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Incidence and factors associated with venous thromboembolism in women with gynecologic cancer

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ABSTRACT

Introduction: Venous thromboembolism (VTE) is a frequent clinical event in patients with gynecologic cancer. However, studies that exclusively address the incidence of VTE according the type of gynecologic cancer are poorly reported.

Objective: To analyze the incidence of VTE and the associated factors in women with different types of gynecologic cancer.

Results: A total of 1.885 women with gynecologic cancer was included. Among them, 40.8% (769) experienced venous thromboembolic events, most of them in the first two years after cancer diagnosis. There was no statistically significant difference in the incidence of VTE according to the type of gynecologic cancer. However, we observed statistically significant difference in the incidence of pulmonary embolism when stratified by type of thromboembolic events. Multiple regression analysis identified the absence of cancer treatment as a factor associated with VTE in patients with gynecologic cancer (OR = 3.14, CI 95% 2.50–3.96), particularly in patients with cervical (OR = 2.48, CI 95% 1.81–3.42), endometrial (OR = 4.18, CI 95% 2.46–7.10), and ovarian (OR = 3.55, CI 95% 2.22–5.68) cancer. For the total study population, especially patients with cervical and endometrial cancer an advanced stage of cancer was found to be associated with the incidence of VTE.

Conclusion: We observed that 40.8% experienced venous thromboembolic events. These events were associated with the treatment modality and the stage of cancer.

1. Introduction

Venous thromboembolism (VTE) consists of two closely connected clinical presentations, namely deep venous thrombosis (DVT) and pulmonary embolism (PE) [1], and it is a frequent clinical event that occurs in cancer patients [2]. VTE is multifactorial and its risk factors are related to patient characteristics (e.g. presence of comorbidities, varicose veins, prior history of VTE and hereditary factors), tumor characteristics (e.g. tumor site, histologic grade, clinical stage, presence of metastasis and time elapsed since the diagnosis of the neoplasm), type of cancer treatment (e.g. surgery, chemotherapy, radiation therapy, blood transfusion, and hospitalization) and the presence of biomarkers (e.g. hematological, D-Dimer, P-selectin, tissue factor, among other) [3,4].

The occurrence of thromboembolic events in cancer patients is associated with a poor prognosis [5]. Aside from drastically increasing morbidity and mortality of cancer patients, VTE can interfere with patient care plans and chemotherapy regimens. It can reduce patients' quality of life as well. Ultimately, VTE in cancer patients increases the consumption of health resources [6,7]. Overall, VTE is a serious health problem.

The association between gynecologic cancer and the presence of VTE was previously observed [8]. However, there is a lack of studies that address the association of different gynecologic cancer types and incidence of VTE [9,10]. This study aims to analyze the incidence of DVT and PE and the associated factors of these conditions in women with gynecologic cancer of different types.

2. Methods

This study was a retrospective cohort study that was approved by the Research Ethics Committee of the Instituto Nacional de Cancer (INCA) under n° 41285015.5.0000.5274. Patients were selected for this study through two screening stages. In the first stage, patients were selected if they were subjected to tests that detected for DVT and PE, such as Doppler echocardiography, Doppler ultrasound imaging of

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limbs and chest angiotomography, from January 2008 to July 2015 in the Hospital do Cancer II (HC II)/INCA (Rio de Janeiro, Brazil) regardless of their results. Patients were excluded if they were diagnosed with thrombosis prior to gynecologic cancer; their exams exhibited thrombosis within recanalized areas (previous thrombosis); or their exams were taken for other objectives that would make VTE evaluation impossible.

In the second stage, data was subsequently obtained from the Hospital Cancer Registry (HCR) of the HC II/INCA for the selected patients and further screened under inclusion and exclusion criteria. Patients with cancer in the cervix, endometrium, ovary, vagina and vulva were included in this study. Patients were excluded if they were under 18 years of age or had rare histological types of gynecologic cancer, such as sarcoma and lymphoma.

Collected data include socio-demographic information, such as age, marital status, education and occupation; clinical information, including tumor topography, staging and histological type; and treatment variables, such as treatment modality. To minimize loss of information, physical and electronic records were consulted when necessary.

Descriptive statistics of the population were expressed as means and standard deviations (SD) for continuous variables and absolute and relative frequencies for categorical variables, ANOVA and chi-square test were performed. The occurrence of VTE was considered an event, and patients who did not experience the event were censored at the date of the last follow-up. In order to identify the factors associated with the risk of developing VTE, a Cox proportional hazards regression model was used. Independent variables that showed $p < 0.20$ in the univariate analysis were included in the multiple regression model. Only independent variables with $p < 0.05$ were retained in the final model. The data were analyzed using the statistical package SPSS (*Statistical Package for Social Science for Windows*, Inc., USA) version 20.0.

3. Results

There were 5747 tests that were conducted for VTE detection. After verification of the eligibility criteria, 1885 women were included (Fig. 1).

Comparison of demographic characteristics of gynecologic cancer patients stratified by topography are presented in Table 1. Patients with cervical cancer showed lower average age ($p < 0.001$), as well as higher alcohol ($p = 0.006$) and tobacco ($p < 0.001$) consumption. Women with vulvar and vaginal neoplasms showed lower educational level ($p < 0.001$) and were more often found to be homemakers or retired ($p = 0.003$).

Endometrial cancer patients were frequently considered to be stage I (33.2%), while ovarian (25.0%) and vulvar and vaginal (28.7%) cancer patients most frequently had stage IV ($p < 0.001$). A total of 74.1% of deaths were identified, being more frequent in ovarian (82.3%) and cervical cancer patients (75.7%) ($p < 0.001$). Most of the women were submitted to some type of cancer treatment (84.7%). However, the absence of treatment was found to be more common for those with ovarian cancer. Among women who received cancer treatment, 40.3% were subjected to surgery, 67.8% received chemotherapy and 64.1% received radiotherapy (Table 2).

As for the incidence of VTE, it was observed that 40.8% of the women experienced at least one thromboembolic event. Specifically, 40.4% of patients experienced DVT, while PE occurred in 1.2% of the patients (Table 3). Of the 769 patients who experienced VTE, 747 (97.1%) only had DVT, 7 (0.9%) only had PE and 15 (2.0%) had DVT and PE simultaneously (data not showed).

There was no statistically significant difference in the incidence of VTE between the different types of gynecologic cancer. However, when stratified by type of event, a statistically significant difference in the incidence of PE according to the topography was observed (Table 3).

In terms of the amount time elapsed between cancer diagnosis and the first occurrence of a thromboembolic event, most patients (74.6%) developed VTE within the first two years of cancer diagnosis, with VTE predominantly occurring within the first six months (Fig. 2).

A univariate analysis was conducted to identify potential variables that could be associated with the risk of developing VTE (Supplementary Tables 1, 2). Multiple regression analysis showed that absence of cancer treatment was associated with the development of VTE in the total study population (OR = 3.14, 95% CI 2.50–3.96), especially in patients with cervical (OR = 2.48, 95% CI 1.81–3.42), endometrial (OR = 4.18, 95% CI 2.46–7.10) and ovarian (OR = 3.55, 95% CI 2.22–5.68) cancer. For the total study population and particularly in patients with cervical and endometrial cancer, advanced stages of cancer were also associated with the incidence of VTE. Our analysis was not able to identify risk factors that were associated with the incidence of VTE for patients with vulvar and vaginal cancer (Table 4).

4. Discussion

VTE is an event that often occurs in patients with malignant neoplasms. In this study, we found that the incidence of VTE in gynecologic cancer patients is associated with the absence of cancer treatment and advanced clinical stages of cancer.

The clinical characteristics of our study population differed from those observed in other epidemiological studies of gynecologic cancer. Graul et al. [10] noted that the most common gynecologic cancer was endometrial cancer, followed by ovarian, cervical and vulvar cancer. In contrast, our study observed that the most prevalent cancer was cervical, followed by endometrial, ovarian, vulvar and vaginal cancer. The high incidence of cervical cancer in this study could be explained by irregular coverage and lack of organization in screening programs. Furthermore, access to health care services for treating precursor lesions of cervical cancer might be difficult, especially in developing countries [11]. Moreover, a greater number of patients at advanced stages (III and IV) of cancer was found in our study population compared to other studies conducted in other countries, where the patient population is enriched with individuals at early stages (I–II) of cancer [12,13]. This observation might reflect the income inequality that exists in Brazil, a reality of developing countries.

In contrast to other studies that indicate surgery as the most frequent treatment option for gynecologic cancer, the frequency of surgery was low (40.3%) in our study population [13]. This observation might be attributed to the advanced stage of cancer in patients at diagnosis, which would limit treatment options of patients to chemotherapy, radiation therapy or a combination of both [14].

In this study, 288 women (15.3%) were found to have not received any oncological treatment. The absence of cancer treatment in these patients might be attributed to the fact that they were diagnosed at an advanced stage of cancer. Indeed, many patients that were not subjected to any kind of cancer treatment were at stage III and IV. Patients at these stages of cancer likely arrived in the hospital without clinical conditions that would not be conducive to any kind of cancer treatment.

We also observed that 40.8% of our study population experienced thromboembolic events, of which 97.1% had DVT, 0.9% experienced PE and 2.0% were found to suffer from both events simultaneously. The low incidence of PE (0.9%) that was observed in this study might reflect misdiagnosis because our study only included patients who had undergone tests for the investigation and confirmation of this complication. Indeed, about 60% of VTE cases are asymptomatic and found through routine testing [15]. In contrast to the low frequency of patients that suffered from both DVT and PE simultaneously, Oranratanaphan et al. [16] observed a high incidence of simultaneous events (46.7%). Although there was a discrepancy in the frequency of our study and Ye et al. [13] and Oranratanaphan et al. [16] observed a high occurrence of DVT (76.4%), which was also observed in this study.

When we assessed the incidence of VTE in gynecologic cancer patients on the basis of cancer topography, we observed no statistically

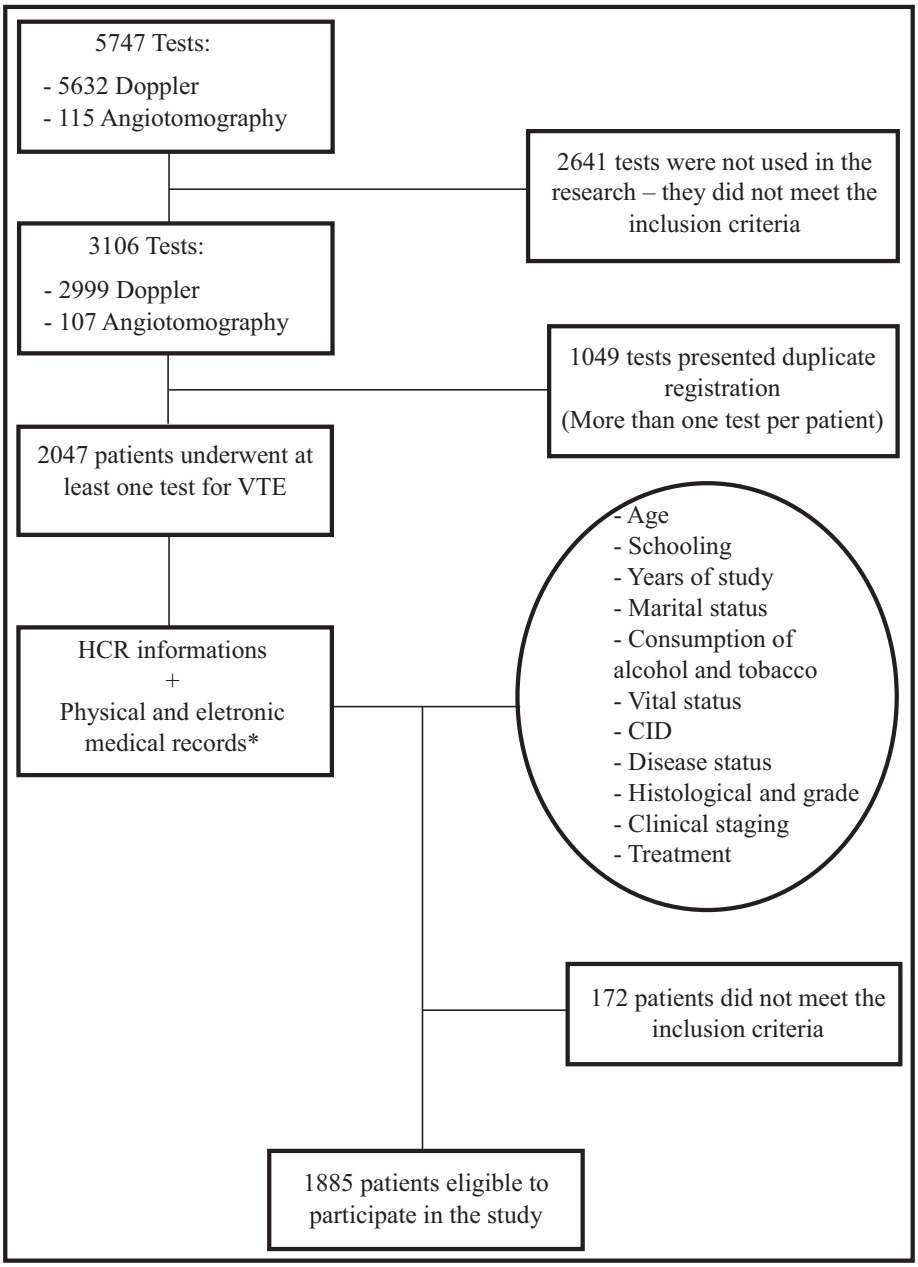

Fig. 1. Flowchart of the tests and patients included in the study.
* In cases with lack of information in electronic records, the physical record was consulted.

significant difference in VTE incidence between the different types of gynecologic cancer. However, we noted that gynecologic cancer patients with the highest incidence of VTE were patients with cervical cancer (41.5%), followed by vulvar and vaginal (41.4%), endometrial (39.9%) and ovarian (39.3%) cancer. This observation diverges from previous reports that suggest patients with ovarian and endometrial cancer have the highest risk of developing VTE [6,17,18]. This divergence might reflect the prevalence of advanced stages of gynecologic cancer in different studies.

We also assessed the amount of time elapsed between cancer diagnosis and VTE development. Specifically, we observed that gynecologic cancer patients were likely to experience a thromboembolic event within two years after diagnosis and such an event predominantly occurred within six months after diagnosis. Our findings were consistent with previous reports that there is an increased risk of a thromboembolic event within the first year of cancer diagnosis [19] and that it is more likely to occur within the first six months [20].

In this study, we report that the advanced clinical stage of cancer and the absence of cancer treatment are two independent factors that are associated with VTE development in gynecologic cancer patients. This finding is consistent with previous reports that cancer patients at more advanced stages have a higher chance of developing VTE due to an increase in circulating procoagulant factors in the blood [21]. On the other hand, the lack of cancer treatment probably occurred due to the advanced oncologic stage and the lack of clinical condition of the patients, together with the presence of comorbidities. Therefore, the hypothesis is that the association between the absence of cancer treatment and a higher incidence of VTE might reflect the association between tumor aggressiveness and VTE development instead [22] and not to the absence of treatment itself.

Since the analysis of the total study population for factors associated with VTE development could mask the effects of these factors on VTE development in specific types of gynecologic cancer, we assessed the factors associated with VTE incidence in our study population for

Table 1
Comparison of demographic characteristics, stratified by tumor topography of women with gynecological cancer.

Variable	Total population (1885) *N* (%)	Cervical cancer (1072) *N* (%)	Endometrial cancer (398) *N* (%)	Ovary cancer (328) *N* (%)	Vulvar/vaginal cancer (87) *N* (%)	*p* value
Age						
Mean (SD)	55.0 (± 13.8)	49.8 (± 13.0)	63.8 (± 10.3)	58.0 (± 12.1)	63.3 (± 14.5)	< **0.001**
Marital status						
With partner	747 (36.6)	422 (39.4)	163 (41.0)	130 (39.6)	32 (36.8)	0.884
No partner	1092 (57.9)	613 (57.2)	231 (58.0)	207 (63.1)	55 (63.2)	
Missing	46 (2.4)	37 (3.5)	4 (1.0)	1 (0.3)	0	
Race/skin color						
White	1032 (54.7)	557 (52.0)	225 (56.5)	199 (60.7)	51 (58.6)	**0.024**
Not white*	846 (44.9)	512 (47.8)	171 (43.0)	127 (38.7)	36 (41.4)	
Missing	7 (0.4)	3 (0.3)	2 (0.5)	2 (0.6)	0	
Schooling (years of study)						
< 8 years of study	1007 (53.4)	602 (56.2)	202 (50.8)	141 (43.0)	62 (71.3)	< **0.001**
≥ 8 years of study	872 (46.3)	468 (43.7)	195 (49.0)	184 (56.1)	25 (28.7)	
Missing	6 (0.3)	2 (0.2)	1 (0.3)	3 (0.9)	0	
Occupation						
Work out	683 (36.2)	413 (38.5)	133 (33.4)	120 (36.6)	17 (19.5)	**0.003**
Homemaker/Retired	1187 (63.0)	650 (60.6)	262 (65.8)	207 (63.1)	68 (78.2)	
Missing	15 (0.8)	9 (0.8)	3 (0.8)	1 (0.3)	2 (2.3)	
Consumption of alcohol						
Yes/ex consumer	171 (9.1)	118 (11.0)	30 (7.5)	19 (5.8)	4 (4.6)	**0.006**
No	1595 (84.6)	884 (82.5)	349 (87.7)	282 (86.0)	80 (92.0)	
Missing	119 (6.3)	70 (6.5)	19 (4.8)	27 (8.2)	3 (3.4)	
Consumption of tobacco						
Yes/ex-smoker	678 (36.0)	444 (41.4)	90 (22.6)	110 (33.5)	34 (39.1)	< **0.001**
No	1095 (58.1)	563 (52.5)	288 (72.4)	194 (59.1)	50 (57.5)	
Missing	112 (5.9)	65 (6.1)	20 (5.0)	24 (7.3)	3 (3.4)	
Cancer family history						
Yes	905 (48.0)	502 (46.8)	207 (52.0)	151 (46.0)	45 (51.7)	0.303
No	830 (44.0)	489 (45.6)	162 (40.7)	143 (43.6)	36 (41.4)	
Missing	150 (8.0)	81 (7.6)	29 (7.3)	34 (10.4)	6 (6.9)	

Vulvar and vaginal cancer were grouped to ensure that categories were comprised of enough cases to wake statistically stable estimates.

* Not white = black, brown, yellow and indigenous; Analysis performed with valid values; In bold are the variables that presented a statistically significant difference between the groups ($p < 0.05$).

associations with specific types of gynecologic cancer. However, in the case of the association between clinical stage of cancer and VTE development, we found that patients with endometrial cancer had a similarly risk of experiencing a thromboembolic event at advanced stages compared to patients with cervical cancer. These findings on endometrial and cervical cancer corroborate with previous reports that advanced cancer stages favored the emergence of VTE [19,23,24].

When the type of gynecologic cancer was considered, an increased risk of VTE was found in patients with cervical, ovarian and endometrial cancer if they did not receive any cancer treatment. Specifically, untreated cervical and ovarian cancer patients had a 2.48 fold ($p < 0.001$) and 3.55 fold ($p < 0.001$) greater risk of developing VTE compared to corresponding treated patients, respectively Endometrial cancer patients had the greatest increase in risk between untreated versus treated patients at 4.18 fold ($p < 0.001$). In previous studies, oncological treatment is associated with the emergence of thromboembolic disease because it favors the prothrombotic condition [25]. In contrast, we report that oncological treatment is a protective factor. This contradiction might be related to the fact that treatment improves the clinical condition of patients by preventing cancer progression, thereby reducing the risk of VTE.

We were unable to identify factors for vaginal and vulvar cancer that were associated with the incidence of VTE in this study. The inability to find any factors that are associated with VTE development for these types of gynecologic cancer might be due to the small sample size of these cancer types. We attempted to combine the data of the two gynecologic cancer types to increase the power of our statistical tests with the justification that they have similar clinical characteristics, treatment modalities and low occurrence. However, this strategy was not able to increase the power of statistical tests to a sufficient level to identify factors that are associated with VTE development in vaginal and vulvar cancer.

This study has several limitations. Despite having collected electronic and physical records to minimize the loss of information on study participants, this study is limited by its retrospective nature and the use of a secondary database that might be lacking in some information. Both factors could introduce biased information in our analysis. Another limitation of this study is that the patients included in this study were identified on the basis of tests that were conducted in clinical routine, for investigation of VTE or others investigations in which it is possible to identify VTE. Thus, our study might underestimate the true impact of gynecologic cancer on VTE occurrence due to the possibility of occurrence of thromboembolic events in patients who did not perform any tests that could identify the presence of VTE.

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5. Conclusion

In our study on 1885 gynecologic cancer patients, 40.8% (769) experienced venous thromboembolic events, supporting the observations that these complications frequently occur in these patients and that most of thromboembolic events occur within the first two years after cancer diagnosis. Importantly, we observed that the mode of treatment was an independent risk factor for VTE development in the

Table 2
Comparison of clinical characteristics, stratified by tumor topography of women with gynecological cancer.

Variable	Total population (1885) *N* (%)	Cervical cancer (1072) *N* (%)	Endometrial cancer (398) *N* (%)	Ovary cancer (328) *N* (%)	Vulvar/vaginal cancer (87) *N* (%)	*p* value
Histological type						
Carcinoma	1002 (53.2)	813 (75.8)	8 (2.0)	108 (32.9)	73 (83.9)	< **0.001**
Adenocarcinoma	726 (38.5)	254 (23.7)	382 (96.0)	76 (23.2)	14 (16.1)	
Cystadenocarcinoma	105 (5.6)	0	0	105 (32.0)	0	
Not specified	52 (2.8)	5 (0.5)	8 (2.0)	39 (11.9)	0	
Clinical stage						
I	379 (20.1)	180 (16.8)	132 (33.2)	47 (14.3)	20 (23.0)	< **0.001**
II	454 (24.1)	328 (30.6)	80 (20.1)	30 (9.1)	16 (18.4)	
III	704 (37.3)	412 (38.4)	121 (30.4)	150 (45.7)	21 (24.1)	
IV	305 (16.2)	145 (13.5)	53 (13.3)	82 (25.0)	25 (28.7)	
Missing	43 (2.3)	7 (0.7)	12 (3.0)	19 (5.8)	5 (5.7)	
Death						
Yes	1397 (74.1)	812 (75.7)	256 (64.3)	270 (82.3)	59 (67.8)	< **0.001**
No	488 (25.9)	260 (24.3)	142 (35.7)	58 (17.7)	28 (32.2)	
Cancer treatment						
Yes	1597 (84.7)	923 (86.1)	347 (87.2)	249 (75.9)	78 (89.7)	< **0.001**
No	288 (15.3)	149 (13.9)	51 (12.8)	79 (24.1)	9 (10.3)	
Surgery*						
Yes	643 (40.3)	138 (15.0)	291 (83.9)	171 (68.7)	43 (55.1)	< **0.001**
No	954 (59.7)	785 (85.0)	56 (16.1)	78 (31.3)	35 (44.9)	
Chemotherapy*						
Yes	1083 (67.8)	676 (73.2)	142 (40.9)	230 (92.4)	35 (44.9)	< **0.001**
No	514 (32.2)	247 (26.8)	205 (59.1)	19 (7.6)	43 (55.1)	
Radiotherapy*						
Yes	1023 (64.1)	814 (88.2)	158 (45.5)	4 (1.6)	47 (60.3)	< **0.001**
No	574 (35.9)	109 (11.8)	189 (54.5)	245 (98.4)	31 (39.7)	
Frequent treatments*						
Exclusive surgery	195 (12.2)	68 (7.4)	80 (23.1)	18 (7.2)	29 (37.2)	< **0.001**
Exclusive radiotherapy	193 (12.1)	163 (17.7)	22 (6.3)	0	8 (10.3)	
Exclusive chemotherapy	134 (8.4)	37 (4.0)	20 (5.8)	77 (30.9)	0	
Surgery + radiotherapy	124 (7.8)	16 (1.7)	101 (29.1)	1 (0.4)	6 (7.7)	
Surgery + chemotherapy	237 (14.8)	4 (0.4)	83 (23.9)	148 (59.4)	2 (2.6)	
Radiotherapy + chemotherapy	624 (39.1)	585 (63.4)	11 (3.2)	1 (0.4)	27 (34.6)	
Surgery + radiotherapy + chemotherapy	81 (5.1)	50 (5.4)	23 (6.6)	2 (0.8)	6 (7.7)	
Other modalities	9 (0.6)	0	7 (2.0)	2 (0.8)	0	

In bold are the variables that presented a statistically significant difference between the groups ($p < 0.05$).
Calculation based on data from patients who received cancer treatment.
Vulvar and vaginal cancer were grouped to ensure that categories were comprised of enough cases to wake statistically stable estimates.
* Only those undergoing treatment (n = 1597).

total study population, especially for patients with cervical, endometrial and ovarian cancer. Furthermore, we identified cancer staging as a second variable associated with the risk of VTE in gynecologic cancer patients. This observation was particularly evident in cervical and endometrial cancer patients. Our study did not identify variables statistically associated with the occurrence of VTE in the group of vulvar and vaginal cancer patients. Although this study further contributed to our understanding on the factors associated with the incidence of VTE in patients with gynecologic cancer, studies will still need to be conducted to develop measures for risk stratification and

Table 3
Incidence of venous thromboembolism in the study population ($N = 1885$).

Variable	Total population (1885) *N* (%)	Cervical cancer (1072) *N* (%)	Endometrial cancer (398) *N* (%)	Ovary cancer (328) *N* (%)	Vulvar/vaginal cancer (87) *N* (%)	*p* value
VTE						
Yes	769 (40.8)	445 (41.5)	159 (39.9)	129 (39.3)	36 (41.4)	0.885
No	1116 (59.2)	627 (58.5)	239 (60.1)	199 (60.7)	51 (58.6)	
DVT						
Yes	762 (40.4)	444 (41.4)	157 (39.4)	125 (38.1)	36 (41.4)	0.715
No	1123 (59.6)	628 (58.6)	241 (60.6)	203 (61.9)	51 (58.6)	
PE						
Yes	22 (1.2)	6 (0.6)	5 (1.3)	10 (3.0)	1 (1.1)	**0.004**
No	1863 (98.8)	1066 (99.4)	393 (98.7)	318 (97.0)	86 (98.9)	

VTE - venous thromboembolism; DVT - deep vein thrombosis; PE - pulmonary embolism.
In bold are the variables that presented a statistically significant difference between the groups ($p < 0.05$).

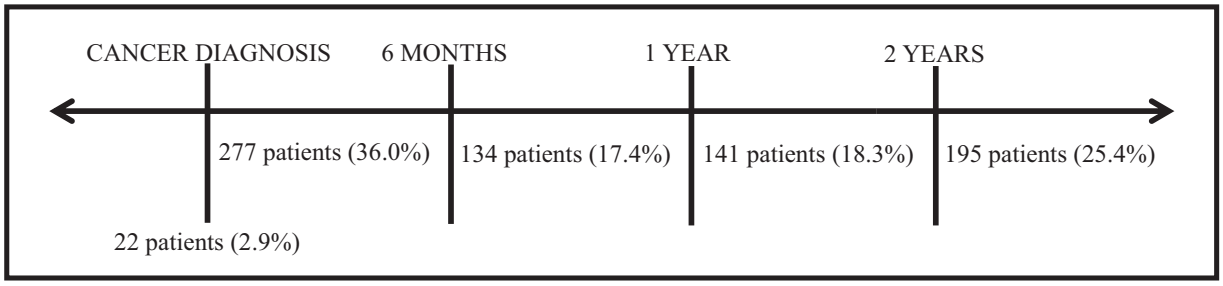

Fig. 2. Elapsed time between the development of venous thromboembolism and the diagnosis of cancer ($N = 769$).

Table 4
Factors associated with the development of venous thromboembolism in patients with gynecologic cancer.

Topography[a]	Variables	HR	95% CI	*p* value
Total population	**Clinical stage**			
	I	1.00		
	II	1.65	1.30–2.09	< **0.001**
	III	2.05	1.64–2.56	< **0.001**
	IV	2.88	2.22–3.75	< **0.001**
	Treatment modality			
	Isolated treatment	1.00	–	–
	Combined treatment	0.81	0.68–0.96	**0.017**
	No treatment	3.14	2.50–3.96	< **0.00**
Cervical cancer	**Clinical stage**			
	I	1.00	–	–
	II	1.61	1.17–2.21	**0.004**
	III	2.30	1.69–3.14	< **0.001**
	IV	3.77	2.58–5.51	< **0.001**
	Treatment modality			
	Isolated treatment	1.00	–	–
	Combined treatment	0.88	0.70–1.11	0.269
	No treatment	2.48	1.81–3.42	< **0.001**
Endometrial cancer	**Clinical stage**			
	I	1.00	–	–
	II	2.47	1.53–3.98	< **0.001**
	III	2.59	1.67–4.03	< **0.001**
	IV	3.42	1.97–5.95	< **0.001**
	Treatment modality			
	Isolated treatment	1.00	–	–
	Combined treatment	0.65	0.44–0.95	**0.026**
	No treatment	4.18	2.46–7.10	< **0.001**
Ovary cancer	**Treatment modality**			
	Isolated treatment	1.00	–	–
	Combined treatment	0.69	0.45–1.06	0.091
	No treatment	3.55	2.22–5.68	< **0.001**

HR - hazard ratio; 95% CI - 95% interval confidence.
In bold are the variables that presented a statistically significant ($p < 0.05$).
[a] No associated factors have been identified for vulva/vagina topography.

effective prophylactic strategies for gynecologic patients.

Declaration of competing interest

"None declared".

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.thromres.2019.11.009.

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