Gynecologic Oncology Reports 54 (2024) 101411

Contents lists available at ScienceDirect

Gynecologic Oncology Reports

journal homepage: www.elsevier.com/locate/gynor

Postoperative venous thromboembolism risk in patients with vulvar carcinoma: An analysis of the National surgical Quality Improvement Program (NSQIP) database

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ARTICLE INFO

Keywords:
Vulvar cancer
Thromboprophylaxis
VTE

ABSTRACT

Objectives: Due to low incidence of vulvar cancer (VC), incidence and predictors for development of venous thromboembolism (VTE) are poorly understood. We examined incidence and risk factors associated with VTE in patients undergoing surgery for VC.

Methods: We included patients who underwent surgery for VC from the National Surgical Quality Improvement Program database. VTE within the 30-day postoperative period was captured with Current Procedural Terminology codes. Baseline demographics and clinical characteristics were compared between patients with and without VTE. Univariable and multivariable-adjusted exact logistic regression models were used to estimate odds ratios (ORs) and 95% confidence intervals (CIs) for associations between risk factors and VTE.

Results: We identified 1414 patients undergoing procedures for VC from the NSQIP database. Overall, 11 (0.8 %) patients developed VTE. Univariable predictors of VTE included surgery type [compared with simple vulvectomy: radical vulvectomy only (OR = 7.97, 95 % CI = 1.44, infinity) and radical vulvectomy plus unilateral IFN (OR = 15.98, 95 % CI = 2.70, infinity)], unplanned readmission (OR = 11.56, 95 % CI = 2.74, 46.38), deep surgical site infection (OR = 16.05, 95 % CI = 1.59–85.50), and preoperative thrombocytosis (OR = 6.53, 95 % CI = 0.00, 34.86). In a multivariable-adjusted model, longer operative time (≥72 min OR = 11.33, 95 % CI = 1.58–499.03) and preoperative functional status [compared with complete independence: total dependence (OR = 53.88, 95 % CI = 0.85, infinity) and partial dependence (OR = 53.88, 95 % CI = 0.85, infinity)] were associated with VTE.

Conclusion: In this cohort of patients with VC undergoing radical vulvectomy, VTE incidence was low. Surgery type, longer operative time, dependent functional status, and wound disruption were identified as risk factors. Our findings highlight opportunities for prophylactic intervention in certain patients.

1. Introduction

Approximately 6,000 new cases of vulvar cancer (VC) are diagnosed in the United States each year, comprising 5 % of gynecologic cancers (Reade and Elit, 2012). For most patients, treatment and staging for VC includes excision by radical vulvectomy, with or without lymphadenectomy (Merlo, 2020; LeBreton et al., 2020). Patients who undergo surgical management of VC are at varying risk of postoperative complications and long-term sequelae, including wound dehiscence, surgical site infection, lymphocele, lymphedema, urinary tract infection, sexual dysfunction, and decreased mobility (LeBreton et al., 2020; Rahm et al., 2022; Bacalbasa et al., 2019; Gitas et al., 2021; van de Berg et al., 2023; Green et al., 2000). Individual patient characteristics and comorbidities have been linked to adverse postoperative events in vulvar surgery. Specifically, preoperative hypoalbuminemia, history of radiation, history of prior excision, longer operating time, longer

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https://doi.org/10.1016/j.gore.2024.101411
Received 2 May 2024; Accepted 4 May 2024
Available online 12 May 2024

hospital stays, and various medical comorbidities have been linked to increased risk of postoperative complications (Rahm et al., 2022; Bacalbasa et al., 2019; Gitas et al., 2021).

Venous thromboembolism (VTE), which includes deep venous thrombosis (DVT) and pulmonary embolism (PE), is one of the most lethal postoperative complications following a diagnosis of gynecologic cancer (Li et al., 2023; Mahdi et al., 2016; Graul et al., 2017 Mar 1). Gynecologic cancers have a risk of DVT and PE of up to 25 % postoperatively, in part due to their anatomic location in the pelvis and often close approximation with pelvic lymphatics and vasculature (Guntupalli et al., 2020). The risk of VTE is highest among patients undergoing laparotomy, but the risk is lower in those undergoing minimally invasive surgery (MIS) (Guntupalli et al., 2020). In a study by Mahdi and colleagues, the rate of VTE following MIS for endometrial, ovarian, and cervical cancers was 0.7 %, with no significant differences based on cancer type, operating time, or performance of lymphadenectomy (Mahdi et al., 2016). In a subsequent study inclusive of patients with VC, the rate of VTE was 1.8 %; however, risk factors were not evaluated (Graul et al., 2017 Mar 1). Further understanding of the incidence and risk factors for VTE following surgery for VC will help in patient counseling and guide decision-making regarding thromboprophylaxis. The purpose of this study was to explore the incidence of and risk factors for postoperative VTE in patients undergoing vulvectomy for VC.

2. Methods

2.1. Data source and study design

We used a multi-institutional dataset from the National Surgical Quality Improvement Program (NSQIP) database. In brief, the NSQIP is an ongoing data-driven, participatory, quality improvement initiative that includes over 700 US hospitals (Raval et al., 2011). Data is collected by trained surgical clinical reviewers who abstract preoperative and 30-day postoperative patient-level information from medical records according to standardized definitions. A systematic sampling protocol includes the first 35 consecutive surgical cases meeting inclusion criteria within an 8-day cycle to reduce selection bias. It is one of the most reliable and complete surgical databases, with an inter-rater reliability audit and an overall disagreement rate of 2 % among participating hospitals (Shiloach et al., 2010). This study was considered exempt by the Institutional Review Board of The Ohio State University.

2.2. Study population

We included women (≥18 years) who underwent vulvectomy for VC between 2014 and 2020. We used International Classification of Diseases 9th Revision [(ICD-9) 184.1, 184.2, 184.3, 184.4] and ICD-10th Revision (C51.0, C51.1, C51.2, C51.8, C51.9) postoperative diagnosis codes to identify patients with VC. Using *Current Procedural Terminology* (CPT) codes, we further restricted the study population to women who underwent a simple (56620, 56625) or radical (56630, 56631, 56632, 56633, 56634, 56637, 56640) vulvectomy, leaving 1,414 women in the analytical sample.

2.3. Venous thromboembolism and other covariates

We defined venous thromboembolism (VTE) as the occurrence of deep vein thrombosis (DVT) or pulmonary embolism (PE) using predefined NSQIP variables. Timing of VTE occurrences were categorized as in hospital (if they occurred during the surgical hospitalization) or post-discharge (<30 days). We also included information on age at diagnosis (<65, ≥65), race (Non-Hispanic White, Non-Hispanic Black, Hispanic, Other, Unknown), body mass index (BMI; <30, 30–39.9, ≥40, Unknown), preoperative albumin (<3, ≥3, Unknown), length of hospital stay (continuous, measured in days), disseminated cancer (yes, no), ASA classification (<3, ≥3), smoking within the last year (yes, no), preoperative dialysis (yes, no), steroid use for a chronic condition (yes, no), preoperative weight loss (yes, no), diabetes mellitus (yes, no), hypertension requiring medicine (yes, no), congestive heart failure (yes, no), bleeding disorder (yes, no), history of severe COPD (yes, no), transferred from a non-home facility (yes, no), functional dependency (independent, partially dependent, totally dependent, unknown), operative time (continuous, measured in minutes and dichotomized at the median of 72 min), procedure type (simple vulvectomy, radical vulvectomy), type of surgery [simple vulvectomy only; radical vulvectomy only; radical vulvectomy plus unilateral inguinofemoral lymphadenectomy (IFLND); radical vulvectomy plus bilateral IFLND; radical vulvectomy plus IFLND, iliac, and pelvic lymphadenectomy], and lymphadenectomy type (none, sentinel, full, IFLND, iliac, pelvic). CPT codes were used to identify unilateral IFLND (56631, 56634), bilateral IFLND (56632, 56637), and IFLND, iliac, and pelvic (56640). Full lymphadenectomy was defined as having either unilateral or bilateral IFLND, while sentinel lymphadenectomy was defined with the additional procedure CPT code 38531.

2.4. Surgical outcomes

For this analysis, we categorized postoperative complications (<30 days after discharge) as major vs. minor, with minor including blood transfusion, urinary tract infection, wound disruption, renal insufficiency, pneumonia, superficial surgical site infection, deep surgical site infection and major including any unplanned readmission, return to the operating room, cardiac arrest, myocardial infarction, stroke, renal failure, venous thromboembolism, deep venous thrombosis, pulmonary embolus, sepsis, shock, organ space surgical site infection, ventilation necessary for > 48 h, or need for reintubation.

2.5. Statistical analysis

Statistical analyses began with frequency distributions of preoperative characteristics, surgical features, and postoperative complications in the overall cohort and according to VTE status (*i.e.,* no vs. yes). We examined the timing of VTE occurrences (in hospital vs. post-discharge) according to surgery type. Exact univariable logistic regression models were used to calculate odds ratios (ORs) and 95 % confidence intervals (CIs) for associations between VTE and each of the preoperative characteristics, surgical characteristics, and postoperative complications. Given the low number of VTE events in this study sample, we chose to include a multivariable exact logistic regression model only adjusting for operative time (<72 min vs. ≥ 72 min) and functional dependency. These variables were selected *a priori* for their suspected importance in driving VTE. Statistical analyses were performed in SAS version 9.4. As the low overall sample size and small number of VTE events produced imprecise estimates, we provide a cautious interpretation of the effect estimates generated from the exact logistic regression analyses.

3. Results

Of the 1414 patients with VC included within this retrospective cohort, overall VTE incidence was 0.8 %. Table 1 displays the clinical characteristics of patients with VC who underwent vulvectomy procedures and univariable associations with VTE odds. Age, race, BMI, medical comorbidities, need for transfer from a non-home facility, smoking status, pre-operative transfusion, preoperative albumin, disseminated cancer, ASA classification, dialysis, or weight loss prior to surgery were not associated with VTE. Functional dependence was associated with VTE, with total (OR = 27.63, 95 % CI 0.54, 275.01) and partial (OR = 8.38, 95 % CI 0.84, 43.92) dependence associated with higher VTE odds compared to fully independent patients. Higher preoperative thrombocytosis was associated with higher VTE odds (OR = 6.53, 95 % CI = 0.00, 34.86).

Table 2 displays the surgical details of patients with VC who

Table 1
Univariable odds ratios (ORs) and 95% confidence intervals (CIs) for associations between clinical characteristics and VTE in vulvar cancer patients.

	Overall (n = 1,414)	No VTE (n = 1,403)	VTE (n = 11)		
Patient characteristics	n (%)	n (%)	n (%)	OR (95 % CI)[1]	p
Age ≥ 65 years	579 (41.0)	829 (59.1)	6 (54.6)	0.83 (0.21, 3.46)	0.77
Race					0.85
Non-Hispanic White	952 (67.3)	942 (67.1)	10 (90.9)	1.00	
Non-Hispanic Black	74 (5.2)	74 (5.3)	0 (0.0)	0.92 (0.00, 4.53)	
Hispanic	61 (4.3)	61 (4.4)	0 (0.0)	1.12 (0.00, 5.51)	
Other	53 (3.8)	53 (3.8)	0 (0.0)	1.29 (0.00, 6.36)	
Unknown	274 (19.4)	273 (19.5)	1 (9.1)	0.35 (0.01, 2.45)	
BMI (kg/m^2)					0.35
<30	744 (52.6)	739 (52.7)	5 (45.5)	1.00	
30–39.9	492 (34.8)	486 (34.6)	6 (54.6)	1.82 (0.46, 7.60)	
≥40	169 (12.0)	169 (12.1)	0 (0.0)	0.65 (0.00, 3.62)	
Unknown	9 (0.6)	9 (0.6)	0 (0.0)	12.59 (0.00, 75.15)	
Medical Comorbidities					
DM	320 (22.6)	319 (22.7)	1 (9.1)	0.34 (0.01, 2.41)	0.47
HTN	820 (58.0)	816 (58.2)	4 (36.4)	0.41 (0.09, 1.63)	0.22
CHF	5 (0.4)	5 (0.4)	0 (0.0)	19.37 (0.00, 113.84)	1.00
Steroid use	62 (4.4)	62 (4.4)	0 (0.0)	1.42 (0.00, 6.91)	1.00
Bleeding disorder	23 (1.6)	23 (1.6)	0 (0.0)	3.96 (0.00, 19.83)	1.00
History of severe COPD	106 (7.5)	105 (7.5)	1 (9.1)	1.24 (0.03, 8.84)	0.58
Renal failure	3 (0.2)	3 (0.2)	0 (0.0)	33.75 (0.00, 232.04)	1.00
Transferred from a non-home facility	31 (2.2)	30 (2.1)	1 (9.1)	4.56 (0.10, 33.95)	0.23
Functional dependency					**0.005**
Independent	1,355 (95.8)	1,347 (96.0)	8 (72.7)	1.00	
Partially dependent	42 (3.0)	40 (2.9)	2 (18.2)	8.38 (0.84, 43.92)	
Totally dependent	7 (0.5)	6 (0.4)	1 (9.1)	27.63 (0.54, 275.01)	
Unknown	10 (0.7)	10 (0.7)	0 (0.0)	2.53 (−infinity, 4.23)	
Smoker within one year of surgery	279 (19.7)	278 (19.8)	1 (9.1)	0.41 (0.01, 2.87)	0.70
Pre-op Thrombocytosis (PLT > 450 K)	20 (1.4)	20 (1.4)	0 (0.0)	6.53 (0.00, 34.86)	**0.04**
Pre-op transfusion of > 4 units PRBCs within 72 h prior	4 (0.3)	4 (0.3)	0 (0.0)	24.62 (0.00, 153.12)	1.00
Preoperative albumin					0.14
<3	15 (1.1)	15 (1.1)	0 (0.0)	1.00	
≥ 3	694 (49.1)	692 (49.3)	2 (18.2)	0.05 (0.01, infinity)	
Unknown	705 (49.9)	696 (49.6)	9 (81.8)	0.26 (0.05, infinity)	
Disseminated cancer	36 (2.6)	36 (2.6)	0 (0.0)	2.49 (0.00, 12.31)	1.00
ASA classification ≥ 3	872 (61.7)	865 (61.7)	7 (63.6)	1.09 (0.28, 5.09)	1.00
On dialysis prior to surgery	13 (0.9)	13 (0.9)	0 (0.0)	7.13 (0.00, 36.86)	1.00
Weight loss prior to surgery	8 (0.6)	8 (0.6)	0 (0.0)	11.80 (0.00, 64.02)	1.00

Statistics displayed as n (%). Bold denotes statistical significance with $p < 0.05$. VTE, venous thromboembolism; BMI, body mass index; HTN, hypertension; DM, diabetes mellitus; CHF, congestive heart failure; COPD, chronic obstructive pulmonary disease; PLT, platelets; ASA, American Society of Anesthesiologists
[1] univariable odds ratios (OR) and 95% confidence intervals (CI) from exact logistic regression

underwent vulvectomy procedures and univariable associations with VTE odds. Approximately 36.9 % (n = 521) of patients underwent simple vulvectomy alone, 31.3 % (n = 443) underwent radical vulvectomy alone, 19.0 % (n = 269) underwent radical vulvectomy with bilateral IFLND and 12.4 % (n = 175) underwent radical vulvectomy with unilateral IFLND (Table 2). Surgery type was associated with postoperative VTE; compared to patients who underwent simple vulvectomy, VTE odds were higher among those receiving radical vulvectomy only (OR = 7.97, 95 % CI = 1.44, infinity) or radical vulvectomy plus unilateral IFN (OR = 15.98, 95 % CI = 2.70, infinity). Longer operative time (OR = 9.89, 95 % CI = 1.40, 430.27), unplanned readmission (OR = 11.56, 95 % CI = 2.74, 46.38), and deep SSI (OR = 16.05, 95 % CI = 1.59, 85.50) were univariably associated with higher VTE odds.

Multivariable-adjusted associations between functional dependency and operative time with VTE odds are shown in Table 3. Notably, total dependence (OR = 53.88, 95 % CI = 0.85, infinity) and partial dependence (OR = 9.12, 95 % CI = 0.89, infinity) were associated with higher VTE odds as was longer operative time (OR ≥ 72 min vs. < 72 min OR = 11.33, 95 % CI = 1.58, 499.03). As shown in Table 4, of the 11 VTE events, DVT alone accounted for most VTE diagnoses (n = 7, 63.6 %), followed by PE alone (n = 3; 27.3 %) and DVT and PE (n = 1; 9.1 %). The majority of VTEs (n = 7; 63.6 %) were diagnosed during the initial surgical hospitalization (Table 4).

4. Discussion

Gynecologic oncology patients are at variable risk of postoperative VTE, the highest being those undergoing laparotomy (Guntupalli et al., 2020). Prior studies have evaluated the incidence and risk factors for VTE among patients with ovarian, endometrial, and cervical cancers. However, the incidence and etiology of VTE in patients with VC is understudied. In this analysis of the NSQIP database, we identified that the overall incidence of VTE after vulvectomy for VC is very low and comparable to rates previously reported in gynecologic oncology patient populations following MIS procedures (Mahdi et al., 2016). Specifically, we observed no VTE after simple vulvectomy and a low incidence (1.2 %) after radical vulvectomy. Given this low incidence of VTE, universal thromboprophylaxis is likely unindicated.

Risk stratification is important to provide more individualized care and reduce morbidity by considering prophylactic anticoagulation only in high-risk patients. The current ACOG guidelines for pharmacologic thromboprophylaxis prior to gynecologic surgery are based on the Caprini score, balancing it with the individual bleeding risk of each patient (College, 2021). We identified several patient and surgical factors that were associated with an increased VTE risk, including surgical procedure type (such as concurrent IFLND), increased functional

Table 2
Univariable odds ratios (ORs) and 95% confidence intervals (CIs) for associations between surgical characteristics and VTE in vulvar cancer patients.

	Overall (n = 1,414)	No VTE (n = 1,403)	VTE (n = 11)		
Surgical details	n (%)	n (%)	n (%)	OR (95 % CI)[1]	p
Procedure type					**0.01**
Simple vulvectomy	521 (36.9)	521 (37.1)	0 (0.0)	1.00	
Radical vulvectomy	893 (63.2)	882 (62.9)	11 (100.0)	9.06 (1.88, infinity)	
Surgery type					**0.01**
Simple vulvectomy only	521 (36.9)	521 (37.1)	0 (0.0)	1.00	
Radical vulvectomy only	443 (31.3)	438 (31.2)	5 (45.5)	7.97 (1.44, infinity)	
Radical vulvectomy + unilateral IFN	175 (12.4)	171 (12.2)	4 (36.4)	15.98 (2.70, infinity)	
Radical vulvectomy + bilateral IFN	269 (19.0)	267 (19.0)	2 (18.2)	4.69 (0.56, infinity)	
Radical vulvectomy + IFN, iliac, and pelvic LN	6 (0.4)	6 (0.4)	0 (0.0)	—-	
Lymphadenectomy type					0.27
None	945 (66.8)	940 (67.0)	5 (45.5)	1.00	
Sentinel	19 (1.3)	19 (1.4)	0 (0.0)	7.47 (0.00, 42.71)	
Full	444 (31.4)	438 (31.2)	6 (54.6)	2.57 (0.65, 10.72)	
IFN, iliac, and pelvic	6 (0.4)	6 (0.4)	0 (0.0)	24.28 (0.00, 151.99)	
Operation time					**0.01**
<72 min	699 (49.4)	698 (49.8)	1 (9.1)	1.00	
≥ 72 min	715 (50.6)	705 (50.3)	10 (90.9)	9.89 (1.40, 430.27)	
Postoperative Complications					
Major					
Unplanned readmission	99 (7.0)	94 (6.7)	5 (45.5)	11.56 (2.74, 46.38)	**<0.001**
Re-operation	38 (2.7)	37 (2.6)	1 (9.1)	3.69 (0.08, 27.15)	0.26
Cardiac arrest	0 (0.0)	0 (0.0)	0 (0.0)	—-	—-
MI	3 (0.2)	3 (0.2)	0 (0.0)	33.75 (0.00, 232.04)	1.00
CVA	2 (0.1)	2 (0.1)	0 (0.0)	53.52 (0.00, 459.23)	1.00
Renal failure	0 (0.0)	0 (0.0)	0 (0.0)	—-	—-
Sepsis	13 (0.9)	12 (0.9)	1 (9.1)	11.52 (0.25, 93.74)	0.10
Shock	2 (0.1)	2 (0.1)	0 (0.0)	53.52 (0.00, 459.23)	1.00
Organ space surgical site infection	7 (0.5)	7 (0.5)	0 (0.0)	13.57 (0.00, 75.00)	1.00
Ventilation necessary for > 48 h	0 (0.0)	0 (0.0)	0 (0.0)	—-	—-
Need for reintubation	2 (0.1)	2 (0.1)	0 (0.0)	53.52 (0.00, 459.23)	1.00
Minor					
Blood tranfusion	25 (1.8)	25 (1.8)	0 (0.0)	3.63 (0.00, 18.14)	1.00
UTI	21 (1.5)	20 (1.4)	1 (9.1)	6.89 (0.15, 52.81)	0.15
Wound disruption	56 (4.0)	54 (3.9)	2 (18.2)	5.54 (0.57, 27.69)	0.07
Renal insufficiency	1 (0.1)	1 (0.1)	0 (0.0)	127.55 (0.00, infinity)	1.00
Pneumonia	2 (0.1)	2 (0.1)	0 (0.0)	53.52 (0.00, 459.23)	1.00
Superficial SSI	126 (8.9)	126 (9.0)	0 (0.0)	0.66 (0.00, 3.21)	0.61
Deep SSI	21 (1.5)	19 (1.4)	2 (18.2)	16.05 (1.59, 85.50)	**0.01**

Statistics displayed as n (%). Bold denotes statistical significance with $p < 0.05$. VTE, venous thromboembolism; IFN, inguinofemoral lymph node dissection; MI, myocardial infarction; LN: lymphadenectomy; CVA, Stroke/Cerebrovascular accident; SSI, surgical site infection

[1] univariable odds ratios (OR) and 95% confidence intervals (CI) from exact logistic regression

Table 3
Multivariable-adjusted ORs and 95% confidence intervals (CIs) for associations between operative time, functional status, and VTE.

	No VTE (n = 1,403)	VTE (n = 11)		
Characteristics	n (%)	n (%)	OR (95 % CI)[1]	p
Functional dependency				0.003
Independent	1,347 (96.0)	8 (72.7)	1.00	
Partially dependent	40 (2.9)	2 (18.2)	9.12 (0.89, 49.57)	
Totally dependent	6 (0.4)	1 (9.1)	53.88 (0.85, infinity)	
Unknown	10 (0.7)	0 (0.0)	12.95 (0.00, 75.41)	
Operation time				0.004
<72 min	698 (49.8)	1 (9.1)	1.00	
≥ 72 min	705 (50.3)	10 (90.9)	11.33 (1.58, 499.03)	

[1] exact logistic regression adjusted for all variables in the table

dependency before surgery, longer operating time, and concurrent postoperative complications, including sepsis, wound disruption, and unplanned hospital readmission. Our study highlights the association between more extensive surgical procedures and longer operating times with increased VTE risk, in line with other reports of gynecologic surgery for other malignancies (Graul et al., 2017 Mar 1; Barber et al., 2015; Swift et al., 2022). In this cohort, there were no VTE events with simple vulvectomies. As expected, more extensive surgical procedures (radical resection with and without lymphadenectomies) were associated with longer operating times. Of note, no VTE events were diagnosed in patients that underwent sentinel lymphadenectomies, but this subgroup

Table 4
Timing and type of VTE, overall and by procedure type.

	Overall	Radical vulvectomy only	Radical vulvectomy + unilateral IFN	Radical vulvectomy + bilateral IFN
	(n = 11)	(n = 5)	(n = 4)	(n = 2)
	n (%)			
PE	**3 (27.3)**	**3 (60.0)**	**0 (0.0)**	**0 (0.0)**
In hospital	0 (0.0)	0 (0.0)	–	–
After discharge	3 (100.0)	3 (100.0)	–	–
DVT	**7 (63.6)**	**2 (40.0)**	**3 (75.0)**	**2 (100.0)**
In hospital	3 (42.9)	1 (50.0)	2 (66.7)	0 (0.0)
After discharge	4 (57.1)	1 (50.0)	1 (33.3)	2 (100.0)
PE + DVT	**1 (9.1)**	**0 (0.0)**	**1 (25.0)**	**0 (0.0)**
In hospital	1 (100.0)	–	1 (100.0)	–
After discharge	0 (0.0)	–	0 (0.0)	–

was small (N = 19). Similar findings were observed for patients undergoing MIS versus open hysterectomy (Graul et al., 2017 Mar 1; Barber et al., 2015). For example, in a study of over 44,000 patients, Barber et al. identified open hysterectomy to be significantly longer than MIS (131.9 vs. 123.1 min, respectively), carrying a two-folder higher postoperative VTE risk (Barber et al., 2015). In another study including 2800 patients, patients with ovarian cancer were found to be at increased risk of VTE when open cases were included, but there was no difference when only minimally invasive surgery was included (Graul et al., 2017 Mar 1). The same study also found that open hysterectomy has a longer operating time and yields a higher risk for VTE. Moreover, when these analyses were stratified by gynecologic cancer type, patients with vulvar cancer had the lowest risk for VTE and the shortest operating time. Importantly, the independent effect of operating time was not examined in this study (Graul et al., 2017 Mar 1). These findings are consistent with the current study.

In addition to surgery duration, we found that functional dependence prior to surgery increases the risk of diagnosis of postoperative VTE. The NSQIP surgical risk calculator places patients into 3 categories of function: independent patients do not require assistance with and activities of daily living, partially dependent patients require assistance with some, and totally dependent require assistance with all (ACS Risk Calculator, 2024). Patients with higher levels of functional dependence were 28 times more likely to develop VTE than their independent peers. Increased VTE risk in vaginal surgery patients with poor functional status has similarly been observed in the urogynecology literature (Escobar et al., 2020). Following vaginal surgery for pelvic organ prolapse, functionally dependent patients showed a two-fold higher VTE risk than functionally independent patients (Escobar et al., 2020). This heightened risk may arise from decreased mobility, which predisposes these patients to VTE through increased venous stasis. However, no objective system to measure levels of immobility that could further tailor recommendations exists (Ye et al., 2016; Samama, 2000). Given patients with decreased mobility may be predisposed to VTE, it is reasonable to consider whether patients included in this study had preexisting DVTs. As this is a retrospective study of a database, it is impossible to evaluate this possibility. Though, a study in patients with various malignancies found that detection of incidental, asymptomatic VTE on imaging prior to surgery was low (1.4 %) (Douma et al., 2010). Further study is warranted to assess how these patients may benefit from tailored interventions to improve mobility before surgery, including physical therapy and prehabilitation programs where clinically appropriate. Independent of surgery, patients with less mobility are at higher risk for developing VTE, and this risk can be compounded by the postoperative state (Samama, 2000).

Prior studies have demonstrated that acute infection is a risk factor for VTE in surgical and non-surgical patients. In hospitalized patients, those admitted with acute infection had significantly increased VTE risk despite not receiving surgery in comparison to admitted patients who did not develop VTE (Alikhan et al., 2004; Pandor et al., 2021). Moreover, acute infection is related to VTE risk in immobile and mobile patients and is related to a 15-fold higher risk of VTE independent of mobility status (Grimnes et al., 2017). We also observed that VC patients who developed deep surgical site infection or sepsis postoperatively were at a substantially increased risk of VTE, a risk observed in other gynecologic malignancies (Swift et al., 2022). Relative immobility in the recovery period and inflammation related to infection may synergistically affect the likelihood of VTE formation. While our study was not designed to assess whether prophylactic anticoagulation is beneficial within these high-risk patients, given the substantially increased risk among those with functional dependency and postoperative infections, these data may facilitate discussion and shared decision making with patients regarding the risks and potential benefits of thromboprophylaxis.

Our study has several significant limitations inherent to performing a retrospective analysis of NSQIP data. Primarily, we are limited by the available data and are missing information on critical patient and oncologic characteristics, including tumor size, tumor location, postoperative adjuvant treatment, and patterns of thromboprophylaxis given pre-procedure and post-operatively. Further, while we established the patient cohort through diagnosis codes specific for VC, we are unable to identify through this dataset the pathologic diagnosis (dysplasia versus carcinoma) that necessitated the surgery. Finally, the low number of VTE events precluded an examination of a multivariable model with multiple predictors and the effect estimates produced in the univariable and minimally-adjusted models were characterized by imprecision. Despite these limitations, our study is one of the first to assess the incidence and risk factors for VTE in women undergoing surgery for VC. Utilizing this large, validated prospective database enables the study of a relatively rare disease within a large denominator of patients with decreased potential biases related to geography, provider surgical techniques, and patient selection. However, multi-institutional studies may be an important mechanism to evaluate rare postoperative outcomes in patients with VC.

In conclusion, within this national cohort, we observed no VTE events following simple vulvectomy, and VTE incidence after radial vulvectomy was low. Several notable risk factors were identified, including longer surgical time, functional dependency, and concurrent postoperative complications. While the current body of evidence does not indicate universal thromboprophylaxis, our findings highlight potential opportunities for individualized prophylactic intervention, especially in patients with functional dependence and those who may undergo extensive and longer procedures.

CRediT authorship contribution statement

Quinn Kistenfeger: Writing – original draft, Writing – review & editing. **Ashley S. Felix:** Formal analysis, Methodology, Writing – original draft, Writing – review & editing. **Caitlin E. Meade:** Formal analysis, Writing – original draft, Writing – review & editing. **Vincent Wagner:** Data curation, Investigation, Writing – review & editing. **Kristin Bixel:** Writing – review & editing. **Laura M. Chambers:**

Conceptualization, Funding acquisition, Investigation, Methodology, Supervision, Writing – review & editing.

Declaration of competing 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.

Acknowledgements

This work was supported by Grant 2021258 for Laura Chambers, DO, from the Doris Duke Charitable Foundation (DDCF) through the COVID-19 Fund to Retain Clinical Scientists collaborative grant program and was made possible through the support of Grant 62288 from the John Templeton Foundation. The opinions expressed in this publication are those of the author(s) and do not necessarily reflect the view of the DDCF, the John Templeton Foundation, the OSU College of Medicine, or the Center for Clinical and Translational Science. Additionally, this project was supported by a Research Grant by a Path to K award from the Ohio State University College of Medicine Office of Research and the Center for Clinical & Translational Science through the Richard P. & Marie R. Bremer Medical Research Fund and William H. Davis Endowment for Basic Medical Research. The content is solely the authors' responsibility and does not necessarily reflect the views of the Davis / Bremer Research Fund, the CCTS, or The Ohio State University Medical Center. Additional grant support includes The Ohio State University National Center for Advancing Translational Sciences, Grant UL1TR001070, and The Pelotonia Institute for Immuno-Oncology.

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