unit of biomedical ethics of medicine at king Abdulaziz university hospital (KAUH). The target sample included children, adolescent, young adults, adults and geriatrics. Both genders, who diagnosed with VTE.

Pregnant women and patients with anticoagulant contraindications were excluded from the study. We used Microsoft office 365, excel 2016 to collected data from medical records with no personal interaction with the patients. The data collection sheet contain age, gender, causes of VTE, number of VTEs, type of anticoagulant and the outcomes. Statistical analysis was performed using statistical package for the social sciences (SPSS) version 25. P-value were considered significant.

Result

In this study, we aimed to explain the predisposing factors of VTE and show the demographic date of the patient and effectiveness of treatment of anticoagulant in king Abdulaziz University. A total of 84 patients diagnosed with VTE between 2010 and 2019 included in this retrospective study. The mean age was 52.73 ± 20.29 years, and patients were classified into five age groups children, adolescent, young adults, adults and geriatrics. 4.8%, 1.2%, 29.8% 31% and 33.3%, respectively. Most of the patients were females 49 (58.3%) and 35 (41.7%) of them were male. 57 of the VTE patients had medical comorbidities and the other 27 hadn't have any medical comorbidity, while 34 patients had hypertensions. (Table 1)

Table 1: Demographic information of patients

Characteristic	Total 84
Age	
Mean ± SD	52.726±20.29
Range	95
Child	4(4.8%)
adolescent	1(1.2%)

Young adults	25 (29.8%)
Adult	26(31%)
Geriatrics	28(33.3%)
Male	35(41.7%)
Female	49(58.3%)
Comorbidity	
Hypertension	57 (67.9%)
Diabetes mellites	34
Another comorbidity	26
Pt outcome	
Recurrence	17(20.2%)
Improve	42(50%)
Died	22(26.2%)
Treatment duration	
Less than 6 months	39(46.4%)
Within 6 months	7(8.3%)
More than 6 months	33(39.3%)

Majority of cases were cancer related such as colon cancer, breast, liver and lung cancer. (Table 2). The most common outcome of cancer patients with VTE was death (12 out of 20 patients). Other causes were hematological malignancies (15.5%) followed by cardiovascular diseases (10.7%), postoperative patients and immobilization (8.3%). (Table 3). 33 patients developed PE. Half of the patients showed an improvement and full recovery 42 (50%), 22(26.2%) died and only 17% had recurrence of VTE (table 2).we noted the improve rate in patient used enoxaparin (46.4%) higher than who used warfarin and UFH 35.7% 21.4%, respectively. Our results showed significant between the causes and outcome p value = 0.003

Table 2: The frequency of cancer types among patients

Characteristic	Frequency
Cancer	22 (26.2%)
Colon cancer	6 (23.07%)
Breast cancer	3 (11.5%)
Lung cancer	3 (11.5%)
Liver cancer	3 (11.5%)
Ovarian cancer	3 (11.5%)
Prostate cancer	2 (7.6%)
Gyn cancer	2 (7.6%)
Skin cancer	1 (3.8%)
Brain cancer	1 (3.8%)
Blood cancer	1 (3.8%)
Duodenum	1 (3.8%)
Total	26

Table 3: The causes of VTE

Characteristic	Frequency	Percent%
Cancer	22	26.1
Hematology	13	15.5
Idiopathic	12	14.3
CVS	9	10.7
Surgery	7	8.3
Immobilization	7	8.3
Ob and Gyn	3	3.6
Orthopedic	2	2.4
Trauma	2	2.4
Obesity	1	1.2
Renal disease	1	1.2
Respiratory disease	1	1.2
Other	4	4.8

In our study we found that the most frequently used anticoagulation drugs used in VTE patients were warfarin, enoxaparin and UFH, while the frequency rate was 73, 55 and 41, respectively. We also found that statistically significant association between Low Molecular weight heparin (LMWH) and outcomes of patients p value = 0.001. There was 39 (46.4%) patients was treated in duration less than 6 months, 33 (39.3%) was treated in duration more than 6 months and 7 treated within 6 months.

Discussion

A retrospective study was conducted among 84 patients who had diagnosed with VTE. We aimed to assess the predisposing factors of VTE, our sample is higher than the observational study conducted in government medical college, Kozhikode. With 56 patients [13].

Based on the results from previous studies, the gender has relation with VTE, we found that the increase incidence rate in female more than male [14-16].

Other finding in this study, the incidence of VTE increased markedly with increase age, the majority of our VTE patients were geriatrics with 33.3% then adults with 31%. This finding consists with results of previous study that confirmed the age has a marked relation with VTE [2,14].

We analyzed the factors associated with increased VTE risk and we found that the cancer is the most common predisposing factor with (26%). In addition, we found the high-risk types of cancer are colon cancer (23%) while Breast, Ovarian, Lung and liver are less common (11%). Then prostate and gynecological malignancies are 7.6%. This result is similar to studies which showed the cancer has high-risk to develop VTE [17,18]. The other causes for VTE in our patients were hematological causes, idiopathic, CVS and Immobilization, Surgery, OB and Gynecological malignancies. Which was similar to causes to reports in previous studies [1,3-6].

The majority of our patients were treated for less than 6 months 39 (46.4%). Also, 33 (39.3%) patients were treated for more than 6 month. 59.1% of patients with cancer related VTE were treated more than 6 months. The current guidelines represented that the duration of anticoagulant treatment in patients with cancer related VTE should be treated for 6 months or more [19]. In our study, patients used enoxaparin showed with high improved rate 46.4% compare with warfarin and UFH 35.7% 21.4%, respectively. Recent studies in 2018, confirmed that the LMWH and Warfarin have similar incidences rate for VTE recurrence, but when compared LMWH and Warfarin with patients who received Rivaroxaban drug showed the Rivaroxaban user have lower risk of recurrence by 26% - 28% than patient warfarin and LMWH users [13].

Regarding to our results there are 20.2% of our patient had VTE recurrent and the adult group showed the highest recurrence rate. In addition, the cancer patients showed 15% who treated with warfarin and had VTE recurrent. While, in previous study there were up to 20% of cancer patient who treated with Warfarin had developed frequency VTE. In addition, the mortality rate was 28.6% of our patients and we noted that up to half of our cancer patients are dead with 12 out of 20 patients. This finding was consistent with a retrospective analysis, Khorana et al they found higher mortality among cancer patients with VTE as compared to only cancer patients [20].

Ethics approval and consent to participate

This study was approved by the Unit of biomedical ethics of medicine at king Abdulaziz university hospital (KAUH).

No informed consent was obtain, it is a record review study

Data Availability

The data was collected from the electronic records of King Abdulaziz University Hospital (<https://hospital.kau.edu.sa/Default-599-EN>)

Conflicts of Interest

The authors declare that there is no conflict of interest regarding the publication of this paper.

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Authors' contributions

All authors contributing in writing, analysing, and interpreting the data of the research

All of them read and approved the final manuscript.

Limitations

These results are subject to certain limitations. Such as, the researchers were not able to reach an adequate sample size, also, the study was only implemented in one hospital

References

- [1] Book: Badireddy M, Mudipalli VR. Deep Venous Thrombosis (DVT) Prophylaxis. [Updated 2018 Dec 3]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2018 Jan-. Available from: (<https://www.ncbi.nlm.nih.gov/books/NBK534865/>)
- [2] Epidemiology of cancer-associated venous thrombosis. Timp JF, Braekkan SK, Versteeg HH, Cannegieter SC Blood. 2013 Sep 5; 122(10):1712-23.
- [3] Crous-Bou, M., Harrington, L. B., & Kabrhel, C. (2016). Environmental and Genetic Risk Factors Associated with Venous Thromboembolism. Seminars in thrombosis and hemostasis, 42(8), 808-820.
- [4] Zakai NA, Wright J, Cushman MJ Thromb Haemost. 2004 Dec; 2(12):2156-61.
- [5] Zakai NA, Callas PW, Repp AB, Cushman MJ Thromb Haemost. 2013 Apr; 11(4):634-41.
- [6] Barsoum MK, et al. Is progestin an independent risk factor for incident venous thromboembolism? A population-based case-control study. Thromb. Res. 2010;126:373-378.
- [7] Heit JA, Spencer FA, White RH. The epidemiology of venous thromboembolism. J Thromb Thrombolysis. 2016;41:3-14
- [8] Ageno W, Gallus AS, Wittkowsky A, Crowther M, Hylek EM, Palareti G. Oral anticoagulant therapy antithrombotic therapy and prevention of thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. Chest. 2012; 141(2):E44s-E88

- [9] Konstantinides SV, Torbicki A, Agnelli G, et al. 2014 ESC guidelines on the diagnosis and management of acute pulmonary embolism. *Eur Heart J* 2014;35:3033–69.
- [10] Grosse SD, Nelson RE, Nyarko KA, et al. The economic burden of incident venous thromboembolism in the United States: a review of estimated attributable healthcare costs. *Thromb Res* 2016;137:3–10.
- [11] Witt DM, Clark NP, Kaatz S, et al. Guidance for the practical management of warfarin therapy in the treatment of venous thromboembolism. *J Thromb Thrombolysis* 2016;41:187–205.
- [12] Cancer-Associated Venous Thromboembolic Disease, Version 1.2015. Streiff MB, Holmstrom B, Ashrani A, Bockenstedt PL, Chesney C, Eby C, Fanikos J, Fenninger RB, Fogerty AE, Gao S, Goldhaber SZ, Hendrie P, Kuderer N, Lee A, Lee JT, Lovrincevic M, Millenson MM, Neff AT, Ortel TL, Paschal R, Shattil S, Siddiqi T, Smock KJ, Soff G, Wang TF, Yee GC, Zakarija A, McMillian N, Engh AMJ *Natl Compr Canc Netw*. 2015 Sep; 13(9):1079-95.
- [13] <https://onlinelibrary.wiley.com/doi/full/10.1002/ajh.25059>
- [14] Heit, J. A., Ashrani, A., Crusan, D. J., McBane, R. D., Petterson, T. M., & Bailey, K. R. (2016). Reasons for the persistent incidence of venous thromboembolism. *Thrombosis and haemostasis*, 117(2), 390–400. doi:10.1160/TH16-07-0509
- [15] Silverstein MD, Heit JA, Mohr DN, Petterson TM, O’Fallon WM, Melton LJ., 3rd Trends in the incidence of deep vein thrombosis and pulmonary embolism: a 25-year population-based study. *Arch Intern Med*. 1998;158:585–593
- [16] Severinsen MT, Johnsen SP, Tjonneland A, Overvad K, Dethlefsen C, Kristensen SR. Body height and sex-related differences in incidence of venous thromboembolism: a Danish follow-up study. *Eur J Intern Med*. 2010;21:268–272.
- [17] Chew HK, WunT, HarveyD, ZhouH, WhiteRH. , Incidence of venous thromboembolism and its effect on survival among patients with common cancers *Arch Intern Med* , 2006, vol. 166(pg. 458-464)
- [18] Hisada Y, Mackman N. Cancer-associated pathways and biomarkers of venous thrombosis. *Blood*. 2017;130(13):1499-1506.
- [19] Kearon C, Akl EA, Comerota AJ, et al: Antithrombotic therapy for VTE disease: Antithrombotic Therapy and Prevention of Thrombosis, 9th ed American College of Chest Physicians Evidence Based Clinical Practice Guidelines. *Chest* 141: e419S-e494S, 2012
- [20] Khorana AA, Ahrendt SA, Ryan CK, Francis CW, Hruban RH, Hu YC, et al. Tissue factor expression, angiogenesis, and thrombosis in pancreatic cancer. *Clin Cancer Res* (2007) 13(10):2870–5. doi:10.1158/1078-0432.CCR-06-2351



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