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Epidemiological, Clinical and Therapeutic Patterns of Venous Thromboembolic Disease in Cancer Patients Followed up in Two Reference Hospitals in Cameroon

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Abstract

Background: Cancer increases the incidence of venous thromboembolic disease (VTE), which represents a significant cause of morbidity, mortality, and economic burden in cancer patients. **Objective:** We aimed to describe the epidemiologic, clinical, and therapeutic pattern of VTE in cancer patients followed-up in two reference hospitals in Cameroon over the past ten years. **Methods:** This was a cross-sectional retrospective study conducted in the oncology department of the General hospitals of Yaoundé and Douala. We included the medical records of all patients aged 18 years and above who had active cancer with a confirmed diagnosis of VTE from 2010 to 2021. **Results:** We analysed 408 patients' medical records. The prevalence of VTE was 7.6%. All those having VTE had solid tumours. There were twenty (64.5%) cases of deep venous thrombosis, five (16.1%) cases of pulmonary embolism, and three (9.7%) cases of both. Poor performance status and chemotherapy were independently associated with the development of VTE. Most of the patients were treated with compression stockings and low molecular weight heparin. **Conclusion:** VTE prevalence is high among cancer patients in Cameroon. It is most frequent in solid tumours originating from the genitourinary system, the lung, the pancreas, and the brain.

Keywords

Venous Thromboembolic Disease, Cancer, Cameroon

1. Introduction

Venous thromboembolic disease (VTE) is a multifactorial disease involving the development of blood clots in veins with or without inflammation. It includes two entities: deep venous thrombosis (DVT) and pulmonary embolism (PE). The major underlying factors, hypercoagulability, haemodynamic changes, and endothelial injury, are known as the Virchow triad from the German physician who described them in the 19th century [1]. Many conditions such as surgery, cancer, trauma, and immobilisation can cause one or more of these alterations [2]. Thrombosis associated with cancer, known as Trousseau's syndrome, was first described by the renowned French physician Armand Trousseau in 1865 [3]. VTE represents a significant cause of morbidity, mortality, and economic burden in cancer patients. The incidence of VTE is increased about six-fold in cancer patients [4]. It is the highest in the case of metastatic disease at diagnosis and fast-growing and biologically aggressive cancers. The incidence is also the highest in the first few months following the diagnosis and may reflect the biology of the tumour or medical interventions such as major surgery and chemotherapy [5]. Other risk factors include advanced age, obesity, comorbidities, primary tumour site, and histologic subtype of cancer [6] [7]. The occurrence of VTE can interrupt essential cancer therapy and cause severe bleeding complications [8]. It also represents the second leading cause of death in cancer patients after the underlying cancer progression [9]. The prothrombotic state caused by cancer is a consequence of tumour and patient-specific factors, including vascular compression, vessel injury, and blood hypercoagulability. The last can result from direct activation of pro-coagulant pathways by cancer cells involving aberrant expression of tissue factor, the release of tumour-derived tissue factor-bearing microparticles, and expression of cell surface proteases that modulate fibrinolytic pathways. Indirect pro-coagulant effects result from the enhanced formation of neutrophil extracellular traps and altered expression of pro-inflammatory cytokines and coagulation factors [8]. There is a scarcity of data regarding cancer and VTE in our country. We, therefore, aimed to describe the epidemiological, clinical, and therapeutic pattern of VTE in cancer patients followed-up in two reference hospitals in Cameroon.

2. Methods

2.1. Study Design and Setting

This was a retrospective cross-sectional study conducted in the oncology department of the General Hospitals of Yaoundé and Douala. It lasted eight months (from January to August 2021) and included ten years spanning from

January 2010 to May 2021.

2.2. Participants

We included the medical records of all patients aged 18 years and above who had active cancer with a diagnosis of VTE confirmed by Doppler-echography or chest CT angiography. Incomplete medical records and cases of thrombosis of a central venous catheter or catheter port were excluded from the study.

2.3. Data Collection

All the data were consecutively collected from the patients' medical records. They included sociodemographic information (age and gender), VTE risk factors (history of VTE, obesity, smoking, chronic kidney disease and recent surgery), cancer-related information (type, extension, biology and treatments), and type of VTE, location, diagnostic methods used and treatments. The data were compiled using Census and Survey Processing System (CSPro) software version 7.2 for Windows®.

A Doppler ultrasound confirmed DVT, and PE was confirmed by thoracic CT angiography.

2.4. Statistical Analysis

Statistical Package for Social Sciences (SPSS) software version 20 for Windows® was used for all statistical analysis. Odds-ratio was calculated to approximate relative risk with 95% confidence intervals. A multiple logistic regression model was used to determine independent factors independently associated with VTE. A P-value of less than 0.05 was considered statistically significant.

3. Results

We found that 408 patients followed up for cancer during the study period. Thirty-one of them had a confirmed diagnosis of VTE. The prevalence of 7.6% of VTE among cancer patients was estimated. The mean age was 51 ± 18 years, and the sex ratio was 0.35.

All the patients with VTE had solid cancers, and the most represented primary tumours were located in the uterus (25.7%), the prostate (12.9%) and the lung (9.7%) (Table 1). Carcinoma was the most frequent histologic subtype of cancer, and most of the patients had metastatic disease.

Table 2 shows the type of VTE disease in our study population. Most of the patients with VTE had DVT (74.2%). In three cases, most DVT was proximal and associated with pulmonary embolism (9.7%). Only three (9.7%) patients had bilateral DVT.

In Table 3, we present the factors associated with the occurrence of VTE. Best rest and chemotherapy administered in the month preceding the diagnosis of VTE were the only factors independently associated with the development of VTE in this study population.

Table 1. Characteristics of cancers in our study population.

Variables	Count	Frequency (%)
Primary site of the tumour		
Uterus	8	25.7
Prostate	4	12.9
Lung	3	9.7
Ovaries	2	6.5
Pancreas	2	6.5
Brain	2	6.5
Bone	2	6.5
Others*	8	25.7
Total	31	100
Histology		
Carcinoma	23	74.2
Others**	8	25.8
Total	31	100
Extension of cancer		
Localised	5	16.1
Locally advanced	6	19.4
Metastatic	20	64.5
Total	31	100
Treatment options		
Chemotherapy	24	77.4
Surgery	2	6.5
Radiation	2	6.5
Total	28	90.4

*liver, kidney, skin, lymphoma, colon, breast, stomach; **sarcoma, lymphoma, melanoma.

Table 2. Differents types and sites of VTE.

Variables	Count	Frequency (%)
DVT	23	74.2
Proximal	11	35.5
Distal	9	29.0
Bilateral	3	9.7
Isolated PE	5	16.1
VTE (DVT + PE)	3	9.7
Total	31	100

DVT: deep venous thrombosis; PE: pulmonary embolism.

Practically, 80.6% of patients were using compression stockings. Two-thirds of cancer patients were treated with low molecular weight heparin, one-third with anti-vitamin K drugs and only 16.1% with direct oral anticoagulants (**Table 4**).

Table 3. Multivariate analysis of factors associated with the occurrence of VTE in the study population compared to patients who did not develop VTE.

Items	OR (95% CI)	P
Low-performance status*	11.7 (3.1 - 44.1)	**<0.001**
Chemotherapy	351.8 (36.2 - 3413.6)	**<0.001**
Metastatic disease	1.4 (0.4 - 4.5)	0.554
History of VTE	/	0.999

*WHO stage 3 or 4. OR: odds-ratio. CI: confidence interval.

Table 4. Treatment of VTE in cancer patients.

Items	Count	Frequency (%)
Compression stockings	25	80.6
LMWH	20	64.5
AVK	9	29.0
DOACs	5	16.1

LMWH: Low molecular weight heparin; AVK: anti-vitamin K; DOACs: direct oral anticoagulants.

4. Discussion

This study aimed to describe the epidemiological, clinical and therapeutic patterns of VTE in cancers patients followed up in two reference hospitals in Cameroon in light of the data available in the literature.

We found a VTE prevalence of 7.6% among all cancer patients. This is close to results previously reported by other research [10] [11] [12]. All those who developed VTE had solid tumours with primary sites being the genitourinary system, the lung, the pancreas and the brain. Previous studies found similar findings [6] [11]. In our research, the genitourinary system came in the first position and was dominated by uterine cancer, specifically cancer of the cervix. The predominance of the female gender may explain this in our sample and the high prevalence of cervical cancer in sub-Saharan Africa [13]. About two-thirds of the patients had a metastatic tumour. The presence of the metastatic disease has been associated with VTE development. In our study, it failed to reach statistical significance after multivariate analysis, but Mulder *et al.* recently found in a study based on Danish medical registries that the presence of metastasis increased the incidence of VTE in cancer patients [14] significantly. They also reported prior VTE as a risk factor which we found was not associated with VTE. High platelet level was reported as a risk factor by Khorana *et al.* in 2008 and Simanek *et al.* one year later, but we did not find a significant association in our study [12] [15]. We found that chemotherapy and low-performance status were the two factors independently associated with VTE development in our sample. For chemotherapy, it is similar to what was previously reported [6] [11] [14]. Although they had a sample different from ours, Guven *et al.* found that patients with metastatic cancer treated with immunotherapy who had a poor perform-

ance status also had an increased risk of thromboembolism [16]. This factor, therefore, need to be taken into account when assessing the thromboembolic risk of cancer patients. Almost all the patients with VTE were prescribed compression stockings, and most of them received low molecular weight heparin (LMWH), sometimes followed by anti-vitamin K drugs (AVK). Only a few of them received direct oral anticoagulants (DOACs). There is only a little evidence concerning the use of DOACs in cancer patients. The AMPLIFY trial published in 2015 concluded that apixaban was a convenient option for cancer patients with VTE [17]. The 2018 guidelines of the International Society on Thrombosis and Haemostasis suggest the use of specific DOACs for cancer patients with an acute diagnosis of VTE, a low risk of bleeding, and no drug-drug interactions with current systemic therapy [18]. Globally the result of this study does not differ too much from what is found in the literature.

The main limitation of this study was its retrospective design. We were unable to get the incidence rate of VTE and determine whether it was highest during the first few months after the cancer diagnosis, as described in many studies.

5. Conclusion

VTE prevalence is high among cancer patients in Cameroon. It is most frequent in solid tumours originating from the genitourinary system, the lung, the pancreas, and the brain. Development of VTE is independently associated with poor performance status and chemotherapy. Most of the patients were treated with LMWH ± AVK, with a few receiving DOACs.

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Authors' Contribution

Conception and design: Chris Nadège Nganou-Gnindjio, Alain PatrickMenanga.
Data collection: Chris Nadège Nganou-Gnindjio, Huguette Atangana Ekobo, Etienne Atangana Okobalemba, Lade Viche, Félicité Kamdem.
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Manuscript drafting: Chris Nadège Nganou-Gnindjio, Dieudonné Danwe.
Manuscript revision: all the authors.
Approval of the final manuscript: all the authors.

Availability of Data and Materials

The datasets used for this study are available from the corresponding author on request.

Ethical Approval and Consent to Participate

The study was approved by the Institutional Ethical Review Board of the Faculty

of Medicine and Biomedical of the University Yaoundé I (Cameroon). Individual informed consent was also obtained from the participants, and all the principles of the declaration of Helsinki were respected.

Competing Interest

The authors declare that they have no competing interests.

References

[1] Louw, V.J. and Ntusi, N.A.B. (2019) Virchow's Triad Revisited. *South African Medical Association*, **109**, 822-823. https://doi.org/10.7196/SAMJ.2019.v109i11.14442

[2] Riva, N., Donadini, M.P. and Ageno, W. (2015) Epidemiology and Pathophysiology of Venous Thromboembolism: Similarities with Atherothrombosis and the Role of Inflammation. *Thromb Haemost*, **113**, 1176-1183. https://doi.org/10.1160/TH14-06-0563

[3] Metharom, P., Falasca, M. and Berndt, M.C. (2019) The History of Armand Trousseau and Cancer-Associated Thrombosis. *Cancers*, **11**, Article 158. https://doi.org/10.3390/cancers11020158

[4] Geerts, W.H., Bergqvist, D., Pineo, G.F., Heit, J.A., Samama, C.M., Lassen, M.R., *et al*. (2008) Prevention of Venous Thromboembolism. *Chest*, **133**, 132S-175S. https://doi.org/10.1378/chest.08-0656

[5] Wun, T. and White, R.H. (2009) Epidemiology of Cancer-Related Venous Thromboembolism. *Best Practice & Research Clinical Haematology*, **22**, 9-23. https://doi.org/10.1016/j.beha.2008.12.001

[6] Khorana, A.A., Francis, C.W., Culakova, E., Kuderer, N.M. and Lyman, G.H. (2007) Frequency, Risk Factors, and Trends for Venous Thromboembolism among Hospitalised Cancer Patients. *Cancer*, **110**, 2339-2346. https://doi.org/10.1002/cncr.23062

[7] Blom, J.W., Doggen, C.J.M., Osanto, S. and Rosendaal, F.R. (2005) Malignancies, Prothrombotic Mutations, and the Risk of Venous Thrombosis. *The Journal of the American Medical Association*, **293**, 715-722. https://doi.org/10.1001/jama.293.6.715

[8] Donnellan, E., Kevane, B., Bird, B.R.H. and Ni Ainle, F. (2014) Cancer and Venous Thromboembolic Disease: From Molecular Mechanisms to Clinical Management. *Current Oncology*, **21**, 134-143. https://doi.org/10.3747/co.21.1864

[9] Khorana, A.A., Francis, C.W., Culakova, E., Kuderer, N.M. and Lyman, G.H. (2007) Thromboembolism Is a Leading Cause of Death in Cancer Patients Receiving Outpatient Chemotherapy. *Journal of Thrombosis and Haemostasis*, **5**, 632-634. https://doi.org/10.1111/j.1538-7836.2007.02374.x

[10] Ay, C., Dunkler, D., Marosi, C., Chiriac, A.-L., Vormittag, R., Simanek, R., *et al*. (2010) Prediction of Venous Thromboembolism in Cancer Patients. *Blood*, **116**, 5377-5382. https://doi.org/10.1182/blood-2010-02-270116

[11] Cronin-Fenton, D.P., Søndergaard, F., Pedersen, L.A., Fryzek, J.P., Cetin, K., Acquavella, J., *et al*. (2010) Hospitalisation for Venous Thromboembolism in Cancer Patients and the General Population: A Population-Based Cohort Study in Denmark, 1997-2006. *British Journal of Cancer*, **103**, 947-953. https://doi.org/10.1038/sj.bjc.6605883

[12] Simanek, R., Vormittag, R., Ay, C., Alguel, G., Dunkler, D., Schwarzinger, I., *et al*. (2010) High Platelet Count Associated with Venous Thromboembolism in Cancer

Patients: Results from the Vienna Cancer and Thrombosis Study (CATS). *Journal of Thrombosis and Haemostasis*, **8**, 114-120. https://doi.org/10.1111/j.1538-7836.2009.03680.x

[13] Jedy-Agba, E., Joko, W.Y., Liu, B., Buziba, N.G., Borok, M., Korir, A., *et al*. (2020) Trends in Cervical Cancer Incidence in Sub-Saharan Africa. *British Journal of Cancer*, **123**, 148-154. https://doi.org/10.1038/s41416-020-0831-9

[14] Mulder, F.I., Horváth-Puhó, E., van Es, N., van Laarhoven, H.W.M., Pedersen, L., Moik, F., *et al*. (2021) Venous Thromboembolism in Cancer Patients: A Population-Based Cohort Study. *Blood*, **137**, 1959-1969. https://doi.org/10.1182/blood.2020007338

[15] Khorana, A.A., Kuderer, N.M., Culakova, E., Lyman, G.H. and Francis, C.W. (2008) Development and Validation of a Predictive Model for Chemotherapy-Associated Thrombosis. *Blood*, **111**, 4902-4907. https://doi.org/10.1182/blood-2007-10-116327

[16] Guven, D.C., Aksun, M.S., Sahin, T.K. *et al*. (2021) Poorer Baseline Performance Status Is Associated with Increased Thromboembolism Risk in Metastatic Cancer Patients Treated with Immunotherapy. *Supportive Care in Cancer*, **29**, 5417-5423. https://doi.org/10.1007/s00520-021-06139-3

[17] Agnelli, G., Buller, H.R., Cohen, A., Gallus, A.S., Lee, T.C., Pak, R., *et al*. (2015) Oral Apixaban for the Treatment of Venous Thromboembolism in Cancer Patients: Results from the AMPLIFY Trial. *Journal of Thrombosis and Haemostasis*, **13**, 2187-2191. https://doi.org/10.1111/jth.13153

[18] Khorana, A.A., Noble, S., Lee, A.Y.Y., Soff, G., Meyer, G., O'Connell, C., *et al*. (2018) Role of Direct Oral Anticoagulants in the Treatment of Cancer-Associated Venous Thromboembolism: Guidance from the SSC of the ISTH. *Journal of Thrombosis and Haemostasis*, **16**, 1891-1894. https://doi.org/10.1111/jth.14219