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A Cross-sectional Study of the Assessment of Venous Thromboembolism Risk and Use of Anticoagulant Thromboprophylaxis

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Abstract

Background: Venous thromboembolism (VTE) is a common and preventable disease among non-surgical hospitalized patients. Its incidence is high and alarming. Acute medical patients have VTE risk during and after hospitalization. The Padua prediction score is a risk model created to identify high VTE risk patients among non-surgical hospitalized patients. *Methods:* We performed a cross-sectional survey of 107 patients admitted to Internal Medicine wards who were assessed as acutely ill patients at Emergency Department, in a period of 4 weeks. The demographic and clinical data were collected using a designed questionnaire. VTE risk was defined as having a Padua Prediction score of ≥4 points. A statistical analysis was done to determine prevalence. The patients at high VTE risk received thromboprophylaxis. *Results*: One hundred and seven eligible patients were included. 84% were found to be at high risk for VTE. Among physiologically unstable patients, 60% of the patients were classified in red color during the time of triage; this means they were severely sick and needed resuscitation. Among the leading diagnosis, severe pneumonia was predominant (29%). Severe pneumonia and uncontrolled DM showed a significant association with high VTE risk. 11.1% of high VTE risk patients were taking anticoagulant thromboprophylaxis prior to the recruitment. *Conclusion:* This study demonstrated a high prevalence of VTE risk among acute ill medical patients and underuse of anticoagulants for thromboprophylaxis in potential patients at Kigali University Teaching Hospital, CHUK. The Padua prediction score should be implemented for early detection of patients at-risk of VTE in severely ill patients and to start anticoagulant thromboprophylaxis on time for reducing mortality and morbidity.

Keywords: Venous Thromboembolism Risk; Rwanda; Anticoagulant Thromboprophylaxis; VTE.

1. Introduction

Venous thromboembolism (VTE), which includes deep venous thrombosis (DVT) and pulmonary embolism (PE), is one of the most causes of morbidity and mortality in acutely ill and critical medical or surgical inpatients [1]. In non-surgical patients, the incidence is ranging between 10 to 30% and is associated with a 10% mortality rate; three fourth

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of all deaths occur in medical patients [2, 3]. The use of VTE prophylaxis decreases its risk in surgical patients, besides the high risk of bleeding due to the multiple comorbidities [1]. The VTE was identified to be among the preventable diseases in order to decrease mortality and morbidity, in 2008, in US, they have introduced the VTE prophylaxis protocols [4, 5]. Risks for VTE include immobility, infections, heart failure, respiratory failure, and active or underlying malignancy; they also include an increase in age, prior VTE, and underlying congenital or acquired thrombophilia. These risks are synergistic, and the more risk factors present, the higher the VTE risk [6].

The guidelines by the American College of Chest Physician (ACCP) recommend the use of anticoagulant thromboprophylaxis with low molecular weight heparin, or low dose unfractionated heparin, or fondaparinux for medical patients at risk of thrombosis; the VTE risk evaluation is done by using the Padua prediction score; and discourage the use of anticoagulants in medical patients with active bleeding or at high risk of bleeding [7]. Despite the ACCP recommendation, globally, half of hospitalized medical patients with a high risk of DVT received thromboprophylaxis [7, 8]. There is a risk assessment model that was predefined by the Padua Prediction Score to assign eleven common VTE risks in medical patients, the score of ≥4 points defined as high risk, and this model provided the best assessment basis, but with some weaknesses. There was the establishment of a bleeding risk score besides not validated and no separation of use versus non-use of prophylaxis [7, 9]. There are major bleeding risks such as bleeding within 3 months prior to admission, a platelet counts less than $50x10^9$/L and active gastro-duodenal bleeding [7, 10].

In the CHUK Emergency Department, they are using the modified South Africa Triage Score (mSATS) during the triage, where the patients are classified into five colors (red, orange, yellow, green, and blue) according to the clinical status [10]. Unstable patients requiring resuscitation are labeled red, yellow and green patients are not severely sick while blue patients are clearly dead [11]. Many interventions may improve the overall compliance of VTE risk assessment in acute medical ill patients and result in a positive attitude towards mortality and morbidity reduction, improvement of adherence to pharmacology thromboprophylaxis as preventive measures, the advocacy of VTE risk assessment is paramount at all levels of health facilities [11]. In the absence of a standard protocol, this study was done to see if all severely ill medical patients at-risk of VTE at CHUK are identified and put on anticoagulant thromboprophylaxis. We assessed the magnitude of VTE risk and the use of anticoagulant thromboprophylaxis in acutely ill medical patients at CHUK, Rwanda.

2. Methods

2.1. Study Design and Methodology

Kigali University Teaching Hospital, CHUK is a public, tertiary hospital in Rwanda, located in Kigali, the capital city of Rwanda. It is the biggest hospital among the three major referral hospitals located in Kigali, with a capacity of 560 beds. Internal Medicine is among the departments based on type of specialty. We performed a non-randomized, cross-sectional, descriptive, and observational study. During 4 weeks, between April and May, 2020; 107 patients aged ≥ 18 years old who were admitted to Internal Medicine through emergency rooms, triaged in red (patients who were physiologically unstable and required resuscitation) or orange (patients who were potentially unstable physiologically or had life-threatening pathology), and accepted or the legal next of kin accepted to give consent, were recruited in the study. At Emergency Department, the triage is done by using a local modified South Africa Triage Score (mSATS). The patients who had active bleeding, gastro duodenal ulcer, platelets count $<50x10^9$/L, known with bleeding risks (like hemophilia or bleeding within 3 months prior to admission), and or incomplete data in their chart from Emergency department were excluded from the study. The data collection was done using a tool of variables; the Padua Prediction Score (Table 1) [9], overall, the cumulative score of ≥4 points was recorded as high VTE risk, and the patients had benefited from anticoagulant thromboprophylaxis. The obesity (BMI≥30) was not assessed; many patients were severely sick and bedridden.

Table 1. Padua prediction score assessment tool: High risk VTE score: ≥ 4 points

Item(s)	Score
Active cancer	3
Previous VTE	3
Bed rest for ≥3 days	3
Thrombophilia	3
Recent trauma (≤ 1 month)	2
Elderly age (≥70 years)	1
Heart failure/Respiratory failure	1
Acute myocardial infection/ischemic stroke	1
BMI ≥30 Kg/m^2	1
Ongoing hormonal therapy	1

2.2. Patient and Public Involvement

All patients admitted to internal medicine wards who were triaged in red or orange color at the emergency department were recruited for the study. Prior to the recruitment of the study participants, by using the local language (Kinyarwanda), the patients were explained the purpose of the study as well as the potential benefits and risks of participating in the study. The investigator told them that they were free to withdraw from the study at any time, without having to give a reason of withdrawing and without affecting their future medical care. They had the opportunity to ask questions. By signing the informed consent, they knew that they authorized access to their medical records to the monitor(s) and the auditor(s), and possibly to the members of the ethical committees or health authorities, for verification of clinical study procedures and/or data. They have been given a copy of the Informed Consent Form. After analyzing the data, the findings were explained to the patients.

3. Analysis

Date entry was done using Epidata version 3.1 and exported to Excel and the statistical package for social science (IBM SPSS Statistics) version 28 for final data cleaning and analysis. We performed descriptive statistics to determine frequency and percentages, and later we did a chi-square test of independence and binary logistic regression to find out the relevant significance of association where by p-value <0.05 under confidence of 95% the predictive variable(s) was considered as significantly associated with the outcome variable. No confounding variables identified in the literature review fit for multinomial logistic regression testing for adjustment.

4. Results

Of 107 patients, almost 59.8% were female; 60.7% were classified in red color in triage at the time of admission to the accident and emergency department; among the leading diagnoses, one in three had severe pneumonia, 84.1% had high VTE risk (Table 2). In assessment of venous thromboembolism by the Padua prediction score, 86.9% did not report active bleeding, 95.3% denied a history of thrombophilic condition, 91.6% were active cancer-free, 91.6% were not in heart failure, 80% were younger than 70 years old, 89.7% did not have an ischemic stroke, and 71% did not have an acute infection (Table 3). During bivariate analysis of the leading diagnosis and Padua prediction score, a severe pneumonia diagnosis had a significant association with venous thromboembolism (p value = 0.004) and the same as uncontrolled Diabetes Mellitus with p value < 0.001 (Table 4). Among the 10 patients who were taking anticoagulant thromboprophylaxis, 3 patients had severe pneumonia (Table 5), and there was no significant association between the Padua prediction score and VTE prophylaxis (p value = 0.234). In the Padua prediction score distribution, in the study population, 62.6% scored 4 points, 7.5% scored the highest score in this study, which was 6 points, and 15.9% scored less than 4 points, which means no VTE risk (Figure 1). In the Padua prediction score distribution by mean age, the patients with 77.3 years old scored 5 points, and the patients with 53.4 years old scored 6 points (Figure 2). Blindly, 11.1% of high VTE risk patients were taking anticoagulant thromboprophylaxis prior to our study recruitment (Table 5).

Table 2. Baseline characteristics of the study participants

Characteristics	Number(n)	Percentage (%)
Gender		
Male	43	40.2
Female	64	59.8
Total	107	100
Triage color of patient		
RED	65	60.7
ORANGE	42	39.3
Total	107	100
Leading Diagnosis		
Acute decompensated heart failure	9	8.4
complicated malaria	11	10.3
Severe pneumonia	31	29.0
Extra-pulmonary TB	6	5.6
Ischemic stroke	11	10.3
Malignancy	9	8.4
DKA	9	8.4
Meningitis	8	7.5
Uncontrolled DM	13	12.1
Total	107	100.0

Padua score		
<4	17	15.9
≥4	90	84.1
Total	107	100

Table 3. Descriptive statistics of Padua prediction score Elements

Characteristics	Number(s)	Percentage(s)
Active bleeding		
Yes	14	13.1
No	93	86.9
Total	107	100
History of thrombophilic condition		
Yes	5	4.7
No	102	95.3
Total	107	100
Active cancer		
No	98	91.6
Yes	9	8.4
Total	107	100
Heart failure(s)		
No	98	91.6
Yes	9	8.4
Total	107	100
Age in years		
<70	86	80.4
≥70	21	19.6
Total	107	100
Ischemic stroke		
No	96	89.7
Yes	11	10.3
Total	107	100
Acute infection		
No	76	71
Yes	31	29
Total	107	100

Table 4. Bivariate analysis of the leading diagnosis and Padua prediction score

Leading Diagnosis	PPS SCORE			P-value
	<4 score	≥4 score	Total	
	Number (%)	Number n (%)	No.	
DKA				0.173
No	17(17.3)	81(82.7)	98	
Yes	0(0)	9(100)	9	
Total	17(15.9)	90(84.1)	107	
Malignancy				0.173
No	17(17.3)	81(82.7)	98	
Yes	0(00	9(100)	9	
Total	17(15.9)	90(84.1)	107	
Heart failure				0.156
No	17(17.3)	81(82.7)	98	
Yes	0(0)	9(100)	9	
Total	17(15.9)	90(84.1)	107	

Complicated Malaria				0.128
No	17(17.7)	79(82.3)	96	
Yes	0(0)	11(100)	11	
Total	17(15.9)	90(84.1)	107	
Severe Pneumonia				0.004***
No	17(22.4)	59(77.6)	76	
Yes	0(0)	31(100)	31	
Total	17(15.9)	90(84.1)	107	
EXTRA PULMONARY TB				0.273
No	17(16.8)	84(83.2)	101	
Yes	0(0)	6(100)	6	
Total	17(15.9)	90(84.1)	107	
ISCHEMIC STROKE				0.128
No	17(17.7)	79(82.3)	96	
Yes	0(0)	11(100)	11	
Total	17(15.9)	90(84.1)	107	
Meningitis				0.234
No	17(17)	83(83)	100	
Yes	0(0)	7(100)	7	
Total	17(15.9)	90(84.1)	107	
Uncontroled DM				<0.001***
No	5(5.4)	88(94.6)	93	
Yes	12(85.7)	2(14.3)	14	
Total	17(15.9)	90(84.1)	107	

Table 5. Anticoagulant thromboprophylaxis use in patients at VTE risk

Leading Diagnosis	**VTE prophylaxis status in VTE Risk patients**		**P-value**
	Yes: numbers (%)	**No: n(%)**	
DKA			0.694
No	6(7.4)	75(92.6)	
Yes	1(11.1)	8(88.9)	
Malignancy			0.694
No	6(7.4)	75(92.6)	
Yes	1(11.1)	8(88.9)	
Heart failure			0.694
No	6(7.4)	75(92.6)	
Yes	1(11.1)	8(88.9)	
Complicated Malaria			0.862
No	6(7.6)	73(92.4)	
Yes	1(9.1)	10(91)	
Severe Pneumonia			0.626
No	4(6.8)	55(93.2)	
Yes	3(9.7)	28(90.3)	
EXTRA PULMONARY			0.462
No	7(8.3)	77(91.7)	
Yes	0(0.0)	6(100)	
ISCHEMIC STROKE			0.862
No	6(7.6)	73(92.4)	
Yes	1(9.1)	10(91)	
Meningitis			0.032**
No	5(6)	78(94)	
Yes	2(28.6)	5(71.4)	

Uncontrolled DM			0.678
Yes	0(0.0)	2(100)	
No	7(8)	81(92)	
Total of the patients taking anticoagulant thromboprophylaxis	10/90	11.1%	0.234

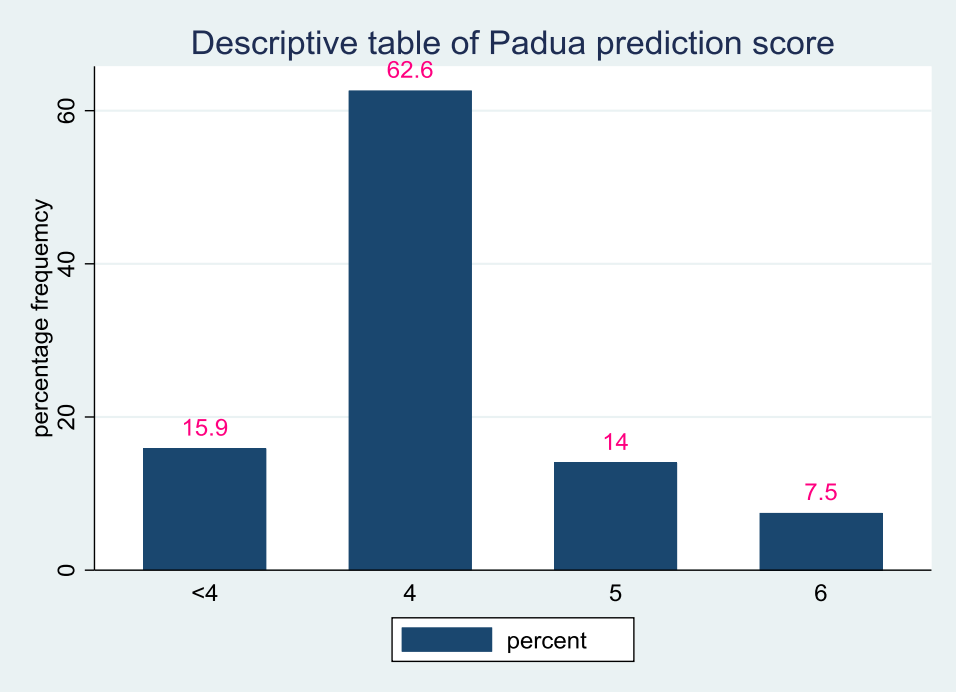

Figure 1. The distribution of Padua prediction score

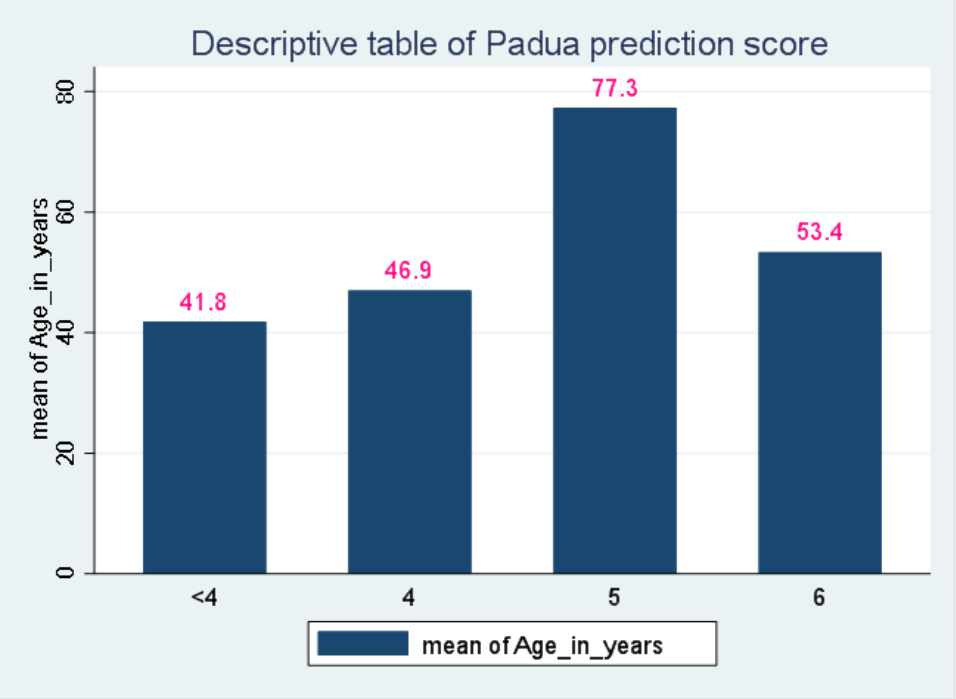

Figure 2. The distribution of Padua score by age in years

5. Discussion

VTE is a major problem in non-surgical hospitalized patients, needs more attention as it leads to substantial costs and is associated with high morbidity and mortality [12]. Every year in the United States, VTE is diagnosed for the first time in 100 persons per 100,000, and its incidence is rising from <5 cases per 100,000 persons in <15 years old to 500 cases per 100,000 persons at the age of 80 years old [13]. The venous thrombophylaxis is extensively under-usage in

hospitalized medical patients. A simple risk assessment model (RAM) was used to assess high-risk VTE patients who received venous thromboprophylaxis in comparison with those who did not, the findings, 2.2% who received VTE prophylaxis developed VTE and 11% in the comparison group [9]. In the group of high-risk VTE patients, the mean age of 77.7 years; reduced mobility; acute infection or rheumatologic disorder; and Heart failure and or respiratory failure showed significant association with VTE with p values <0.01 [9]; and the relative risk was 38.8 (95% CI, 10.4–146.5) [9]. The VTE free cumulative proportion was increasing with absence of VTE prophylaxis use and increased length of hospital stay [9]. The patients who scored ≥ 4 and did not receive prophylaxis had 30 times risk of developing in-hospital VTE and adequate thrombophylaxis reduced the risk to 90% [9]. In a previous study conducted in two tertiary hospitals in Rwanda, the prevalence of proximal DVT was 5.5% in patients who were admitted to the Internal Medicine and Obstetrics-Gynecology Departments, among them 75% were taking anticoagulant drugs, and this study has documented the low use of anticoagulant thromboprophylaxis [14].

According to our findings in CHUK, the severely ill medical patients are not assessed properly, and there is an underuse of anticoagulant thromboprophylaxis in eligible patients. Among 107 recruited patients, 90 (84.1%) patients had VTE risk or they should be even many if we were able to assess BMI (Table 2) and among them only 10 (11.1%) patients were taking anticoagulant thromboprophylaxis (Table 5). Among the patients who were physiologically unstable, 60.7% were classified in red color (Table 2), this is explained by referring system in public hospitals where the patients are getting the first treatment at health post or health center and if no improvement, they are referred at district hospital, referral hospital or provincial hospital then later to the Teaching Hospital, the patients may delay and their health conditions become worse. Among leading diagnoses, severe pneumonia was predominant, followed by complicated malaria and ischemic stroke (Table 2). Four of five patients were aged below 70 years old, compared to the previous study where the mean age was 77.7 years and showed significant association with VTE risk [9]. Contrary to the previous study, in our study, around 10 patients who scored 5 points were aged 78 years old (Figures 1 and 2). In this study, severe pneumonia and uncontrolled DM showed a significant association with VTE risk (Table 4); this study shared the same finding as a previous one with one parameter of infection [9]. This study showed that aging was associated with increased VTE risk. Patients with a mean age of 41.8 years had no risk of VTE, while the patients with a mean age of 46.9 years, 77.3 years, and 53.4 years scored 4 points, 5 points, and 6 points, respectively (Figure 2). 62.6% of the patients who had a mean age of 46.9 years old scored 4 points (Figures 1 and 2). This was explained by the fact that young age is associated with high mobility and less Padua prediction score (9).

6. Conclusion

Based on our study findings, there was a high risk of developing VTE in admitted patients and underuse of anticoagulant thromboprophylaxis in potential candidates at CHUK. The Padua prediction score should be implemented at the point of entry to assess high-risk patients and start anticoagulant thrombophylaxis on time in non-surgical patients. To the best of our knowledge, this is the first study assessing VTE risk and the use of anticoagulant thromboprophylaxis in CHUK as well as Rwanda. Due to the lack of a national standard protocol on the use of anticoagulant thromboprophylaxis in severely ill non-surgical patients, the Padua prediction VTE risk assessment should be implemented to detect all patients at VTE risk among physiologically unstable patients as well the accessibility of anticoagulant thrombophylaxis in all hospitals in Rwanda to reduce mortality and morbidity.

Due to the time frame limitation and lack of external funds, we were not able to do follow-up with our patients during hospitalization and after discharge to assess the treatment response for those who received prophylaxis in terms of success rate.

7. Declarations

7.1. Author Contributions

Conceptualization, E.A. and E.N.; methodology, E.U.; software, R.N.; validation, E.N., O.S., and F.M.; formal analysis, R.N.; investigation, A.B.; resources, E.A.; data curation, O.S.; writing—original draft preparation, E.A.; writing—review and editing, E.N.; visualization, A.B.; supervision, F.M.; project administration, O.S. All authors have read and agreed to the published version of the manuscript.

7.2. Funding

The authors received no financial support for the research, authorship, and/or publication of this article.

7.3. Data Availability Statement

The data presented in this study are available on request from the corresponding author.

7.4. Ethical Approval

All subjects gave their informed consent for inclusion before they participated in the study. The study was conducted in accordance with the Declaration of Helsinki, and the protocol was approved by the Ethics Committee of Institutional Review Board of College of Medicine and Health Sciences (No 032/CMHS/IRB2020) and Ethics committee of CHUK (Ref: EC/CHUK/017/2020).

7.5. Informed Consent Statement

Informed consent was obtained from all subjects involved in the study. They were explained the objective of the study, and they were granted freedom of withdrawing from the study at any time, without giving a reason of withdrawing or affecting their future medical care.

7.6. Conflict of Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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