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Original Research Article

Evaluation of pharmacological prophylaxis for deep venous thrombosis in hospitalized patients with risk factors at the university teaching hospitals, Lusaka, Zambia

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ABSTRACT

Background: Deep venous thrombosis is a common clinical problem accounting for high rates of morbidity and mortality. The existence of risk factors, which include trauma, venous stasis, and hypercoagulability, is linked to the occurrence of the condition. Objective of current study was to evaluate DVT risk factors and prophylaxis pattern of use for patients who were admitted at the University Teaching Hospitals in Lusaka, Zambia.
Methods: A cross-sectional study was conducted using medical files for patients who were hospitalized at the University Teaching Hospitals in Lusaka, Zambia from May 2020 to June 2021. Two hundred and ninety-six patient files were reviewed, and the Caprini risk assessment model was used to stratify patients into DVT risk categories. Multilinear regression analysis was used to identify factors associated with DVT prophylaxis.
Results: Of the 296 patient files that were sampled from ICU, medical, and surgical wards, 198 (66.9%) (>2 caprini score) were eligible for DVT prophylaxis, but only 77 (38.9%) of these eligible patients received prophylaxis. The number of eligible patients for DVT prophylaxis per department was as follows; ICU 50 (100%), Medical 71 (57.7%) and Surgery 77 (62.6%) wards. However, DVT prophylaxis was given to 21 (42%), 33 (46.5%), and 23 (29.9%) patients from the ICU, medical, and surgery, respectively. Enoxaparin was the most commonly used anticoagulant for Venous thromboembolism (VTE) prophylaxis with a mean dose of 60mg (SD±5). Across all departments, the most common predisposing risk factors for DVT were bed confinement for >72 hours (167, 56.4%) and age of 41-60 years (118, 39.8%). In the adjusted model, swollen legs (AOR: 3.6, CI: 1.97, 6.57) and history of VTE (AOR: 21.3, CI: 9.87, 46.08) were significantly associated with a higher likelihood of DVT prophylaxis.
Conclusions: Pharmacologic thromboprophylaxis is underutilized in patients in ICU, medical and surgical wards at the university teaching hospitals in Lusaka, Zambia. This study underscores the importance of implementing a DVT risk assessment technique for patients in ICU, medical and surgical wards and administering prophylaxis unless contraindicated.

Keywords: Pharmacological prophylaxis, Risk factors, Thromboembolism, Caprini score, Deep vein thrombosis

INTRODUCTION

Deep venous thrombosis (DVT) is a life-threatening condition with high mortality and morbidity rates worldwide.[1,2] Usually, deep veins of the legs or pelvis are the ones prone to DVT.[3] It manifests when a blood clot forms in the deep veins, and pulmonary embolism (PE) is potentially a deadly complication that happens when part of or all of the clot detaches and moves to the lungs.[4,5] Venous thromboembolism (VTE) is undoubtedly the most common preventable cause of death among hospitalized surgical patients with risk factors.[6] Each year, approximately 2 million people experience deep vein thrombosis, and on average, 0.6 million of these patients experience a PE. Currently, PE leads to the death of nearly 0.2 million patients each year, after heart attack and cardiovascular accidents (CVA), e.g. stroke.[7,8] In a given study, it was found that assessment of patients who were at risk of developing DVT prior to admission to the medical ward was crucial because it was a suitable step for thromboprophylaxis.[9,10] Analytical studies indicated that the occurrence of the most serious complication of VTE, fatal PE, could be underrated in population studies. For roughly two-thirds of PE patients, the first clinical presentation is unexpected death.[11] Furthermore, as out-of-hospital diagnosis and therapy were becoming more common, study populations needed to also consider outpatients to evaluate the burden of VTE.[12] VTE is frequently a very dangerous disease in patients hospitalized in medical departments, but the rate of its diagnosis, treatment, and prevention in medical wards is poor. Prophylactic treatments using anticoagulant drugs such as enoxaparin are effective and can be used in the prophylaxis of VTE.[13] Undeniably, a decrease in the rate of VTE was witnessed in surgical and orthopedic wards due to the enactment of preventive programs, while no such reductions were seen in medical wards.[14,15] Consequently, it was important to raise awareness of VTE risk and develop effective prevention techniques in medical wards. To recognize patients who are at high risk for VTE, risk factors should be well established. A plethora of studies have outlined numerous risk factors, e.g., acute illness, older age, obesity, former VTE events, as well as genetic factors like protein C, S deficiency, factor V Leiden, high fibrinogen levels, and immobilization, malignancy, varicose veins, chronic use of oestrogen ,and renal failure.[14,16-18] Henceforth, this study was designed to determine the rate of DVT prophylaxis and associated factors for DVT prophylaxis eligibility.

METHODS

Study area and period

This study was conducted at the adult university teaching hospital (AUTH) in Lusaka, which is the biggest primary referral healthcare facility in Zambia. It lies around 4 kilometres east of the city centre in the capital city of Lusaka. With approximately 1655 beds, its estimated population is around 2 million. The study was conducted in the medical, surgical and ICU wards from August 2021 to October 2021.

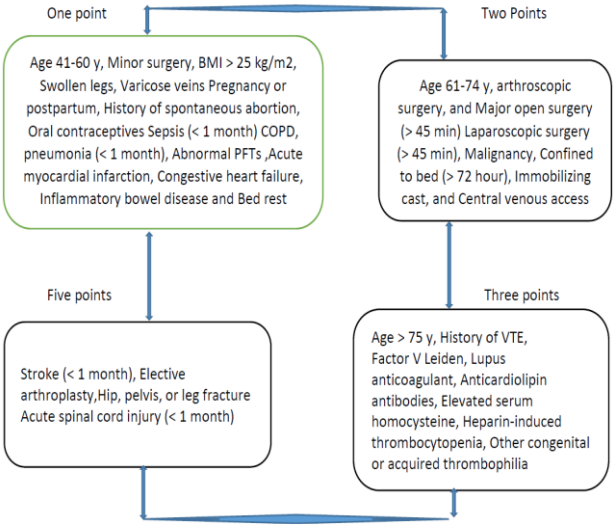

Figure 1: Caprini DVT RAM; Score 0= very low risk, Score 1-2= Patients considered low risk, Score 3-4=moderate risk, Score ≥5= High-risk patients.

Study design and sample

This cross-sectional study assessed the rate of patient's eligibility for DVT prophylaxis and factors associated with DVT prophylaxis. Medical files of adult patients who were admitted to ICU, medical and surgical wards of the University Teaching Hospitals from May 2020 to June 2021 were included in the study. Patients who were admitted due to DVT, had prophylaxis within the past month before admission or any contraindications for DVT, received low molecular heparin, warfarin and new oral anticoagulants were excluded from the study. A sample size of 303 patients' files was obtained using the single proportion formula at a 95% confidence interval

$$n = [Z / 2]\, 2P\,(1 - P) / d2)$$

Where Zα/2=1.96, d=5% and P=27% prevalence based on similar study in the USA were patients admitted to medical-surgical ICUs received anticoagulant only.[19] However, only 97.7% (n= 296) out the total sample patient medical files from May 2020 to June 2021 were reviewed and we are confident that 2.3% shortfall may not significantly affect the statistical power of the sample. The sample size was distributed to the three departments using probability proportional to size. A systemic sampling method was used to select every 4th of the files for inclusion in the study.

Data collection and management

All hospital records in medical, Surgical and ICU wards were reviewed for sociodemographic, clinical features, the core purpose for hospital admission and the existence

of risk factors for VTE. As shown in figure 1, the Caprini RAM for the assessment of thrombosis risk in adult hospitalized patients was employed to group patients into risk factors, and therefore, identify the necessary thrombo-prophylactic mode.

The patients' risk factors were classified into four categories as follows: "Very low risk" (0 points): A group of individuals in whom early and frequent ambulation without mechanical or pharmaceutical prophylaxis is advised. "Low risk" (1-2 points): This group benefits from mechanical prophylaxis with intermittent pneumatic compression versus no prophylaxis. "Moderate risk" (3-4 points): The suggested methods for this group are mechanical prophylaxis with IPC or pharmacological (LMWH, or fondaparinux twice daily) and "highest risk" (5 points): for these individuals, both pharmacologic and mechanical prophylaxis should be given to people who are not at high risk of bleeding.[7,20] For this study, we considered individuals with ≤2 caprini score as low risk and >2 as high risk (requiring both machinical and pharmacological prophylaxis.

Data analysis and processing

The obtained data was cross-examined manually for accuracy. Statistical programs i.e., STATA version 15.1 was used to analyze the data. Furthermore, the analyzed data was presented in reader mode tables to produce the result. In order to identify factors associated with DVT prophylaxis, we performed unadjusted logistic regression analysis for each independent variable separately, and we included independent variables with a p-value of less than 0.2 in the multivariate logistic regression model to account for any confounding among the independent variables. The p value for significance was set at <0.05 with a 95% confidence interval. Consent to access patient records was obtained from the adult university teaching hospital's clinical service director. Only the research team handled any information derived from the data gathered throughout the investigation.

RESULTS

Sociodemographic and clinical details of patients

The study included 296 patients who were admitted to internal medicine, ICU, and surgery wards for the period starting May2020 to May 2021 at the university teaching hospital. The sociodemographic characteristics of the 296 patients are presented in the (Table 1). Of these patients, the majority were females 165 (55%). The median age of the participants was 57 (IQR: 44, 66). The mean Systolic blood pressure, diastolic blood pressure, and heart rate with their corresponding standard deviation values were 125mmHg (±19), 80.9mmHg (±11), and 90 beats per minute (±16) respectively. The distribution of the 296 eligible patient files was; ICU 50(16.8%), surgery 123 (41.6%), and internal medicine 123 (41.6).

Table 1: Sociodemographic and clinical details of patients (n= 296).

Variables	N (%)
Gender	
Male	131 (44.3)
Female	165 (55.7)
Age median (IQR)	57 (44,66)
Systolic BP mean (SD)	125 (±19)
Diastolic BP mean (SD)	80.9 (±11)
Heart rate mean (SD)	90 (±16)
Sensorium	
Unconscious	36 (12.2)
Conscious	260 (87.8)
Department	
ICU	50 (16.8)
Internal medicine	123 (41.6)
Surgery	123 (41.6)

Primary cause of admission

As depicted in (Table 2) below, the main cause of hospitalization was, infectious diseases 69 (23.3% mainly COVID-19 and urinary tract infections). Others 66 (22.3% comprising surgical problems, burns, and body injuries) was the second cause of admission.

Table 2: Primary cause of admission (n=296).

Primary cause of admission	N (%)
Infectious diseases	69 (23.31)
Cardiovascular disorders	62 (20.9)
Diabetes mellitus	9 (3.0)
Orthopedics	19 (6.4)
Renal diseases	22 (7.4)
Respiratory diseases	15 (5.1)
GIT disorders	11 (3.7)
Endocrine disorders	8 (2.7)
Hematological disorders	7 (2.4)
Neurological disorders	8 (2.7)
Others	66 (22.3)

Risk factors for deep vein thrombosis

This table below indicates that the most predisposing risk factors were, bed confinement for >72 hours 167 (56.4%), age 24-60 118 (39.8%), swollen legs 86 (29.1%), and history of VTE 66 (22.3%).

Eligible patients for DVT prophylaxis for all the three departments

The rate of eligible patients for DVT prophylaxis per department is depicted in (Figure 1). A total of 198 patients (66.9%) were found to be at risk for DVT. Of these, ICU recorded 50/50 (100%) high risk patients, with Surgery 77/123 (62.6%) patients while Internal medicine had 71/123 patients (57.7%).

Table 3: Risk factors for DVT in patients as defined by Caprini's Score (n=296).

Risk factor	N (%)
Age 41-60	118 (39.8)
Swollen legs	86 (29.1)
Pregnancy or postpartum	36 (12.2)
Oral contraceptives	29 (9.8)
COPD, pneumonia <1mo	46 (15.5)
Congestive heart failure	26 (8.9)
Age 61-74 years	88 (29.7)
Confined to bed for >72hrs	167 (56.4)
Central venous access	42 (14.2)
Age >75 years	22 (7.4)
History of VTE	66 (22.3)
Hip, pelvis, or leg fracture	16 (5.4)
Acute spinal cord injury (<1 month)	13 (4.4)

Number of patients who received prophylaxis per department

The number of patients who received prophylaxis were 21 (27.3%) from ICU, surgery 23(29.9%) and internal medicine 33 (42.9%) are depicted in (Figure 2). The total number of patients who received prophylaxis for DVT was 77 representing a (38.9%).

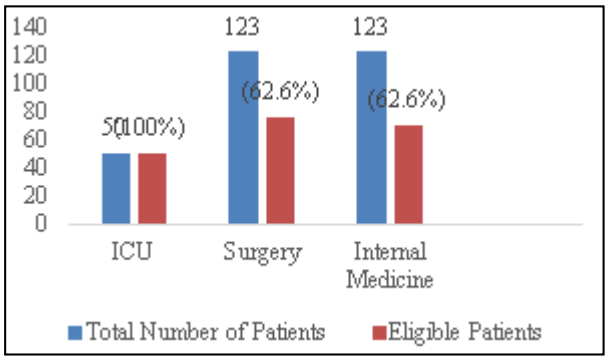

Figure 1: Eligible patients for DVT prophylaxis across the department.

Most prescribe anticoagulant for DVT prophylaxis

As shown in (Figure 3), the most prescribed anticoagulant was the low molecular weight anticoagulant enoxaparin 74 (96.1%) with the mean dose of 60 mg (SD±5) and oral anticoagulant warfarin 3 (3.9%) with the mean dose of 2.5mg (SD±0).

Bivariate and multivariate findings of factors associated with DVT prophylaxis

Results in unadjusted model showed that swollen legs (COR: 3.6, CI: 1.97, 6.57), confined to bed (>72 hour) (COR: 2.6, CI: 1.16, 5.83), central venous access (COR: 3.3, CI: 1.65, 6.78), history of VTE (COR: 21.3, CI:9.87, 46.08), Hip, pelvis or leg fracture (COR: 5.4, CI:1.67, 17.42), stroke (<1 month) (COR: 3.5, CI: 1.66, 7.23) were significantly associated with higher likelihood of DVT prophylaxis. In adjusted model, only swollen legs (AOR: 3.6, CI: 1.97, 6.57) and history of VTE (AOR: 21.3, CI: 9.87, 46.08) were associated with DVT prophylaxis.

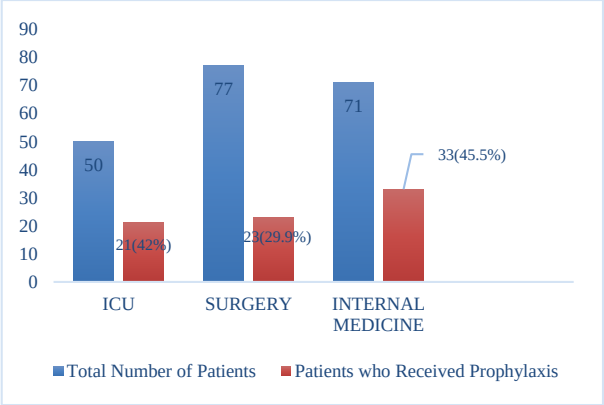

Figure 2: Number of patients who received prophylaxis per department (n=198).

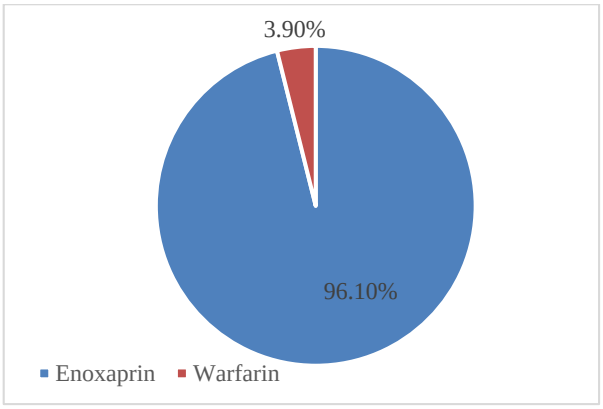

Figure 3: Most prescribed anticoagulant for DVT prophylaxis (n=77).

DISCUSSION

In hospitalized patients, VTE is a common preventable cause of morbidity and mortality.[21,22] The use of anticoagulants for thromboprophylaxis has proven to be both effective and safe.[10] As a result, evidence-based guidelines recommend thromboprophylaxis for critically ill patients who are hospitalized in medical wards and are at risk of developing VTE.[23] Despite these recommendations, barely one-third of patients at risk of developing VTE receive the appropriate treatment.[22] In this study, 296 patients were enrolled and assessed using Caprine RAM for VTE. The total risk caprine score ranged from 0 to 19, with a mean score of 5.5 (±4.5). Of those assessed, 66.9% were at risk of developing VTE according to the 2004 ACCP risk definition. This figure is lower than the 77% reported in South Africa and 77.8% Northern Cyprus.[8,24] However, our findings were within the range of 44 - 80% as reported by the Endorse study.[12]

Table 4: Bivariate and multivariate logistic regression analysis of factors associated with DVT prophylaxis.

Variable	Category	Unadjusted			Adjusted		
		COR	95% CI	P value	AOR	95% CI	P value
Age		1.01	0.98, 1.02	0.881			
Sex	Male	1	0.35,1.12	0.117	1	0.43, 2.51	0.937
	Female	0.6			1.0		
Department	ICU	1					
	Surgery	0.9	0.46, 1.96	0.886			
	Medicine	0.7	0.32, 1.41	0.288			
Sensorium	Unaltered	1	0.23, 1.07	0.075	1	0.11, 1.22	0.102
	Altered	0.5			0.4		
Age 41-60 years	No	1	0.62, 2.01	0.713			
	Yes	1.1					
Swollen legs	No	1	1.97, 6.57	0.0001**	1	1.44, 8.55	0.006*
	Yes	3.6			3.5		
Oral contraceptive	No	1	0.16, 1.29	0.142	1	0.97, 14.54	0.055
	Yes	0.6			3.76		
OPD, pneumonia (< 1 month)	No	1	0.76, 2.00	0.248			
	Yes	1.5					
Congestive heart failure	No	1	0.27, 1.61	0.365			
	Yes	0.7					
Age 61-74 years	No	1	0.45, 1.49	0.515			
	Yes	0.8					
Confined to bed (<72hour)	No	1	1.16, 5.83	0.020**	1	0.62, 5.80	0.264
	Yes	2.6			1.9		
Central venous access	No	1	1.65, 6.78	0.001**	1	0.90, 7.38	0.076
	Yes	3.3			2.6		
Age 75	No	1	0.45, 2.71	0.837			
	Yes	1.1					
History of VTE	No	1	9.87, 46.08	0.0001**	1	10.68, 70.54	0.0001*
	Yes	21.3			27.4		
Hip, pelvis or leg fracture	No	1	1.67, 17.42	0.005**	1	0.59, 13.52	0.194
	Yes	5.4			2.8		
Acute spinal cord injury (<1 month)	No	1	0.62, 5.93	0.259			
	Yes	1.9					
Stroke (< 1 month)	No	1	1.66, 7.23	0.001**	1	0.93, 7.14	0.070
	Yes	3.5			2.6		
Immobilizing cast	No	1	0.26, 5.45	0.827			
	Yes	1.2					

COR: Crude odds ratio, AOR: Adjusted odds ratio, CI: Confidence interval, **: p< 0.05 in unadjusted model,*: p<0.05 in adjusted model, No: Absence of risk DVT risk factors, Yes: Presence of DVT risk factors

The low rate of risk for developing VTE observed in this study could be attributed to the inability to measure some Caprini parameters such as Factor V Leiden, anticardiolipin antibodies, and elevated serum homocysteine due to limitations of the institution's laboratories. In addition, the lack of simple risk stratification tools or written standardized VTE prophylaxis protocols in our setting may also account for the low rate of risks for developing DTE reported in this study. In our study, the ICU reported the highest (100%) risk for VTE, followed by Surgery (62.6%) and the lowest risk was from the Medical wards (57.7%). These findings are comparable to another study in Senegal in which 57.4% and 60.3% of medical and surgical patients were reported to be at risk of developing VTE, respectively. [2] In our study, only 38.9% of patients identified to be at risk of developing VTE received prophylaxis in accordance with the recommended guidelines. Although the application of prophylaxis to eligible patients was low, this finding is similar to those reported by studies in Saudi Arabia and ENDORSE (a multinational cross-sectional survey) which reported a thromboprophylaxis rate of 39.3% and 39.5% respectively.[12,25] In contrast to our study, a higher thromboprophylaxis rate of 52.3% was documented in Northern Cyprus and 70.9% in South Africa. [8,26] The

observed low rate of VTE prophylaxis reported in our study could be due to the perceived high cost of VTE prophylaxis. Although VTE preventive therapy may be inaccessible and generally costly for some low-income settings, research has consistently found that providing prophylaxis for high-risk patient populations is a cost-effective strategy. Our findings may be further explained by the presence of a high bleeding risk among the hospitalized patients and the existence of several active comorbidities where the focus by attending physicians is to manage the illness on presentation and not prevention of potential illness. Our study further reported a higher provision of VTE prophylaxis to patients in the medical wards (45.5%) compared to those in ICU (42%) and surgical wards (29.9%). This finding conflicts with that from the ENDORSE study's subgroup analysis of participants, which concluded that less than 40% of people at risk in the medical patient community receive prophylaxis for VTE.[27]

A slightly greater rate of VTE prophylaxis reported in our study may be attributable to some hospital physicians' strong perceptions of the risk of VTE and their sufficient understanding of the benefits of prophylaxis. Surprisingly, our study observed that VTE prophylactic coverage among surgery patients was very low (29.9 %). In contrast, the ENDORSE global study found that surgical patients were substantially more likely to receive prophylaxis, with rates ranging from 50 to 88%.[12] In another study, 86% of ICU patients received thromboprophylaxis in the first 24 hours, a much higher rate than that reported in our study. These findings demonstrate an urgent need for intensified awareness and training of physicians and surgeons regarding the long-term impact of VTE on individual patients and the burden on institutions. The most prevalent risk factors for VTE in this study were bed confinement of more than 72 hours and an age group of 41-60 years. This finding is supported by other studies done elsewhere. [24,28,29] In contrast, a study conducted in Iran found that old age was the most pervasive risk factor.[30] This disparity could be explained by the fact that most patients with risk factors in our study included patients who were relatively younger. Furthermore, the study found that the most (96.1%) prescribed anticoagulant was LMWH enoxaparin at a mean dose of 60mg. This is in agreement with a study conducted in South Africa and Spain which found 89.1% and 97% LMWH as commonly used prophylactic measures, respectively. [31,32] A multivariate logistic regression showed that swollen legs and a history of VTE were independently associated with a higher likelihood of greater use of DVT prophylaxis. This finding is similar to a study conducted in Canada.[33] Although it is reassuring that the use of prophylaxis was associated with a greater presence of known VTE precipitants (swelling legs and history of VTE), the total prevalence of usage in our study was relatively low.

Limitations

Since we were reviewing medical files for data collection, some vital data (Factor V Leiden, anticardiolipin antibodies, and elevated serum homocysteine, body mass index) were not found on patients' medical files. This could have led exclusion of some patients who were at risk for VTE. It was challenging to evaluate additional non-pharmacologic options such early ambulation and leg elevation since they were not noted on the patients' medical files.

CONCLUSION

There was a low rate of thromboprophylaxis use in ICU, medical and surgery patients, despite the fact that more than half of the patients were at risk of developing VTE and published agreement guidelines and high quality, unswerving evidence that back its safety and effectiveness. The hospital across all the departments should create a quality improvement strategy to enhance VTE risk assessment and prophylaxis prescribing by utilizing a validated instrument and embedding it in patient charts for better evaluation and decision-making for VTE prophylaxis.

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Ethical approval: The study was approved by the Institutional Ethics Committee

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