



The modified 5-item frailty index is a predictor of post-operative complications in vulvar cancer: a National Surgical Quality Improvement Program (NSQIP) analysis

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ABSTRACT

Objective To determine whether frailty is associated with post-operative complications following surgery for vulvar cancer.

Methods This retrospective study used a multi-institutional dataset from the National Surgical Quality Improvement Program (NSQIP) database (2014–2020) to analyze the relationship between frailty, procedure type, and post-operative complications. Frailty was determined using the modified frailty index-5 (mFI-5). Univariate and multivariable-adjusted logistic regression analyses were performed.

Results Of 886 women, 49.9% underwent radical vulvectomy alone, and 19.5% and 30.6% underwent concurrent unilateral or bilateral inguofemoral lymphadenectomy, respectively; 24.5% had mFI ≥ 2 and were considered frail. Compared with non-frail women, those with an mFI ≥ 2 were more likely to have an unplanned readmission (12.9% vs 7.8%, $p=0.02$), wound disruption (8.3% vs 4.2%, $p=0.02$), and deep surgical site infection (3.7% vs 1.4%, $p=0.04$). On multivariable-adjusted models, frailty was a significant predictor for minor (OR 1.58, 95% CI 1.09 to 2.30) and any complications (OR 1.46, 95% CI 1.02 to 2.08). Specifically, for radical vulvectomy with bilateral inguofemoral lymphadenectomy, frailty was significantly associated with major (OR 2.13, 95% CI 1.03 to 4.40) and any complications (OR 2.10, 95% CI 1.14 to 3.87).

Conclusion In this analysis of the NSQIP database, nearly 25% of women undergoing radical vulvectomy were considered frail. Frailty was associated with increased post-operative complications, especially in women concurrently undergoing bilateral inguofemoral lymphadenectomy. Frailty screening prior to radical vulvectomy may assist in patient counseling and improve post-operative outcomes.

INTRODUCTION

Vulvar cancer accounts for 5.5% of gynecologic malignancies in the USA.¹ Despite a shift towards less morbid surgical procedures to treat vulvar cancer, the incidence of post-operative complications remain high.² Historical studies have characterized numerous risk factors that are predictive of post-operative complications after vulvar cancer surgery, including stage, diabetes, obesity, smoking, hypoalbuminemia,

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Frailty has consistently proven to be a predictor of adverse post-operative events in women undergoing surgery for ovarian, endometrial and cervical cancer; however, limited data exist to examine the relationship between frailty and post-operative outcomes among women undergoing surgery for vulvar cancer.

WHAT THIS STUDY ADDS

⇒ 25% of women undergoing surgery for vulvar cancer were considered to be frail. Frailty was associated with post-operative complications, especially with bilateral inguofemoral lymphadenectomy.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ Understanding the relationship between frailty and surgical outcomes in a population with a high percentage of frail patients provides an opportunity to consider practical and effective interventions to improve outcomes for women experiencing a vulvar cancer diagnosis.

and increasing age.^{2–9} Frailty assessments can provide a more comprehensive assessment of a patient's global medical and performance status than individual risk factors.

Frailty is a condition of decreased physiologic strength, function and endurance, independent of chronologic age.^{10–11} Several tools to measure frailty have been validated for surgical decision-making and prediction of complications.^{12–19} Recent studies have consistently observed that frail women with ovarian, endometrial, and cervical cancers are at increased risk for post-operative complications, hospital readmission, need for critical care support, and early mortality compared with non-frail women.^{7 8 20–26} Studies in patients with non-gynecologic cancers have demonstrated that pre-operative interventions, or 'prehabilitation', such as exercise programs or nutrition supplementation, may be beneficial.²⁷ In a cost-effectiveness study by Dholakia and colleagues, prehabilitation of medically frail women prior to



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Original research

surgical intervention for ovarian cancer was potentially cost effective by reducing post-operative complications and care facility needs.²⁸

While prior studies have demonstrated that frailty negatively impacts post-operative outcomes following gynecologic cancer surgery, the relationship of frailty on outcomes following vulvar cancer surgery is not yet determined. Given that women with vulvar cancer experience a high rate of post-operative complications following vulvar cancer surgery, frailty assessments and subsequent interventions have the potential to improve outcomes. The purpose of this study is to determine whether frailty is associated with post-operative complications following surgery for vulvar cancer.

METHODS

Data Source and Study Design

This retrospective study used a multi-institutional dataset from the National Surgical Quality Improvement Program (NSQIP) database.²⁹ NSQIP is an ongoing data-driven, participatory, quality improvement initiative including over 700 US hospitals.³⁰ Data collection is performed by trained clinical reviewers who abstract pre-operative and 30-day post-operative information from medical records according to standardized definitions.³¹ 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.³¹ This study was considered exempt by the Institutional Review Board of The Ohio State University.

Study Population

We included women (≥ 18 years) who underwent vulvectomy for vulvar cancer between 2014 and 2020. We used International Classification of Diseases 9th revision (ICD-9) (184.1, 184.2, 184.3, 184.4) and ICD-10 (C51.0, C51.1, C51.2, C51.8, C51.9) diagnosis codes to identify vulvar cancer patients. We further restricted the study population to women who underwent radical vulvectomy using Current Procedural Terminology (CPT) codes (56630, 56631, 56632, 56633, 56634, 56637, 56640), identifying 893 women. Of those, we excluded seven women who were missing information on variables needed to calculate the frailty score, leaving 886 in the analytical sample (online supplemental table 1).

Modified Frailty Index and Other Covariates

Frailty was determined using the modified frailty index-5 (mFI-5) scoring as previously described.^{12–17} All five mFI-5 components were available in NSQIP: (1) diabetes mellitus, (2) hypertension requiring medication, (3) chronic obstructive pulmonary disease, (4) congestive heart failure, and (5) functional dependency.³¹ The number of frailty variables present were summed, with each patient receiving a score between 0 and 5 points (higher scores indicate increased frailty). Based on previous literature, patients were categorized as non-frail (0 or 1 frailty indicator) and frail (≥ 2 frailty indicators).^{17 24 26} In addition, we 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 kg/m², unknown), pre-operative albumin (< 3 , ≥ 3 g/dL, unknown), length of hospital stay (days), disseminated cancer, American Society of Anesthesiologists (ASA) classification (< 3 , ≥ 3), smoking within the last year, pre-operative dialysis,

steroid use for a chronic condition, pre-operative weight loss, operation time (minutes), and type of surgery (radical vulvectomy only, radical vulvectomy plus unilateral inguofemoral lymphadenectomy, and radical vulvectomy plus bilateral inguofemoral lymphadenectomy). The following CPT codes were used to identify unilateral inguofemoral lymphadenectomy (56631) and bilateral inguofemoral lymphadenectomy (56632).

Surgical Outcomes

Within the NSQIP dataset, 21 surgical complications were recorded: deep organ space surgical site infection, deep surgical site infection, wound disruption, superficial surgical site infection, pneumonia, pulmonary embolism, acute renal failure, progressive renal insufficiency, urinary tract infection, stroke, deep venous thrombosis, myocardial infarction, cardiac arrest, any unplanned readmission, return to the operating room, venous thromboembolism, sepsis, shock, ventilation necessary for > 48 hours, need for reintubation, and blood transfusion. For this analysis, we defined four classes of post-operative complications: (1) Minor (blood transfusion, urinary tract infection, wound disruption, renal insufficiency, pneumonia, superficial surgical site infection, deep surgical site infection); (2) Major (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 hours, need for reintubation); (3) Wound-related (deep organ space surgical site infection, deep surgical site infection, superficial surgical site infection, surgical wound disruption); and (4) Any (occurrence of any of the 21 surgical complications listed above).

Statistical Analysis

Statistical analyses utilized frequency distributions of pre-operative characteristics in the overall cohort and according to frailty status (non-frail vs frail). We also examined distributions of frailty and specific post-operative complications. Univariate and multivariable-adjusted logistic regression models were used to calculate odds ratios (ORs) and 95% confidence intervals (95% CIs) for the association of dichotomous mFI-5 and each of the post-operative complication categories. In the main analyses we controlled for pre-operative characteristics that were significantly ($p < 0.05$) associated with frailty and each specific class of post-operative complication. Therefore, the inclusion of adjustment variables differs between models as some pre-operative characteristics were not significantly associated with each post-operative complication class. We took this approach to minimize the degrees of freedom included in each model. For each model, adjustment factors are listed in the relevant tables. In a secondary analysis, we controlled for covariates based on prior literature demonstrating an association with frailty or surgical complications. All analyses were performed with SAS with statistical significance considered as a p value < 0.05 .

RESULTS

Patient Demographics

In total, our retrospective cohort included 886 women with vulvar cancer who underwent either radical vulvectomy alone ($n=442$, 49.9%), radical vulvectomy with unilateral inguofemoral lymphadenectomy ($n=173$, 19.5%), or radical vulvectomy with bilateral

inguinofemoral lymphadenectomy (n=271, 30.6%) between 2014 and 2020. Of these patients, 75.5% (n=669) had mFI-5 scores of 0 or 1, and were considered non-frail, and 24.5% (n=217) had mFI-5 scores of ≥ 2 and were considered frail. The mFI-5 scores were 0 in 35.0% (n=310), 1 in 40.5% (n=359), 2 in 21.2% (n=188), 3 in 3.2% (n=28), 4 in 0.1% (n=1), and 5 in 0.0% (n=0).

Clinical characteristics in the overall study population and according to frailty status are described in Table 1. Compared with non-frail women, women categorized as frail were older than 65 (70.1% vs 54.0%, $p < 0.0001$), had a higher BMI (BMI 30–39.9: 41.9% vs 34.5%, BMI ≥ 40 : 22.1% vs 10.2%, $p < 0.0001$), and had an ASA classification ≥ 3 (84.3% vs 58.2%, $p < 0.0001$). Diabetes mellitus (77.4% vs 4.2%, $p < 0.0001$), functional dependency (12.4% vs 0.5%, $p < 0.0001$), congestive heart failure (1.8% vs 0.0%, $p = 0.004$), history of severe chronic obstructive pulmonary disease (24.0% vs 3.0%, $p < 0.0001$), and hypertension (98.2% vs 46.0%, $p < 0.0001$) were significantly more common among frail as compared with non-frail women. Frail women were also more likely to have dialysis prior to surgery (2.3% vs 0.5%, $p = 0.02$) compared with the non-frail group. There were no significant differences in race ($p = 0.11$), surgery type ($p = 0.83$), length of stay ($p = 0.05$), disseminated cancer ($p = 0.32$), smoking within 1 year of surgery ($p = 0.45$), steroid use ($p = 0.05$), weight loss prior to surgery ($p = 1.00$), and operation time ($p = 0.37$) between frail and non-frail women.

Univariate Analysis

In Table 2, frequencies of individual post-operative complications are described according to frailty status. Compared with non-frail women, women categorized as frail were significantly more likely to have an unplanned readmission (12.9% vs 7.8%, $p = 0.02$), have a wound disruption (8.3% vs 4.2%, $p = 0.02$), and have a deep surgical site infection (3.7% vs 1.4%, $p = 0.04$). We did not observe significant differences in the frequency distributions of other post-operative complications according to frailty.

Multivariable Analysis

In Table 3, multivariable analysis for mFI-5 score and composite complications are shown for the overall study population. In unadjusted models, frailty was significantly associated with minor complications (OR 1.49, 95% CI 1.03 to 2.16), major complications (OR 1.82, 95% CI 1.18 to 2.80), and any complications (OR 1.59, 95% CI 1.13 to 2.23), but not with wound complications (OR 1.33, 95% CI 0.90 to 1.97). In multivariable-adjusted models, frailty remained a significant predictor for minor complications (OR 1.58, 95% CI 1.09 to 2.30) and any complications (OR 1.46, 95% CI 1.02 to 2.08), but was not significantly associated with major complications (OR 1.46, 95% CI 0.93 to 2.31) or wound complications (OR 1.41, 95% CI 0.95 to 2.11). When we further adjusted the wound complications model for BMI—a covariate that has been associated with wound complications in other gynecologic malignancies—the association between frailty and wound complications remained non-significant (OR 1.42, 95% CI 0.94 to 2.15, data not tabled).

Table 4 demonstrates the multivariable analysis for mFI-5 score, and composite complications are shown for patients according to surgical procedure. The multivariable-adjusted association between frailty and odds of post-operative complications stratified by procedure type revealed that among patients undergoing

bilateral inguinofemoral lymphadenectomy, frailty was significantly associated with major complications (OR 2.13, 95% CI 1.03 to 4.40) and any complications (OR 2.10, 95% CI 1.14 to 3.87) (Table 4).

DISCUSSION

Summary of Main Results

Our analysis identified that frailty was predictive of any post-operative complication and any minor complication following vulvar cancer surgery, when controlling for pre-operative patient-specific factors associated with frailty. When stratified by surgical procedures, frailty was associated with increased risk for any post-operative complication and major complications following radical vulvectomy with bilateral inguinofemoral lymphadenectomy.

Results in the Context of Published Literature

Over the last decade, frail status has consistently proven to be a predictor of adverse post-operative events in women undergoing surgery for ovarian, endometrial, and cervical cancer.^{21–26} Our analysis identified that frail status is common in women undergoing vulvar cancer surgery, accounting for 24.5% of the population. In other studies assessing the impact of frailty on post-operative outcomes in women with ovarian, endometrial, and cervical cancer, lower rates of frailty were reported.^{7–20, 22–24, 26} Specifically, in another analysis of NSQIP data using the mFI-5 score, the rate of frailty was 9.61% for cervical cancer, 10.12% for ovarian cancer, and 19.9% for uterine cancer.²⁰ While women with vulvar cancer are on average older at diagnosis, compared with other gynecologic cancers, we understand that other variables exist that may impact post-operative and oncologic outcomes and that many women are diagnosed at a younger age. For example, Black women may be diagnosed with vulvar cancer at an earlier age, with more advanced disease, and have significantly worse outcomes.^{32–34} Due to the relative rarity of vulvar cancer, there is limited research to support how specific medical comorbidities influence oncologic and surgical outcomes. Therefore, frailty assessments, which are independent of chronological age, may provide a more comprehensive, practical assessment in this disease across the entire spectrum of women with this diagnosis.

Although vulvar cancer accounts for a minority of gynecologic cancer diagnoses in the USA, the majority of women are diagnosed with early-stage disease, and surgical management is considered to be the optimal primary treatment approach.³⁵ In recent years, there has been a shift prioritizing less radical surgeries, but patients may ultimately need to undergo more than one operation between diagnosis and treatment based on margin status and lymph node status at initial surgery. This underscores the importance of understanding potential strategies to predict and mitigate peri-operative risk. In women undergoing surgery for vulvar cancer, frailty was associated with any complication and, when analyzed by type of complication, minor complications. When stratified by procedure type, frail patients undergoing radical vulvectomy with bilateral inguinofemoral lymphadenectomy were at higher risk of any complication, including both minor and major complications, even when controlling for medical comorbidities.

The association between frailty and major complications for women undergoing vulvectomy with bilateral inguinofemoral lymphadenectomy may be a reflection of the increased morbidity

Table 1 Clinical characteristics of 886 women with vulvar cancer overall and according to frailty, National Surgical Quality Improvement Program, 2014–2020

Characteristics	Overall (n=886)	N (%)		P value
		Non-frail (n=669)	Frail (n=217)	
Age ≥65 years	513 (57.9)	361 (54.0)	152 (70.1)	<0.0001
Race				0.11
Non-Hispanic White	624 (70.4)	473 (70.7)	151 (69.6)	
Non-Hispanic Black	44 (5.0)	31 (4.6)	13 (6.0)	
Hispanic	37 (4.2)	24 (3.6)	13 (6.0)	
Other	23 (2.6)	14 (2.1)	9 (4.2)	
Unknown	158 (17.8)	127 (19.0)	31 (14.3)	
mFI				---
0	310 (35.0)	310 (46.3)	0 (0.0)	
1	359 (40.5)	359 (53.7)	0 (0.0)	
2	188 (21.2)	0 (0.0)	188 (86.6)	
3	28 (3.2)	0 (0.0)	28 (12.9)	
4	1 (0.1)	0 (0.0)	1 (0.5)	
5	0 (0.0)	0 (0.0)	0 (0.0)	
Body mass index (kg/m ²)				<0.0001
<30	441 (49.8)	365 (54.6)	76 (35.0)	
30–39.9	322 (36.3)	231 (34.5)	91 (41.9)	
≥40	116 (13.1)	68 (10.2)	48 (22.1)	
Unknown	7 (0.8)	5 (0.8)	2 (0.9)	
Surgery type				0.83
Radical vulvectomy only	442 (49.9)	336 (50.2)	106 (48.9)	
Radical vulvectomy+unilateral IFN	173 (19.5)	132 (19.7)	41 (18.9)	
Radical vulvectomy+bilateral IFN	271 (30.6)	201 (30.0)	70 (32.3)	
Pre-operative albumin (mg/dL)				0.003
<3	14 (1.6)	6 (0.9)	8 (3.7)	
≥3	441 (49.8)	324 (48.4)	117 (53.9)	
Unknown	431 (48.7)	339 (50.7)	92 (42.4)	
Pre-operative albumin, mean (SD)	4.0 (0.5)	4.0 (0.4)	3.8 (0.5)	0.0005
Length of stay (days)	1 (1–3)	1 (1–2)	2 (1–3)	0.05
Disseminated cancer	25 (2.8)	21 (3.1)	4 (1.8)	0.32
ASA classification ≥3	572 (64.6)	389 (58.2)	183 (84.3)	<0.0001
Smoker within 1 year of surgery	180 (20.3)	132 (19.7)	48 (22.1)	0.45
On dialysis prior to surgery	8 (0.9)	3 (0.5)	5 (2.3)	0.02
Steroid use for chronic condition	42 (4.7)	37 (5.5)	5 (2.3)	0.05
Weight loss prior to surgery	5 (0.6)	4 (0.6)	1 (0.5)	1.00
Operating time (minutes)	100.5 (62–152)	99 (62–148)	101 (63–166)	0.37
mFI components				
Diabetes mellitus	196 (22.1)	28 (4.2)	168 (77.4)	<0.0001
Functional dependency	30 (3.4)	3 (0.5)	27 (12.4)	<0.0001
Congestive heart failure	4 (0.5)	0 (0.0)	4 (1.8)	0.004
History of severe COPD	72 (8.1)	20 (3.0)	52 (24.0)	<0.0001
Hypertension requiring medication	521 (58.8)	308 (46.0)	213 (98.2)	<0.0001

ASA, American Society of Anesthesiologists; COPD, chronic obstructive pulmonary disease; IFN, inguino-femoral lymphadenectomy; mFI, modified frailty index.

Table 2 Frequency of post-operative complications according to mFI status among 886 women with vulvar cancer, National Surgical Quality Improvement Program, 2014–2020

Complication	Non-frail	Frail	P value
	n=669 n (%)	n=217 n (%)	
<i>Major</i>			
Any unplanned readmission			0.02
Yes	52 (7.8)	28 (12.9)	
No	617 (92.2)	189 (87.1)	
Return to the OR			0.37
Yes	22 (3.3)	10 (4.6)	
No	647 (96.7)	207 (95.4)	
Cardiac arrest			NE
Yes	0 (0.0)	0 (0.0)	
No	669 (100.0)	217 (100.0)	
Myocardial infarction			0.06
Yes	0 (0.0)	2 (0.9)	
No	669 (100.0)	215 (99.1)	
Stroke/cerebrovascular accident			0.43
Yes	1 (0.2)	1 (0.5)	
No	668 (99.9)	216 (99.5)	
Renal failure			NE
Yes	0 (0.0)	0 (0.0)	
No	669 (100.0)	217 (100.0)	
Venous thromboembolism			1.00
Yes	9 (1.4)	2 (0.9)	
No	660 (98.7)	215 (99.1)	
Deep venous thrombosis			0.69
Yes	7 (1.1)	1 (0.5)	
No	662 (99.0)	216 (99.5)	
Pulmonary embolus			1.00
Yes	3 (0.5)	1 (0.5)	
No	666 (99.6)	216 (99.5)	
Sepsis			0.33
Yes	8 (1.2)	5 (2.3)	
No	661 (98.8)	212 (97.7)	
Shock			0.24
Yes	0 (0.0)	1 (0.5)	
No	669 (100.0)	216 (99.5)	
Organ space surgical site infection			1.00
Yes	4 (0.6)	1 (0.5)	
No	665 (99.4)	216 (99.5)	
Ventilation necessary for >48 hours			NE
Yes	0 (0.0)	0 (0.0)	
No	669 (100.0)	217 (100.0)	
Need for reintubation			0.06
Yes	0 (0.0)	2 (0.9)	
No	669 (100.0)	215 (99.1)	
<i>Minor</i>			

Continued

Table 2 Continued

Complication	Non-frail	Frail	P value
	n=669 n (%)	n=217 n (%)	
Blood transfusion			0.66
Yes	15 (2.2)	6 (2.8)	
No	654 (97.8)	211 (97.2)	
Urinary tract infection			0.33
Yes	8 (1.2)	5 (2.3)	
No	661 (98.8)	212 (97.7)	
Wound disruption			0.02
Yes	28 (4.2)	18 (8.3)	
No	641 (95.8)	199 (91.7)	
Renal insufficiency			0.24
Yes	0 (0.0)	1 (0.5)	
No	669 (100.0)	216 (99.5)	
Pneumonia			0.24
Yes	0 (0.0)	1 (0.5)	
No	669 (100.0)	216 (99.5)	
Superficial SSI			0.54
Yes	76 (11.4)	28 (12.9)	
No	593 (88.6)	189 (87.1)	
Deep SSI			0.04
Yes	9 (1.4)	8 (3.7)	
No	660 (98.7)	209 (96.3)	

mFI, modified frailty index; NE, not evaluable; OR, operating room; SSI, surgical site infection.

with a more radical vulvar cancer procedure. The decision for unilateral versus bilateral inguofemoral lymphadenectomy is based on the laterality of the lesion relative to the midline, with more midline masses at an increased risk to drain via dermal lymphatics to the contralateral side.³⁶ While our analysis is limited by lack of information related to the tumor size and location, bilateral inguofemoral lymphadenectomy is more likely to be performed in tumors in closer proximity to vital midline structures, and potentially in larger tumors necessitating a larger area of resection, both of which may increase risk for post-operative complications. Regardless, incorporating frailty measures into pre-operative assessments may aid in patient counseling, communication of expectations, and shared decision-making regarding surgery-related morbidity.

Frailty was not associated with post-operative wound complications. When further adjusted for BMI as a covariate, the association between frailty and wound complications remained non-significant (OR 1.42, 95% CI 0.94 to 2.15). Prior studies have demonstrated that extent of surgery, peri-operative glucose control, and smoking are significant predictors of surgical site infection and wound-related morbidity after vulvar cancer surgery.^{4,37} While frail women who undergo surgery for vulvar cancer are at increased risk for post-operative complications, their inherent risk for wound complications is not higher. These findings are important for surgical planning and patient counseling.

Frailty is a medical condition defined by a reduction in physical status and physiologic reserves, and generalized deconditioning.³⁸

Table 3 Multivariable ORs and 95% CIs for associations between mFI status and composite complications among 886 women with vulvar cancer, National Surgical Quality Improvement Program, 2014–2020

mFI status	Minor complications			Major complications			Wound complications			Any complications						
	n (%)	Yes (n=172)	OR (95% CI)	P value	n (%)	Yes (n=781)	OR (95% CI)	P value	n (%)	Yes (n=148)	OR (95% CI)	P value	n (%)	Yes (n=214)	OR (95% CI)	P value
Non-frail	550 (77.0)	119 (69.2)	1.00	0.02	601 (77.0)	68 (64.8)	1.00	0.10	564 (76.4)	105 (71.0)	1.00	0.09	522 (77.7)	147 (68.7)	1.00	0.04
Frail	164 (23.0)	53 (30.8)	1.58 (1.09 to 2.30)		180 (23.1)	37 (35.2)	1.46 (0.93 to 2.31)		174 (23.6)	43 (29.1)	1.41 (0.95 to 2.11)		150 (22.3)	67 (31.3)	1.46 (1.02 to 2.08)	

Minor complications adjusted for: age (<65, ≥65).
Major complications adjusted for: BMI (<30, 30–40, ≥40, unknown), ASA classification (1–2, ≥3), on dialysis prior to surgery (no vs yes).
Wound complications adjusted for: age (<65, ≥65).
Any complications adjusted for: ASA classification (1–2, ≥3), on dialysis prior to surgery (no vs yes).
ASA, American Society of Anesthesiologists; BMI, body mass index; mFI, modified frailty index.

While there are numerous strategies and validated scales to measure frailty, there is no standardized tool for measuring frailty in surgical populations. The modified frailty index is commonly used in surgical research, has been well-validated, and historically utilized 11 variables contained within the NSQIP database.¹⁹ However, a study by Gani et al demonstrated that due to optional reporting of variables contained in the 11-item modified frailty index after 2013, the vast majority of patients included in NSQIP had missing data points, which led to the evolution of the 5-point mFI-5 scale.¹⁸ While further study is ongoing to understand the optimal assessment of frailty, the mFI-5 assessment allows for a quick, practical assessment of frailty that is clinically relevant and has been shown to be predictive of adverse post-operative events across different surgical settings in addition to patients with gynecologic cancer.^{12–17}

Strengths and Weaknesses

Our study is the first to assess the impact of frailty using the mFI-5 score in women undergoing surgery for vulvar cancer. Utilization of this large, validated, prospective database enables us to study a relatively rare disease. Further, using a national dataset allows for increased generalizability of our findings and decreases some potential for biases related to geography, provider surgical techniques, and patient selection. Nonetheless, external validation would be important.

Our study has several important limitations, which are inherent to performing a retrospective analysis of prospectively collected data from NSQIP. Primarily, we are limited by the available data within the dataset and are missing information on important patient and oncologic characteristics, including tumor size, tumor location, and post-operative adjuvant treatment. Other instruments to measure frailty similarly could not be assessed. The lack of information about the use of neoadjuvant therapy, or the use of sentinel lymph node rather than complete lymph node dissection, could influence the conclusions drawn from these analyses had those practices been employed, and they also reduced the risk of post-operative complications. Further, the mFI-5 score was applied retrospectively after the data were collected, so there is potential for miscalculation or inaccuracy in the frailty scoring.

Implications for Clinical Practice and Future Research

Understanding the relationship between frailty and surgical outcomes in a population with a high percentage of frail patients provides an opportunity to improve outcomes for women with vulvar cancer. As frailty is a dynamic state, there is an opportunity for optimizing surgical candidacy with respect to frailty status, potentially via implementation of prehabilitation programs.³⁹ This highlights the importance of considering frailty in the pre-operative assessment of women undergoing vulvar surgery, and allows for improved communication with patients pre-operatively about expected post-operative risk.

CONCLUSIONS

This NSQIP analysis of outcomes among women undergoing surgery for vulvar cancer revealed that frailty is predictive of any post-operative complication, with the risk of major complications highest in those who underwent radical vulvectomy with bilateral inguino-femoral lymphadenectomy.

Table 4 Multivariable ORs and 95% CIs for associations between mFI status and composite complications stratified by procedure type, National Surgical Quality Improvement Program, 2014–2020

mFI status	Minor complications			Major complications			Wound complications			Any complications							
	n (%)	OR (95% CI)	P value	n (%)	OR (95% CI)	P value	None (n=384)	Any (n=58)	n (%)	OR (95% CI)	P value	None (n=353)	Any (n=89)	n (%)	OR (95% CI)	P value	
Non-frail	286 (76.9)	1.00	0.25	305 (76.3)	1.00	0.99	293 (76.3)	43 (74.1)	271 (76.8)	65 (73.0)	0.60	271 (76.8)	65 (73.0)	1.00	0.82		
Frail	86 (23.1)	1.40 (0.79 to 2.51)	0.25	95 (23.8)	1.11 (0.62 to 1.99)	0.71	91 (23.7)	15 (25.9)	82 (23.2)	24 (27.0)	1.19 (0.63 to 2.25)	82 (23.2)	24 (27.0)	1.07 (0.62 to 1.84)	0.82		
Radical vulvectomy+unilateral IFN																	
None (n=134)	Any (n=39)	None (n=154)	Any (n=19)	None (n=140)	Any (n=33)	None (n=128)	Any (n=45)	None (n=191)	Any (n=80)	None (n=227)	Any (n=63)	None (n=214)	Any (n=57)	None (n=191)	Any (n=80)	None (n=191)	Any (n=80)
n (%)	OR (95% CI)	P value	n (%)	OR (95% CI)	P value	n (%)	OR (95% CI)	P value	n (%)	OR (95% CI)	P value	n (%)	OR (95% CI)	P value	n (%)	OR (95% CI)	P value
Non-frail	28 (71.8)	1.00	120 (77.9)	1.00	0.36	109 (77.9)	12 (63.2)	1.00	101 (78.9)	31 (68.9)	0.28	101 (78.9)	31 (68.9)	1.00	0.29		
Frail	30 (22.4)	1.46 (0.64 to 3.23)	34 (22.1)	1.63 (0.55 to 4.82)	0.38	31 (22.1)	7 (36.8)	1.61 (0.68 to 3.79)	27 (21.1)	14 (31.1)	1.53 (0.69 to 3.35)	27 (21.1)	14 (31.1)	1.53 (0.69 to 3.35)	0.29		
Radical vulvectomy+bilateral IFN																	
None (n=208)	Any (n=63)	None (n=227)	Any (n=44)	None (n=214)	Any (n=57)	None (n=191)	Any (n=80)	None (n=214)	Any (n=57)	None (n=191)	Any (n=80)	None (n=191)	Any (n=80)	None (n=191)	Any (n=80)	None (n=191)	Any (n=80)
n (%)	OR (95% CI)	P value	n (%)	OR (95% CI)	P value	n (%)	OR (95% CI)	P value	n (%)	OR (95% CI)	P value	n (%)	OR (95% CI)	P value	n (%)	OR (95% CI)	P value
Non-frail	160 (76.9)	1.00	176 (77.5)	1.00	0.05	162 (75.7)	25 (56.8)	1.00	150 (78.5)	51 (63.8)	0.20	150 (78.5)	51 (63.8)	1.00	0.02		
Frail	48 (23.1)	1.87 (1.00 to 3.48)	51 (22.5)	2.13 (1.03 to 4.40)	0.05	52 (24.3)	19 (43.2)	2.13 (1.03 to 4.40)	41 (21.5)	29 (36.3)	1.54 (0.80 to 2.96)	41 (21.5)	29 (36.3)	2.10 (1.14 to 3.87)	0.02		

Minor complications adjusted for: age (<65, ≥65).
 Major complications adjusted for: BMI (<30, 30–40, ≥40, unknown), ASA classification (1–2, ≥3), on dialysis prior to surgery (no vs yes).
 Wound complications adjusted for: age (<65, ≥65).
 Any complications adjusted for: ASA classification (1–2, ≥3), on dialysis prior to surgery (no vs yes).
 ASA, American Society of Anesthesiologists; BMI, body mass index; IFN, ??????; mFI, modified frailty index.

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REFERENCES

- Siegel RL, Miller KD, Fuchs HE, et al. Cancer statistics, 2022. *CA Cancer J Clin* 2022;72:7–33.
- Wills A, Obermair A. A review of complications associated with the surgical treatment of vulvar cancer. *Gynecol Oncol* 2013;131:467–79.
- Gitas G, Proppe L, Baum S, et al. A risk factor analysis of complications after surgery for vulvar cancer. *Arch Gynecol Obstet* 2021;304:511–9.
- Hinten F, van den Einden LCG, Hendriks JCM, et al. Risk factors for short- and long-term complications after groin surgery in vulvar cancer. *Br J Cancer* 2011;105:1279–87.
- Sullivan SA, Van Le L, Liberty AL, et al. Association between hypoalbuminemia and surgical site infection in vulvar cancers. *Gynecol Oncol* 2016;142:435–9.
- Di Donato V, Page Z, Bracchi C, et al. The age-adjusted Charlson comorbidity index as a predictor of survival in surgically treated vulvar cancer patients. *J Gynecol Oncol* 2019;30:e6.
- Nakha M, Eakin CM, Mandelbaum A, et al. Frailty is independently associated with worse outcomes and increased resource utilization following endometrial cancer surgery. *Int J Gynecol Cancer* 2022;ijgc-2022-003484.
- Mah SJ, Anpalagan T, Marcucci M, et al. The five-factor modified frailty index predicts adverse postoperative and chemotherapy outcomes in gynecologic oncology. *Gynecol Oncol* 2022;166:154–61.
- Handley KF, Sood AK, Molin GZD, et al. Frailty repels the knife: the impact of frailty index on surgical intervention and outcomes. *Gynecol Oncol* 2022;166:50–6.
- Morley JE, Vellas B, van Kan GA, et al. Frailty consensus: a call to action. *J Am Med Dir Assoc* 2013;14:392–7.
- Dent E, Martin FC, Bergman H, et al. Management of frailty: opportunities, challenges, and future directions. *Lancet* 2019;394:1376–86.
- Panayi AC, Haug V, Kauke-Navarro M, et al. The modified 5-item frailty index is a predictor of perioperative risk in head and neck microvascular reconstruction: an analysis of 3795 cases. *Am J Otolaryngol* 2021;42:103121.
- Ornaghi PI, Afferi L, Antonelli A, et al. Frailty impact on postoperative complications and early mortality rates in patients undergoing radical cystectomy for bladder cancer: a systematic review. *Arab J Urol* 2020;19:9–23.
- Wachal B, Johnson M, Burchell A, et al. Association of modified frailty index score with perioperative risk for patients undergoing total laryngectomy. *JAMA Otolaryngol Head Neck Surg* 2017;143:818–23.
- Dauch J, Hamidi M, Arrington AK, et al. The impact of frailty on patients undergoing liver resection for colorectal liver metastasis. *J Gastrointest Surg* 2022;26:608–14.
- Goldwag J, Harris A, Bettis AD. 5-item modified frailty index as a preoperative predictor of morbidity following minimally invasive partial nephrectomy. *Urology* 2021;157:138–42.
- Chimukangara M, Helm MC, Frelich MJ, et al. A 5-item frailty index based on NSQIP data correlates with outcomes following paraesophageal hernia repair. *Surg Endosc* 2017;31:2509–19.
- Gani F, Canner JK, Pawlik TM. Use of the modified frailty index in the American College of Surgeons national surgical improvement program database: highlighting the problem of missing data. *JAMA Surg* 2017;152:205–7.
- Velanovich V, Antoine H, Swartz A, et al. Accumulating deficits model of frailty and postoperative mortality and morbidity: its application to a national database. *J Surg Res* 2013;183:104–10.
- AlHilli MM, Schold JD, Kelley J, et al. Preoperative assessment using the five-factor modified frailty index: a call for standardized preoperative assessment and prehabilitation services in gynecologic oncology. *Gynecol Oncol* 2022;166:379–88.
- Di Donato V, Caruso G, Bogani G, et al. Preoperative frailty assessment in patients undergoing gynecologic oncology surgery: a systematic review. *Gynecol Oncol* 2021;161:11–9.
- Sia TY, Wen T, Cham S, et al. The effect of frailty on postoperative readmissions, morbidity, and mortality in endometrial cancer surgery. *Gynecol Oncol* 2021;161:353–60.
- Filippova OT, Tin AL, Alonso J, et al. Frailty based on the Memorial Sloan Kettering frailty index is associated with surgical decision making, clinical trial participation, and overall survival among older women with ovarian cancer. *Gynecol Oncol* 2021;161:687–92.
- Chambers LM, Chalif J, Yao M, et al. Modified frailty index predicts postoperative complications in women with gynecologic cancer undergoing cytoreductive surgery and hyperthermic intraperitoneal chemotherapy. *Gynecol Oncol* 2021;162:368–74.
- Mullen MM, McKinnish TR, Fiala MA, et al. A deficit-accumulation frailty index predicts survival outcomes in patients with gynecologic malignancy. *Gynecol Oncol* 2021;161:700–4.
- Uppal S, Igwe E, Rice LW, et al. Frailty index predicts severe complications in gynecologic oncology patients. *Gynecol Oncol* 2015;137:98–101.
- Molenaar CJ, van Rooijen SJ, Fokkenrood HJ, et al. Prehabilitation versus no prehabilitation to improve functional capacity, reduce postoperative complications and improve quality of life in colorectal cancer surgery. *Cochrane Database Syst Rev* 2022;5:CD013259.
- Dholakia J, Cohn DE, Straughn JM, et al. Prehabilitation for medically frail patients undergoing surgery for epithelial ovarian cancer: a cost-effectiveness analysis. *J Gynecol Oncol* 2021;32:e92.
- Raval MV, Pawlik TM. Practical guide to surgical data sets: National Surgical Quality Improvement Program (NSQIP) and pediatric NSQIP. *JAMA Surg* 2018;153:764–5.
- Fink AS, Campbell DA, Mentzer RM, et al. The National Surgical Quality Improvement Program in non-veterans administration hospitals: initial demonstration of feasibility. *Ann Surg* 2002;236:344–53.
- American College of Surgeons National Surgical Quality Improvement Program. User guide for the 2021 ACS NSQIP participant use. 2022.
- Chase DM, Lin CC, Craig CD, et al. Disparities in vulvar cancer reported by the National Cancer Database: influence of sociodemographic factors. *Obstet Gynecol* 2015;126:792–802.
- Zhou WL, Yue YY. Trends in the incidence of vulvar and vaginal cancers with different histology by race, age, and region in the United States (2001–2018). *Int J Public Health* 2022;67:1605021.
- Rauh-Hain JA, Melamed A, Schaps D, et al. Racial and ethnic disparities over time in the treatment and mortality of women with gynecological malignancies. *Gynecol Oncol* 2018;149:4–11.
- NCCN Clinical Practice Guidelines in Oncology. Vulvar cancer. Version 2.2022. 2022.
- Coleman RL, Ali S, Levenback CF, et al. Is bilateral lymphadenectomy for midline squamous carcinoma of the vulva always necessary? An analysis from Gynecologic Oncology Group (GOG) 173. *Gynecol Oncol* 2013;128:155–9.
- Rahm C, Adok C, Dahm-Kähler P, et al. Complications and risk factors in vulvar cancer surgery—a population-based study. *Eur J Surg Oncol* 2022;48:1400–6.
- Lang PO, Michel JP, Zekry D. Frailty syndrome: a transitional state in a dynamic process. *Gerontology* 2009;55:539–49.
- Hanna K, Ditillo M, Joseph B. The role of frailty and prehabilitation in surgery. *Curr Opin Crit Care* 2019;25:717–22.