

Factors Associated with Venous Thromboembolic Disease in a Group of Sub-Saharan African Population Followed-Up for Cervical Cancer in an Urban Setting

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How to cite this paper: Nganou-Gnindjio, C.N., Hamadou, B., Okobalemba, E.A., Oumbe, R.M., Ebong, C., Yondo, J., Ndobu, J.V. and Meka, E. (2026) Factors Associated with Venous Thromboembolic Disease in a Group of Sub-Saharan African Population Followed-Up for Cervical Cancer in an Urban Setting. *World Journal of Cardiovascular Diseases*, **16**, 147-154.

<https://doi.org/10.4236/wjcd.2026.162015>

Received: December 27, 2025

Accepted: February 25, 2026

Published: February 28, 2026

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Abstract

Background: Venous thromboembolic disease (VTE), including deep vein thrombosis and pulmonary embolism, is a common complication of cancer which significantly increases its morbidity and mortality rates. Very few studies in our context have focused on this complication in cervical cancer. **Objective:** The main aim of this study was to assess the prevalence of VTE as well as associated factors in patients followed up for cervical cancer in 3 hospitals in Yaoundé. **Methods:** This was a 5-year retrospective cross-sectional study from 2020-2024 carried out at the Yaoundé General, Central and Gynaeco-Obstetrics and Pediatric Hospitals. The patients included were those with a confirmed diagnosis of cervical cancer who were being followed up at one of the 3 study sites. Data, including sociodemographic, clinical, and risk factors for VTE, and information about VTE were collected from medical records from January 1 to August 31, 2024. Additional information was obtained by phone call after obtaining informed consent from the participants. The data analysis was done using the R software. Odds ratios and their 95% confidence intervals were used to assess the associations between the factors studied. The significance threshold was set at a p-value of less than 0.05. Logistic regression was done to eliminate confounding factors. **Results:** We included 200 patients. The average age of our population was 53.8 ± 12 years, with extremes of 25 and 94 years. The prevalence of VTE was 13.5% (27/200). Factors significantly associated with the occurrence of VTE were age greater than 40 years (OR = 3.84; 95% CI = 1.55, 9.33; P = 0.003), obesity (OR = 1.09; 95% CI = 1.03, 1.58;

P = 0.010), and advanced cancer stage (OR=9.31; 95% CI= 1.21, 88.0; P = 0.039). **Conclusion:** This study shows that VTE is highly prevalent in patients with cervical cancer in our population, mostly in women over 40 years, obese and at advanced stages of cancer.

Keywords

Cervical Cancer, Venous Thromboembolic Diseases, Yaoundé

1. Introduction

Cervical cancer is a significant public health challenge in developing countries which bear the highest incidence and mortality rates [1]. Sub-Saharan Africa in particular carries a disproportionately high burden accounting for 15.7% of all new cancer cases [2]. In Cameroon, more than 2500 new cases of cervical cancer were registered in 2022 amongst which 1852 died [3]. Several factors contribute to death in cervical cancer including local progression of the disease, metastasis and related complications like venous thromboembolism (VTE) [4]. VTE is a clinical entity that regroups deep venous thrombosis and pulmonary embolism. It is a common complication in cancer patients due to hypercoagulability status, chronic inflammation and vascular stasis, which create a favorable milieu for its development [5]. Also, venous compression due to tumor size and anticancer treatment contributes to the high incidence of VTE, especially in cervical cancer. Though the incidence of VTE in cervical cancer is well known worldwide [6] [7], very few observational studies in sub-Saharan Africa have reported the factors associated with its occurrence in this specific population. Thus, the aim of our study was to assess the prevalence of VTE as well as associated factors in patients followed up for cervical cancer in Yaoundé.

2. Methodology

2.1. Study Design and Setting

This was a hospital-based cross sectional study performed in two hospitals of Yaoundé Cameroon after revision and approval of the study protocol by the local Ethics and Research Committee (N°634/CIERSH/DM/2024). Study participants were recruited in the Oncology and Gynaeco-obstetric units of the Yaoundé Central Hospital, the Yaoundé General Hospital and Yaoundé Gynaeco obstetric and Pediatric Hospital from January to August 2024.

2.2. Study Population

All consecutive patients who were followed up exclusively for cervical cancer in one of the 3 study sites and who had given their informed consent were included in the study. Patients with incomplete medical files were excluded.

2.3. Data Collection

The data collected using a pre-established questionnaire included sociodemographic characteristics of participants (age, profession, region of origin, matrimonial status, educational level), clinical data about cancer (associated comorbidities like HIV, hepatitis B, type and histologic stage of cancer, treatment received, delay from diagnosis to treatment), risk factors for VTE (past history of VTE, obesity, smoking, hypertension, diabetes, chronic kidney disease, recent surgery, immobilization and absence of preventive therapy) as well as data about VTE (type, localizations, symptoms and signs, diagnostic method, paraclinical data, delay from the diagnosis of cancer to that of VTE and treatment initiation) were collected from medical records from January 1 to August 31, 2024. Additional information was obtained by phone call after obtaining informed consent from the participants.

2.4. Statistical Analysis

The data obtained during the study period were inserted and analyzed using the R software. The qualitative variables were expressed in frequency and percentages and were compared using Chi-square or Fischer exact tests as needed. The quantitative variables were expressed in terms of means and standard deviation in the case of a normal distribution, or medians and interquartile ranges otherwise. Odds ratios and their 95% confidence intervals were used to assess the associations between the factors studied. Logistic regression was performed to eliminate confounding factors. A p-value < 0.05 was used to define statistical significance.

3. Results

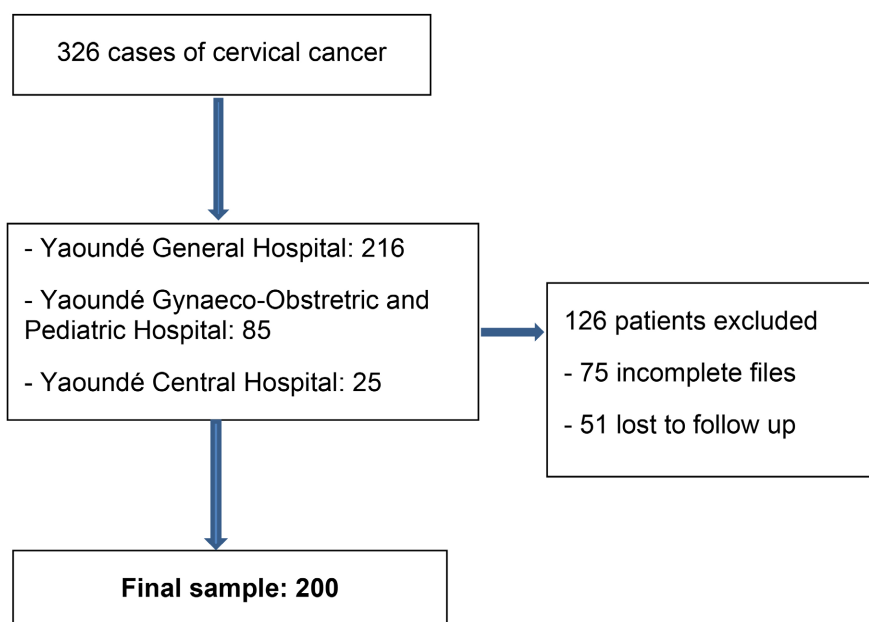
During our study period, we found 326 medical files of patients with a diagnosis of cervical cancer notably 25 in the Yaoundé Central Hospital, 216 in the Yaoundé General Hospital and 85 in the Yaoundé Gynaeco obstetric and Pediatric Hospital (**Figure 1**). The average age of our population was 53.8 ± 12 years, with extremes of 25 and 94 years and modal age group of 55 - 95 years. The participants were mostly married, housewives with an average level of education (**Table 1**). The prevalence of VTE was 13.5% (27/200), amongst which 20 were deep venous thrombosis cases and 7 pulmonary embolisms. Very little number of patients (7) had the diagnosis of VTE contemporary to that of cervical cancer. Factors significantly associated with the occurrence of VTE (**Table 2**) were age greater than 40 years (OR = 3.84; 95% CI = 1.55, 9.33; P = 0.003), obesity (OR = 1.09; 95% CI = 1.03, 1.58; P = 0.010), and advanced cancer stage (OR = 9.31; 95% CI = 1.21, 88.0; P = 0.039). The diagnostic methods were mostly Doppler ultrasound (55.5%) for deep venous thrombosis; rarely angioCT scan (7.4%), but mostly clinical suspicion (29.7%) for pulmonary embolism according to the Wells score (**Table 1**). With regards to management of VTE, 48.1% of patients were placed on low molecular weight heparin and the rest (51.8%) on oral anticoagulation plus compression stockings (63%). More than half (51.8%) of the patients presenting with VTE died.

Table 1. Clinical and paraclinical characteristics of participants.

| Variables | |
|-----------------------------------|------------|
| Mean age (SD), years | 53.8 (12) |
| Matrimonial status, n(%) | |
| Married | 75 (37.5) |
| Single | 46 (23.0) |
| Widow | 36 (19.5) |
| Fianced | 36 (18.0) |
| Divorced | 4 (2.0) |
| Profession, n(%) | |
| Housewife | 120 (60.0) |
| Private sector | 53 (26.5) |
| Public sector | 20 (10.0) |
| Retired | 4 (2.0) |
| Student | 3 (1.5) |
| Level of education, n(%) | |
| None | 2 (1.0) |
| Primary | 70 (35.0) |
| Secondary | 92 (46.0) |
| University | 36 (18.0) |
| Type of VTE, n(%) | |
| DVT | 20 (74.1) |
| PE | 7 (25.9) |
| Diagnostic method, n(%) | |
| Venous doppler ultrasound | 15 (55.5) |
| Clinical scores | 8 (29.7) |
| AngioCT scan | 2 (7.4) |
| D-Dimers | 2 (7.4) |
| Treatment modality, n(%) | |
| LMWH | 13 (48.1) |
| Oral anticoagulants | 14 (51.8) |
| Compression stockings | 17 (62.9) |
| Short term evolution, n(%) | |
| Favorable | 13 (48.2) |
| Death | 14 (51.8) |

Table 2. Factors associated with VTE occurrence.

| Variables | VTE+ | VTE- | OR | 95% CI | p value |
|----------------------|-------------------|--------------------|-------------|--------------------|--------------|
| | n = 27 | n = 173 | | | |
| Age > 40.0 | 17(10.2%) | 150 (89.8%) | 3.84 | 1.55 – 9.33 | 0.003 |
| Obesity | 13 (27.7%) | 34 (72.3%) | 1.24 | 1.10 -1.59 | 0.002 |
| Radio + chemotherapy | 2 (4.0%) | 48 (96.0%) | 4.57 | 0.17 - 85.1 | 0.319 |
| Stage III | 6 (8.8%) | 62 (91.2%) | 9.31 | 1.21 - 88.0 | 0.039 |
| Stage IV | 9 (9.1%) | 90 (90.9%) | 6.37 | 0.84 - 56.8 | 0.080 |
| Immobilisation | 11 (22.9%) | 37 (77.1%) | 2.95 | - | 0.119 |
| Symptomatic cancers | 23 (12.2%) | 166(87.8%) | 3.94 | 0.87 - 16.1 | 0.060 |

**Figure 1.** Flow chart of participants.

4. Discussion

The main aim of our study was to assess the prevalence and factors associated with VTE in cervical cancer patients. The prevalence of VTE in our population was 13.5%, twice greater than that published by Zhao and colleagues in 2020 in Japan as well as other authors in Asia [8]-[10]. This could be explained by the fact that the prevalence of cervical cancer is higher in sub-Saharan African countries with the diagnosis mostly made in advanced stages of the disease with more frequent complications like thromboembolic diseases [11] [12]. Also, we had a larger study period from diagnosis to treatment of patients contrary to the abovementioned studies. Our participants were mostly in their 50's with extremes of 26 and 95 years, in accordance with data found in recent literature. Indeed, this age range

bears the greater proportion of active human papilloma virus infection [13] and other STDs [14]. The factors significantly associated with the occurrence of VTE in cervical cancer were age above 40 years, obesity and cancer stage. Our findings join those published by several authors on the prevalence and factors associated with the occurrence of VTE worldwide [15]-[17]. Concerning advanced age and obesity, it is well known both are associated with reduced mobility, increased coagulability and a certain degree of chronic inflammation [5]. Not surprisingly, advanced cancer stages III and IV were also associated with VTE as these stages are usually characterized by larger tumor size with important venous compression, pronounced inflammation and increased clotting factors [18]. However, in contrast with other authors [15] [16] [18], we did not find significant association between cancer treatment and occurrence of VTE after exclusion of confounding factors. This might be due to our smaller sample size and shorter delay between diagnosis of cervical cancer and VTE.

Limitations

The retrospective nature of the study subjects it to recall bias. However, to minimize this effect, patients were called for additional information.

Conclusion

This study shows that VTE is highly prevalent in patients with cervical cancer in our population, mostly in women over 40 years, obese and at advanced stages of cancer.

Acknowledgements

The authors would like to thank the staff of the Gynaeco-obstetrics departments of the Yaoundé Central Hospital, the Yaoundé General Hospital and Yaoundé Gynaeco Obstetric and Pediatric Hospital for their cooperation in data collection for the study.

Availability of Data and Materials

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

Ethical Approval and Consent to Participate

The study was approved by the Centre Regional Ethics Committee for Human Health Research (N°634/CIERSH/DM/2024). All the participants read and signed informed consent before their inclusion in the study regarding the Helsinki declaration.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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Abbreviations

ASCO: American Society of Clinical Oncology

DVT: Deep Venous Thrombosis

HPV: Human Papilloma Virus

LMWH: Low Molecular Weight Heparin

PE: Pulmonary embolism

SPSS: Statistical Package for Science

STDs: Sexually Transmitted Diseases

VTE: Venous thromboembolism