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Estimation of the Direct Cost of Management of Venous Thromboembolism in Three Reference Hospitals in the City of Yaoundé: A Retrospective Study over a Three-Year Period

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Abstract

Background: Venous thromboembolism (VTE) is a major public health problem due to its increasing frequency, mortality and management cost. This cost may require major financial efforts from patients, especially in developing countries like ours where less than 7% of the population has health insurance. This study aimed to estimate the direct cost of managing VTE in three reference hospitals in Yaoundé. **Methods:** This was a cross-sectional retrospective study over a three-year period (from January 1st 2018 to December 31 2020) carried out in the Cardiology departments of the Central and General Hospitals, and the Emergency Centre of the city of Yaoundé. All patients managed during the study period for deep vein thrombosis and pulmonary embolism confirmed by venous ultrasound coupled with Doppler and computed tomography pulmonary angiography respectively were included. For each patient, we collected sociodemographic and clinical data as well as data on the cost of consultation, hospital stay, workups and medications. These data were analysed using SPSS version 23.0. **Results:** A total of 92 patient's records were analysed. The median age was 60 years [48 - 68] with a sex ratio of 0.53. The median direct cost of management of venous thromboembolism was 766,375 CFAF [536,455 - 1,029,745] or $1415 USD.

Management of pulmonary embolism associated with deep vein thrombosis was more costly than isolated pulmonary embolism or deep vein thrombosis. Factors influencing the direct cost of management of venous thromboembolism were: hospital structure ($p = 0.015$), health insurance ($p < 0.001$), type of pulmonary embolism ($p = 0.021$), and length of hospital stay ($p = 0.001$). **Conclusion:** Management of VTE is a major financial burden for our patients and this burden is influenced by the hospital structure, health insurance, type of pulmonary embolism and length of hospital stay.

Keywords

Cost, Management, Venous Thromboembolism, Yaoundé

1. Introduction

Venous thromboembolism (VTE) is an entity which includes deep vein thrombosis and pulmonary embolism as manifestations [1]. It occurs as a result of a sudden obstruction of a vascular network, most often by a blood clot that prevents normal blood flow [2]. Venous thromboembolism is the third most common cardiovascular condition in whites after myocardial infarction and stroke [3]. The overall incidence is 100 - 200 per 100,000 [1]. Venous thromboembolism is increasingly common in sub-Saharan Africa [2]. A recent systematic review in Africa showed a prevalence of venous thromboembolism ranging from 2.4% to 9.6% [4]. In Cameroon, the prevalence of venous thromboembolism is 1.6% according to a study conducted by Etoundi *et al.*, 2015 [2]. Venous thromboembolism complicates 2% - 3% of hospital admissions [3] and is a significant cause of mortality especially in low-income countries [5]. In Cameroon in 2020, Nkoke *et al.* found an estimated hospital mortality of 10% [4]. Various complications of venous thromboembolism exist and can be prevented by effective drugs, though costly and non-pharmacological measures [3]. The cost of managing venous thromboembolism remains a major concern [6]. In Togo, the cost of treatment per patient varies between $900 USD (450,000 CFAF) and $1200 USD (600,000 CFAF) [7]. In Cameroon, a study conducted by Owoundi in 2013 revealed that 51% of the population lives on less than two dollars a day [8]. The average propensity of total household medical consumption is very high [8]. In fact, 32% of households spend less than half of their income on health, while 16% spend more and 52% spend all of their income; this corresponds to a 68% weight in health expenditure [8]. Some population groups are so poor that they spend almost no income on priority items such as health and education [9]. According to a study conducted by Okouloma in 2018 in Cameroon, the rate of health insurance is less than 7% [10], this implies that the cost of care depends mainly on patients and their families, with the exception of some employees of the private sector who have health insurances. Given the scarcity of data on the direct cost of management of venous thromboembolism, we found it necessary

to estimate the direct cost of treating venous thromboembolism in three reference hospitals in the city of Yaoundé.

2. Methods

2.1. Study Design and Setting

This was a cross-sectional descriptive and analytical study over a three-year retrospective period from 1 January 2018 to December 31 2020. It was carried out in the Cardiology departments of the Yaoundé Central Hospital (YCH), Yaoundé General Hospital (YGH) and the Yaoundé Emergency Centre (YEC).

2.2. Study Population

Our study population consisted of records of patients managed for VTE during the study period.

2.2.1. Inclusion Criteria

- All patients managed for VTE and confirmed by established diagnostic criteria by computerised tomography pulmonary angiography for pulmonary embolism and lower limb venous ultrasound coupled to Doppler for DVT;
- Any patient whose verbal informed consent had been obtained (or in the absence of such consent, that of a relative) to participate in the study.

2.2.2. Exclusion Criteria

The following were excluded from our study:

- Any file that could not be used (socio-demographic, clinical and cost data not obtained due to incomplete completion of the files).
- Any patient file for which verbal informed consent had not been obtained.

2.3. Procedure

Data were collected on the costs of consultation, hospitalisation, various complementary exams and medication from the cardiology department senior health care assistants and the persons in charge of bills of the various hospitals, if it's necessary, patients were reached by telephone call to complete the data. Participants reached via phone calls gave their consent verbally after they had been counselled on the study in the simplest language they could comprehend. To ensure confidentiality, participants were given codes instead of using their names for identification. Data collected were recorded in a pre-designed questionnaire. No test was performed to test for the validity or reliability of the questionnaire.

2.4. Operational Definition of Terms

- Massive pulmonary embolism: PE with arterial hypotension (systolic blood pressure < 90 mm Hg) or peripheral signs of shock;
- Sub-massive pulmonary embolism: PE with acute pulmonary heart (dilatation of the right ventricle and paradoxical septum) without arterial hypoten-

sion or peripheral signs of shock;
- Low-risk pulmonary embolism: PE without hypotension or peripheral signs of shock or acute pulmonary heart;
- Prolonged bed rest: bed rest for more than three (03) days;
- Long trip: trip lasting more than 5 hours;
- Recent surgery: surgery less than three months;
- Recurrence of VTE: PE, DVT or PE + VTE diagnosed for the second or subsequent time;
- Cost; expenditure incurred on a good or activity;
- Direct cost: expenditure directly related to the disease which may be medical or non-medical;
- Indirect cost: expenditure related to the consequence of the disease. Indirect cost: expenditure related to the consequence of the disease. This is referred to as loss;
- Intangible cost: this is difficult to measure and includes elements such as time, pain etc.
- Total cost: direct cost + indirect cost;
- Very low social class: monthly income less than or equal to 36,270 CFAF;
- Low social class: monthly income above 36,270 CFAF and below 100,000 CFAF;
- Middle social class: monthly income higher than 100,000 CFAF and lower than 200,000 CFAF;
- High social class: monthly income above 200,000 CFAF;
- Bantu: nationals of the central, coastal, eastern and southern regions of Cameroon;
- Semi-Bantu: nationals of the North-West, South-West and West regions;
- Sudanese: nationals of the Adamawa, North and Far North regions of Cameroon.

The variables analysed were the following:
- Socio-demographic variables: age, gender, ethnicity, educational level, occupation, marital status, place of residence, monthly income, health insurance, guarantor.
- Clinical variables: diagnosis, type of pulmonary embolism, length of hospital stay, type of anticoagulation prescribed at discharge, comorbidities.
- Economic variables: direct cost of care (cost of consultation, hospital stay, additional tests and treatment).

The costs of consultation, hospitalisation, complementary examinations and treatment were obtained by multiplying the unit price by the quantities consumed.

2.5. Data Analysis

Data were analyzed using Statistical Package for Social Sciences (SPSS) version 23 software. The Kolmogorov Smirnov test was performed to determine the normality of the distributions of quantitative variables. The quantitative variables were presented as medians and interquartile ranges while the qualitative variables

were presented as counts and percentages. The Kruskal-Walis test was used to calculate the statistical relationship between the median costs and the different variables in a bivariate analysis. A multivariate analysis was used to determine the independent factors influencing the direct cost of VTE management. A 95% confidence interval was considered.

2.6. Ethical Considerations

Research authorizations were obtained from the ethical clearance of the Institutional Ethics Committee of the Université des Montagnes (CIE-UdM) under authorization N˚ 2021/050/UdM/PR/CIE number, the Centre Regional ethics committee for human health research under reference N˚ 1133/CRERSHC/2021 and the administration of the three hospitals in which we conducted our study.

3. Results

During the study period, 6282 cases were identified in the registers of the cardiology departments of the Yaoundé Central Hospital, Yaoundé General Hospital and the Yaoundé Emergency Center. 108 cases of VTE were found, of which 92 cases were included and 16 excluded. Our study population consisted of 92 cases, representing prevalence of 1.5% (Figure 1).

The majority of our study population was made up of females (65.2%); with a male to female sex ratio of 0.53. Their median age was 60 years [48 - 69] with extremes of 30 and 80 years. The most represented level of education was secondary school at 46.7% and more than half of the patients lived in Yaoundé

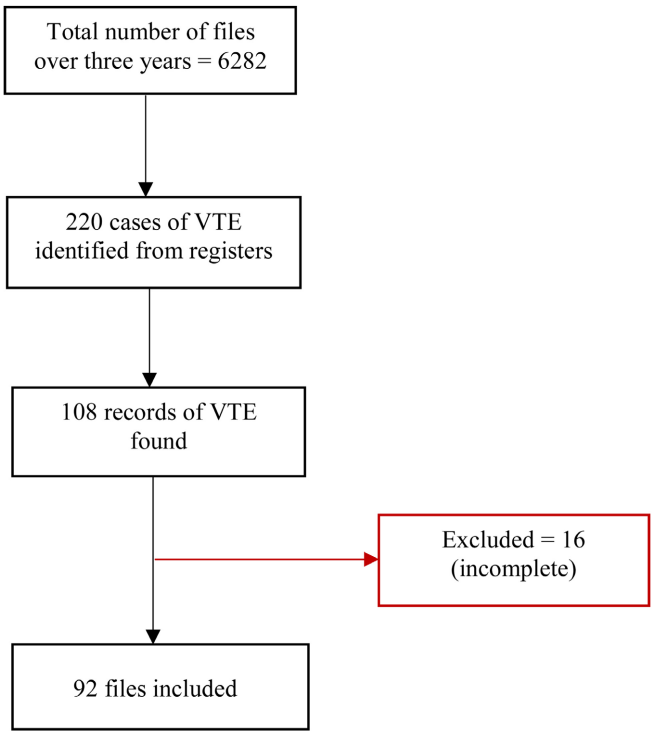

Figure 1. Flow chart of participants.

(83.7%), most of these patients worked in the informal sector (45.7%) and had a family member as a sponsor (80.4%) (Table 1).

In our study, 68.5% of the patients had a monthly income less than or equal to 100,000 CFAF with 26.1% having a monthly income less than or equal to 36,270 CFAF; thus, the majority of our study population belonged to a low or very low social class (68.5%) with 26.1% from a very low social class and 42.4% from a low social class their median income was 55,000 CFAF [35,000 - 172,500] with extremes of 20,000 CFAF and 1,500,000 CFAF (Figure 2).

In this study, only 10.9% of our patients had health insurance. Most patients managed at YEC (69.6%) (Figure 3).

Pulmonary embolism was found in 57.6% of cases; DVT in 29.4% and combined PE + VTE in 13.0%. Recurrence concerned 17.4% of the population. Most

Table 1. Distribution of patients by level of education, place of residence, profession, sponsor and social class.

Variables	Frequency (N = 92)	Percentage (%)
Level of education achieved		
No education	7	7.6
Primary	24	26.1
Secondary	43	46.7
Superior	18	19.6
Place of residence		
Yaoundé	77	83.7
Out of Yaoundé	15	16.3
Profession		
Informal sector	42	45.7
Retired	15	16.3
State employee	13	14.1
Private employee	12	13.0
Housekeeper	10	10.9
Sponsor		
Family member	74	80.4
Myself	14	15.2
Others*	4	4.3
Social class		
Very low	24	26.1
Low	39	42.4
Average	10	10.8
High	19	20.7

*Others = Charities.

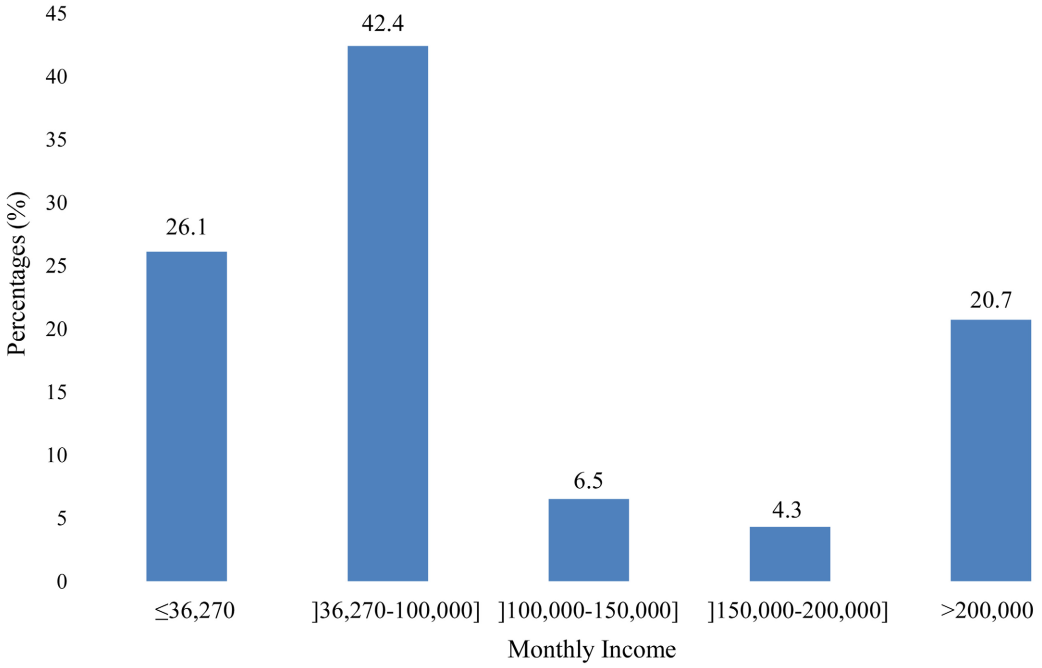

Figure 2. Distribution of patients by monthly income.

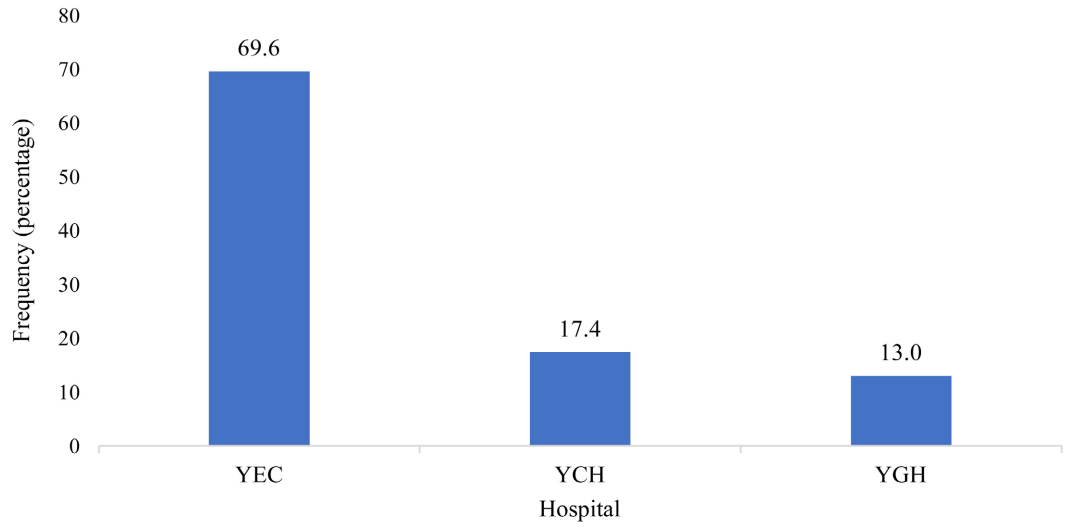

Figure 3. Distribution of patients by hospital.

common comorbidity in our study was hypertension at 63.0% followed by obesity at 59.8% meanwhile, immobilization was the main risk factor for VTE followed by cardiovascular disease at 34.8% and 26.1% respectively. The majority of the patients were hospitalized (95.7%) in the conventional hospital ward (81.2%) and took direct oral anticoagulants on discharge (78.3%). Less than half of them (46.7%) took anticoagulation therapy during 6 months. The median length of stay was 7.5 days [4 - 12] with extremes of 0 and 58 days (Table 2).

The median cost of managing VTE was 766,375 CFAF [536,455 - 1,029,745] or $1415 USD, corresponding to 21 times the SMIG with extremes of 112,376

Table 2. Distribution of patients according to venous thromboembolic event, recurrence, place of care, type of hospital ward and type of pulmonary embolism.

Variables	Frequency (N = 92)	Percentage (%)
Venous thromboembolic event		
Pulmonary embolism	53	57.6
DVT	27	29.4
Pulmonary embolism + DVT	12	13.0
Reoccurence		
Absent	76	82.6
Present	16	17.4
Place of care		
Inpatient	88	95.7
Outpatient	4	4.3
Type of hospital ward		
High class	16	18.8
Classic	69	81.2
Type of anticoagulant prescribed at discharge		
vitamin K antagonists	16	17.4
Direct oral anticoagulants	72	78.3
Direct oral anticoagulants then vitamin K antagonists	4	4.3
Duration of treatment		
3 months	32	34.8
6 months	43	46.7
More than 6 months	17	18.5
Type of pulmonary embolism	**Frequency (N = 65)**	**Percentage (%)**
Massive	26	40.0
Sub-massive	21	32.3
Low risk	18	27.7

and 2,420,000 CFAF. Cost of medication accounted for more than half of expenditure with a median of 490,952 CFAF [218,488 - 578,105] or $906.46 USD. This was followed by the cost of workups and consultations (Table 3). This study revealed that the cost of management of pulmonary embolism was higher than that of deep venous thrombosis. The cost was even highest when both diseases where associated with a median of 860,585 CFAF [758,245 - 938,359] CFAF or $1589 USD (Table 4).

Factors which significantly influenced the direct cost of VTE management were: Being treated in the Yaoundé General Hospital, absence of a health insurance, type of pulmonary embolism and length of hospital stay (Table 5 and Table 6).

Table 3. Cost per consumption item.

Variables	Median Cost (IQR) (FCFA)	Minimum (FCFA)	Maximum (FCFA)
Cost of consultations	105,000 [5200 - 20,000]	0	70,000
Cost of hospital stay	76,500 [42,000 - 149,500]	0	809,500
Cost of workups	233,575 [153,175 - 283,500]	26,640	385,750
Cost of medications	490,952 [218,488 - 578,105]	62,176	1,940,000
Total (direct cost)	**766,375 [536,455 - 1,029,745]**	**112,376**	**2,420,000**

Table 4. Cost by venous thromboembolic event.

Variables	Median Cost (IQR) (CFAF)	Minimum (CFAF)	Maximum (CFAF)
Pulmonary embolism	837,170 [575,196 - 1,075,720]	150,920	2,420,000
Deep veinous thrombosis	540,710 [426,300 - 831,050]	112,376	2,190,000
Pulmonary embolism + Deep veinous thrombosis	860,585 [758,245 - 938,359]	208,543	1,950,000

4. Discussion

4.1. Sociodemographic Data

In our study, the prevalence of VTE was 1.5%. This result is similar to that found by Nkoke *et al.* in 2020 in Cameroon [1] and close to the 1.6% found by Etoundi *et al.* in 2015 [2] also in Cameroon and the 1.7% found by Diall *et al.* in Mali in 2011 [11]. However, it is higher than the 1.15% found by Enyengue *et al.* in Mali in 2021 [12] this could be explained by the fact that most of the patients treated for VTE did not have confirmatory workups, therefore leading to smaller sample size. However, Palud *et al.* in France found a prevalence of 42.6% [13]. This could be explained by the fact that the European population is older and therefore at greater risk of developing VTE. The female sex predominated at 65.2%. This value is similar to that obtained by Nkoke *et al.* in Cameroon in 2020 [14], by Coulibaly *et al.* in Mali [15] and Hodkinson KE and Mahlangu JN in South Africa in 2017 [16]. It is also similar to that obtained by Spencer *et al.* in the United States [17]. This female predominance was classic in the literature and could be explained by risk factors specific to the female gender. In our study, the median age of our patients was 60 years (48 - 69). This value is higher than that found by Diall *et al.* and Coulibaly *et al.* all in Mali who found a mean age of (51 ± 16.9) years and (54 ± 17.8) years, respectively [11] [15] and is similar to that found by Fanikos *et al.* [18]. This value could be explained by the fact that the incidence of VTE increases with age. However, it is different from the 46 years (38 - 57) found by Hodkinson KE and Mahlangu JN in South Africa [16] and the 40 years (19 - 90) found by Goldstein and Wu [19]. This could be explained by the fact that HIV, the main risk factor for VTE, was more common in patients

Table 5. Multivariate analysis of factors associted to the cost of management of VTE.

Variables	Direct cost median [IQR]	*Adjusted p-value*
Hospital structure		
YEC	772,858 [469,021 - 1,029,745]	
YCH	601,251 [536,455 - 834,860]	**0.015**
YGH	1,021,823 [782,994 - 1,525,508]	
Health insurance		
Not insured	817,723 [573,388 - 1,046,305]	**<0.001**
Insured	324,289 [192,903 - 508,089]	
Type of pulmonary embolism		
Massive	1,102,145 [644,399 - 1,493,623]	
Sub-massive	864,150 [740,330 - 1,040,998]	**0.021**
Low risk	669,263 [454,458 - 939,981]	
Venous thromboembolic event		
PE	837,170 [575,196 - 1,075,720]	
DVT	540,710 [426,300 - 831,050]	0.739
PE + DVT	860,585 [758,245 - 938,359]	
Type of anticoagulant prescribed at discharge		
Vitamine K antagonists	529,728 [430,410 - 568,075]	
DOA	843,128 [635,940 - 1,056,719]	0.161
DOA then AVK	979,805 [616,501 - 1,192,708]	
Reoccurence		
Present	1,102,145 [608,066 - 1,517,235]	0.395
Absent	757,705 [469,021 - 936,055]	

Table 6. Correlation between age, number of consultations, length of hospital stays and direct cost.

Variables	Correlation coefficient (R)	P-value
Age	0.091	0.388
Number of consultations	0.002	0.985
Length of stay in hospital	0.462	**0.001**

around this age. The median age of 60 years found in our study was lower than the 65 years found by Spencer *et al.* in the United States [17], which could be explained by the fact that the American population is ageing and its patients have more risk factors for VTE. In our study, 83.7% of the patients lived in the city of

Yaoundé which is an urban area. This result is lower than that found by Diall *et al.* in Mali who found 93% of patients living in urban areas [11]; this could be explained by the fact that in our study patients were classified according to their residence, either in Yaoundé or out of Yaoundé. It could be that patients residing outside Yaoundé came from other urban areas of the country and also that those in rural areas were not diagnosed due to lack of doctors in these areas or lack of financial means to travel to the city. In our study, the sponsor was the family in 80.4% of cases. This could be explained by the fact that the study population belonged for the most part to the lower social class corresponding to a monthly income of less than 100,000 FCFA, which does not allow them to pay for their care alone. In our study, only 10.9% of patients had health insurance. This rate is higher than the 7% found in 2018 by Okoulouma in Cameroon [10]. This low rate of health insurance could be explained by the fact that subscriptions to insurance companies are expensive, so inaccessible to our patients belonging mostly to the lower social class. More than half of our patients were treated at Yaoundé Emergency Center (69.6%). This could be explained by the fact that the YEC is responsible for receiving patients with a life-threatening prognosis; that is, patients in severe distress suffering from a myocardial infarction, a pulmonary embolism or suffering from various fractures following an accident. It is a specialist hospital for emergencies. As such, it receives many suspect patients referred from other hospitals.

4.2. Clinical Data

Most patients in our study had pulmonary embolism (57.6%) followed by DVT (29.3%) and finally pulmonary embolism associated with DVT (13.0%). This predominance of pulmonary embolism is similar to the result found by Coulibaly *et al.* in Mali [15] and that of Fofana *et al.* also in Mali [20] who found more pulmonary embolism in their studies. This result is nevertheless different from the results found by Spencer *et al.* [17], Bullano *et al.* [21] in the United States and Goldstein and Wu in South Africa, as well as those obtained by Etoundi *et al.* [2] and Nkoke *et al.* in Cameroon, who obtained mostly DVT [1]. This could be explained by the fact that their populations were younger. Therefore, DVT being the prerogative of the young subject makes this result understandable. The recurrence rate in our study was 17.4%. This result is close to that found by Spencer *et al.* in the United States [17] in two successive cohorts, but is lower than the 27.1% to 44.3% and 50.7% to 57.8% found by Spyropoulos and Lin in the United States [22] respectively at 30 and 90 days follow-up and the 21% found by Hansson *et al.* at 5 years follow-up [23]. This could be explained by the fact that unlike their studies, we did not use the same approach to assess recurrence in our study. The assessment of recurrence at 30 days and 8 years would explain the 5% and 30% obtained by Bullano *et al.* in the United States [21] respectively. In our study, the median length of hospital stay was 7.5 days (4 - 12). This result is close to that found by Nkoke *et al.* in Cameroon [1], but different

from the 15 days found by Diall *et al*. in Senegal and the 14 days (4 - 36) found by Goldstein and Wu in South Africa. This could be explained by the fact that the relay of anticoagulation in these patients was done by AVK, which would require an increase in the duration of hospitalization in order to obtain the desirable INR margin before discharge. In our study, most of our patients were receiving DOAs (78.3%), a result similar to that found by Eyengue in Mali [12]. In contrast to our study, all patients in the studies by Diall *et al*. in Mali [11] and Nkoke *et al*. in Cameroon [1] were treated with LMWH followed by VKA. In accordance with the literature, DOAs were the first-line treatment, which justifies their extensive use in our study. In our study, the majority of patients received anti-coagulant therapy for 6 months, *i.e*. 46.7%. This could be explained by the fact that most of our patients had VTE for which the risk factor had not been determined, thus reducing the duration of treatment to at least 6 months. Hypertension was the main comorbidity. This result is similar to the one found by Coulibaly *et al*. in Mali in 2018 [15] and to the one found by Fofana *et al*. also in Mali in 2019 [20]. It is however different from the one obtained by Etoundi *et al*. in Cameroon in 2015 who found obesity as the main comorbidity. This could be due to the fact that the risk of developing hypertension increases with age and that our study population consisted of older patients compared to theirs, thus justifying this difference. Immobilization was the main risk factor for VTE. This result is similar to that found by Abah *et al*. in Cameroon [24] and that found by Enyegue in Mali [12] but differs from that found by Coulibaly *et al*. who found cardiovascular disease as the main risk factor for VTE [15].

4.3. Data on Cost

In our study, the median cost of management of VTE was 766,375 FCFA (536,455 - 1,029,745) FCFA with extremes of 112,376 FCFA and 2,420,000 FCFA. This result is higher than the 600,000 FCFA reported by Pessinaba *et al.* in Togo in 2017 [7]. This could be explained by the fact that the anticoagulation protocol in their study was LMWH followed by VKA; a treatment regimen that would cost less than OADs and therefore make management less expensive. Our result is much lower than the $20,000 US (10,820,000 FCFA) reported by Dobesh in the USA [25]. This could be explained by the difference in the technical platform and the standard of living. The median direct cost of managing pulmonary embolism was 837,170 FCFA (575,196 - 1,075,720) FCFA or $1558.69 USD. This result is lower than the $16,644 USD found by Spyropoulos and Lin in the United States [22] and the $4040 USD (2,206,100 CFAF) found by Annemans *et al.* in Belgium [26]. As for deep vein thrombosis, the median cost of treatment found in our study was 540,710 CFAF [426,300 - 831,050] or $1006.72 USD, in contrast to the $10,804 USD found by Spyropoulos and Lin in the United States [22]. This could be explained by the high standard of living of the American population compared to ours. In our study, the cost of treatment constituted the largest proportion of expenditure for the management of VTE. This

result is contrary to that found by Fanikos *et al.* [18], which may be explained by the fact that in their studies only in-hospital costs were considered.

In our study, the cost of VTE management was influenced by the hospital structure ($p = 0.015$); indeed, management at the Yaoundé General Hospital was more expensive. This could be due to the higher costs of consultation and hospitalization, especially in intensive care, compared to the other two hospitals. Health insurance was one of the factors influencing the direct cost of VTE management ($p < 0.001$). Patients who were uninsured spent more in our study. This could be explained by the fact that being uninsured required paying the full cost while the insured paid just 20% of the total expenses. Our study showed that the type of embolism was a factor influencing the direct cost of VTE management ($p = 0.021$): patients with massive pulmonary embolism spent more. This could be explained by the fact that these patients spent more time in intensive care, where hospitalization costs are higher. The length of hospital stay in our study was a factor influencing the direct cost of VTE management ($p = 0.001$). This could be explained by the accumulation of hospital costs. The small sample size could explain why the type of anticoagulant prescribed at discharge was not a factor influencing the direct cost of VTE management, contrary to the results found by Clay *et al.* in England [27] and Yang and Wu in China [28]. This small sample size would also explain why recurrence did not influence the direct cost of VTE management in this study, contrary to the literature.

5. Limitations of the Study

The limitations of our study were as follows:

- Data on cost in most cases was obtained from the patient or his guardian and not the sponsor, constituting a bias.
- The retrospective nature of the study makes it difficult to access all the data.
- This study was not extended to private hospitals.
- The poor quality of the archive restricted us to a small sample as many of the files could not be found.

6. Conclusion

Managing VTE in Yaoundé is expensive. The cost was independently associated with the hospital facility, existence of health insurance, type of VTE and length of hospital stay. It is urgent to establish universal health coverage in order to reduce the financial burden of the management of VTE on families.

Disclosures

The authors declare that this work is devoid of any conflict of interest.

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