



## Frailty in ovarian cancer identified the need for increased postoperative care requirements following cytoreductive surgery

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### HIGHLIGHTS

- Frail patients with advanced ovarian cancer undergoing cytoreductive surgery more often require postoperative ICU care.
- Frail patients with advanced ovarian cancer undergoing cytoreductive surgery are more likely to require non-home discharge.
- Frail patients with advanced ovarian cancer undergoing cytoreductive surgery require longer hospital length of stay.
- Frailty is a measurable factor that influences postoperative outcomes and should be considered in preoperative planning.

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### ABSTRACT

**Objectives.** We sought to examine the relationship between frailty and complicated postoperative courses, including intensive care unit (ICU) admission and non-home discharge, in patients with advanced ovarian cancer (OC) undergoing primary debulking surgery (PDS) for curative intent.

**Methods.** Patients were identified from a retrospectively collected database at a single institution between 1/1/2003–12/31/2011. A frailty index was derived from 30 items representing comorbidities and activities of daily living, each scored as 0, 0.5, or 1, and calculated as the total summated score divided by the total number of non-missing items. Frailty was defined as an index  $\geq 0.15$ . Associations with binary outcomes were assessed using logistic regression.

**Results.** A total of 535 patients met inclusion criteria. Frail patients were older, mean age 67.8 versus 63.2 years ( $p < 0.001$ ), but there was no difference in grade, stage, or serous histology. Almost half of the frail patients (48.9%, 64/131) were admitted to the ICU compared to 20.5% (83/404) of non-frail patients. Frailty remained an independent predictor of 30-day ICU admission (adjusted odds ratio (aOR) 3.20, 95% CI: 2.03–5.06) in a multivariable model including age, preoperative albumin, surgical complexity, and residual disease. Frail patients were also more likely to have a non-home discharge (24.2% vs. 7.0%). Frailty independently predicted non-home discharge (aOR 2.58, 95% CI: 1.35–4.93) after adjusting for age, BMI, and stage.

**Conclusion.** Frailty is a measurable, objective clinical syndrome that has impact on postoperative outcomes in advanced OC and should be considered when decision-making about treatments and counseling patients.

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### 1. Introduction

Epithelial ovarian cancer (EOC) is the leading cause of gynecologic cancer death in the United States. More than 80% of EOC patients present at advanced stages and 5-year overall survival is between 30% to

50% [1]. Patients with advanced EOC usually receive one of two treatment avenues: primary debulking surgery (PDS) followed by platinum-based chemotherapy or neoadjuvant chemotherapy (NACT) followed by interval debulking surgery (IDS). Treatment is associated with high rates of morbidity and mortality, and personalizing treatment plans to the individual is a clinical necessity. Multiple factors have been associated with increased perioperative risks including patient's age, functional status, social support, comorbidities, and nutritional status [2–6]. These factors can predict surgical morbidity, but also can predict other important outcomes such as delay to chemotherapy initiation,

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intensive care unit (ICU) admissions, longer hospital stay, and non-home discharge. Age, poor performance status, and elevated Ca125 have all been associated with independent risk for non-home discharge in EOC [7,8].

Frailty is a clinical condition that is related to both age and cancer [9]. It is characterized by a lack of physiologic reserve and increased vulnerability to stressors, such as surgery, cancer, and chemotherapy. We have previously shown that frailty is common in advanced EOC patients, and that these patients have worse outcomes including an increased risk of severe postoperative complication, death within 90 days of surgery, and lower overall survival, even after adjusting for known risk factors [10]. In other tumor types and surgery, frailty is associated with costly hospital interventions such as ICU stays, postoperative readmission, and non-home discharge [11–15]. Therefore, we sought to understand the relationship between frailty and these secondary outcomes in patients with advanced EOC undergoing surgery to assist in perioperative decision-making and supportive care planning.

## 2. Methods

After obtaining approval from Mayo Clinic Institutional Review Board, data was abstracted for patients who underwent PDS for stage IIIC or IV ovarian cancer, fallopian tube, or primary peritoneal cancer from 1/2/2003 to 12/30/2011. Each patient's medical record was assessed for the presence of a complete institutional form called the Current Visit Information Form. This is administered to all patients prior to an outpatient clinic visit and contains information on activities of daily living as well as other self-reported medical information.

Exclusion criteria included patients who received NACT, patients undergoing palliative or diagnostic surgeries only, patients without frailty index available, and patients who denied access to their medical record. Length of stay was calculated from the day of surgery (day 0) to the day of discharge. Non-home discharge was defined as those who were discharged to a sub-acute rehabilitation facility or nursing home. ICU admission was considered if a patient received any amount of intensive care at any point during the first 30 days after surgery. Patients who died in the hospital during initial hospitalization were excluded from the analysis investigating non-hospital discharge and length of stay.

Frailty was determined by previously published methods using a list of deficits evaluated for each patient. In brief, each deficit was scored as no = 0, or yes = 1 or in the case of climbing 2 flights of stairs without rest or body mass index (BMI), assigned 0, 0.5, or 1 as listed in Table 1. Frailty index was calculated as the total summated score divided by the total number of non-missing items [10,16–18]. Patients with a deficit score of  $\geq 0.15$  were considered to be frail as previous publications describe for this cohort.

Baseline patient characteristics were compared between frail and non-frail patients using the chi-square test or Fisher's exact test for categorical variables and the *t*-test for age and BMI. Univariate and multivariable logistic regression models were fit to evaluate the association between patient characteristics and each binary outcome; associations were summarized by calculating the odds ratio (OR) and corresponding 95% confidence interval (CI). Patient characteristics with a *p*-value < 0.20 based on univariate analysis were considered in the multivariable analysis. Parsimonious multivariable models were identified using stepwise and backward selection methods. The overall discriminatory ability of each multivariable logistic model was measured using the *c*-index. The predictive ability of each multivariable logistic model was summarized by the *c*-index, which is equivalent to the area under a receiver operating characteristic curve (AUC). The AUC estimates were compared between nested models using the DeLong, DeLong, and Clarke-Pearson nonparametric method. The length of stay distribution was compared between frail and non-frail patients using the Wilcoxon rank sum test. Univariate and multivariable linear regression models were fit to evaluate the association between patient characteristics and length of stay, after applying a logarithmic transformation to length

**Table 1**  
Variables and scoring of the deficit index.

Deficit index	Assigned points
1. Need help preparing meals	No = 0, yes = 1
2. Need help feeding yourself	No = 0, yes = 1
3. Need help dressing yourself	No = 0, yes = 1
4. Need help using the toilet	No = 0, yes = 1
5. Need help with housekeeping	No = 0, yes = 1
6. Need help climbing stairs	No = 0, yes = 1
7. Need help bathing	No = 0, yes = 1
8. Need help walking	No = 0, yes = 1
9. Need help using transportation	No = 0, yes = 1
10. Need help getting in and out of bed	No = 0, yes = 1
11. Need help managing medications	No = 0, yes = 1
12. Depend on assistive devices (walker, cane, etc.) or other people to perform activities of daily life	No = 0, yes = 1
13. Dependent on device for normal breathing	No = 0, yes = 1
14. Climb 2 flights of stairs without rest	No, can't do at all = 1 Yes, with difficulty = 0.5 Yes, with no difficulty = 0
15. Myocardial infarction	No = 0, yes = 1
16. Diabetes	No = 0, yes = 1
17. Peripheral vascular disease	No = 0, yes = 1
18. Cerebrovascular disease	No = 0, yes = 1
19. Dementia	No = 0, yes = 1
20. Chronic obstructive pulmonary disease	No = 0, yes = 1
21. Peptic ulcer	No = 0, yes = 1
22. Hemiplegia/paraplegia	No = 0, yes = 1
23. Renal disease	No = 0, yes = 1
24. Moderate/severe liver disease	No = 0, yes = 1
25. Rheumatologic disease	No = 0, yes = 1
26. Hypertension	No = 0, yes = 1
27. Hyperlipidemia	No = 0, yes = 1
28. Body mass index	Underweight/obese = 1 Overweight = 0.5 Normal = 0
29. Depression	No = 0, yes = 1
30. Anemia	No = 0, yes = 1

of stay. All calculated *p*-values were two-sided and *p*-values < 0.05 were considered statistically significant. Statistical analysis was performed using the SAS version 9.4 software package (SAS Institute, Inc.; Cary, NC).

## 3. Results

A total of 617 patients with stage IIIC/IV EOC were eligible for the study. Of those, 535 were included in the total analysis, 75 were excluded due to lack of frailty data available within 30 days of surgery and 7 were excluded because they had 3 or more items missing from the deficit index. Patient characteristics are available in Table 2. Frail patients were older with a mean age of 67.8 versus 63.2 years (*p* < 0.001) and had a higher BMI, 31.7 versus 26.9 kg/m<sup>2</sup> (*p* < 0.001), but there was no difference in grade, stage, or serous histology. Frail patients were more likely to have a preoperative albumin < 3.5 g/dL (19.8% versus 10.6%, *p* = 0.01), and to have an American Society of Anesthesiologists (ASA) score of  $\geq 3$ , (71.8% versus 37.6%, *p* < 0.001). Frail patients were significantly more likely to have a low complexity surgery performed (20.6% vs 12.6%, *p* = 0.02) and have suboptimal surgical resection (24.4% vs 13.1%, *p* = 0.002).

The majority of patients (*n* = 388, 72.5%) did not experience an ICU admission within 30 days of surgery, however 147 (27.5%) did. Almost half of frail patients, 48.9% (64/131), were admitted to the ICU within 30 days of surgery compared to only 20.5% (83/404) of non-frail patients. This is despite having a higher likelihood of low complexity surgery. Table 3 summarizes the variables evaluated for an association with 30-day ICU admission. On univariate analysis, age, BMI, ASA score, preoperative albumin, grade, stage, and frailty were all significantly associated with 30-day ICU admission (*p* < 0.05). In addition high surgical complexity and presence of residual disease were associated with 30-day ICU admission. On multivariate analysis, frailty remained an

**Table 2**  
Demographic characteristics.

Characteristic	Total N = 535	Non-frail N = 404	Frail N = 131	p <sup>a</sup>
Age (years), mean (SD)	64.3 (11.3)	63.2 (11.2)	67.8 (10.8)	<0.001
BMI (kg/m <sup>2</sup> ), mean (SD)	28.1 (6.6)	26.9 (5.7)	31.7 (7.6)	<0.001
ASA score, N (%)				<0.001
<3	289 (54.0)	252 (62.4)	37 (28.2)	
≥3	246 (46.0)	152 (37.6)	94 (71.8)	
Preoperative albumin (g/dL), N (%)				0.02
≥3.5	274 (51.2)	212 (52.5)	62 (47.3)	
<3.5	69 (12.9)	43 (10.6)	26 (19.8)	
Not available	192 (35.9)	149 (36.9)	43 (32.8)	
FIGO grade, N (%) <sup>b</sup>				0.29
1	8 (1.5)	5 (1.3)	3 (2.3)	
2	18 (3.4)	16 (4.0)	2 (1.5)	
3	504 (95.1)	379 (94.8)	125 (96.2)	
FIGO stage, N (%)				0.92
IIIC	419 (78.3)	316 (78.2)	103 (78.6)	
IV	116 (21.7)	88 (21.8)	28 (21.4)	
Histology, N (%)				0.69
Non-serous	80 (15.0)	59 (14.6)	21 (16.0)	
Serous	455 (85.0)	345 (85.4)	110 (84.0)	
Surgical complexity, N (%)				0.03
Low	78 (14.6)	51 (12.6)	27 (20.6)	
Intermediate	272 (50.8)	204 (50.5)	68 (51.9)	
High	185 (34.6)	149 (36.9)	36 (27.5)	
Residual disease, N (%)				<0.001
Microscopic	235 (43.9)	196 (48.5)	39 (29.8)	
Measurable (≤1 cm)	215 (40.2)	155 (38.4)	60 (45.8)	
Suboptimal (>1 cm)	85 (15.9)	53 (13.1)	32 (24.4)	

Abbreviations: ASA, American Society of Anesthesiologists; BMI, body mass index; FIGO, International Federation of Gynecology and Obstetrics; SD, standard deviation.

Results are reported as N (% of non-missing) unless otherwise noted.

<sup>a</sup> Chi-square p value reported for categorical variables and t-test reported for continuous variables.

<sup>b</sup> FIGO grade not available on 5 patients.

**Table 3**  
Predictors of ICU admission within 30 days of surgery.

Characteristic	No. (%) with outcome	Univariate analysis		Multivariable analysis	
		Unadjusted OR (95% CI)	p	Adjusted OR (95% CI)	p
Age (years) <sup>a</sup>	–	1.49 (1.24, 1.79)	<0.001	1.38 (1.13, 1.69)	0.002
BMI (kg/m <sup>2</sup> ) <sup>a</sup>	–	1.20 (1.04, 1.38)	0.01		
ASA score			<0.001		
<3 (N = 289)	58 (20.1)	Reference			
≥3 (N = 246)	89 (36.2)	2.26 (1.53, 3.33)			
Preoperative albumin			<0.001		0.002
≥3.5 g/dL (N = 274)	72 (26.3)	Reference		Reference	
<3.5 g/dL (N = 69)	36 (52.2)	3.06 (1.78, 5.27)		2.29 (1.27, 4.13)	
Not available (N = 192)	39 (20.3)	0.72 (0.46, 1.11)		0.73 (0.45, 1.18)	
FIGO grade <sup>b</sup>			0.19		
1 (N = 8)	0 (0.0)	Reference			
2 (N = 18)	2 (11.1)	2.57 (0.09, 71.08)			
3 (N = 504)	142 (28.2)	6.68 (0.32, 138.23)			
FIGO stage			0.02		
IIIC (N = 419)	105 (25.1)	Reference			
IV (N = 116)	42 (36.2)	1.70 (1.10, 2.63)			
Histology			0.28		
Non-serous (N = 80)	18 (22.5)	Reference			
Serous (N = 455)	129 (28.4)	1.36 (0.78, 2.39)			
Surgical complexity			0.03		0.005
Low (N = 78)	18 (23.1)	Reference		Reference	
Intermediate (N = 272)	65 (23.9)	1.05 (0.58, 1.90)		1.70 (0.85, 3.37)	
High (N = 185)	64 (34.6)	1.76 (0.96, 3.24)		3.05 (1.47, 6.33)	
Residual disease			<0.001		0.005
Microscopic (N = 235)	42 (17.9)	Reference		Reference	
Measurable (≤1 cm) (N = 215)	76 (35.3)	2.51 (1.63, 3.88)		1.98 (1.23, 3.18)	
Suboptimal (>1 cm) (N = 85)	29 (34.1)	2.38 (1.36, 4.16)		2.41 (1.24, 4.67)	
Frailty (deficit index ≥ 0.15)			<0.001		<0.001
No (N = 404)	83 (20.5)	Reference		Reference	
Yes (N = 131)	64 (48.9)	3.69 (2.43, 5.62)		3.20 (2.03, 5.06)	

Abbreviations: ASA, American Society of Anesthesiologists; BMI, body mass index; CI, confidence interval; FIGO, International Federation of Gynecology and Obstetrics; OR, odds ratios.

<sup>a</sup> Odds ratio per 10-year increase in age and 5-unit increase in body mass index.

<sup>b</sup> Firth's bias correction applied due to zero cell issue.

independent predictor of ICU admission within 30 days of surgery (OR 3.20, 95% CI: 2.03–5.06), along with age, preoperative albumin, surgical complexity, and residual disease (Table 3). The overall predictive ability of a multivariable logistic model that included the five fore-mentioned variables, as measured by the c-index, was 0.71 (95% CI, 0.66–0.76). The addition of frailty to this multivariable model significantly increased the c-index to 0.75 (95% CI, 0.70–0.79) ( $p = 0.020$ ).

Patients were assessed for place of discharge, with discharge to a sub-acute rehabilitation center or a nursing home considered as non-home discharge. Eight patients were excluded from this analysis due to death within the initial hospitalization in the postoperative period; 3 of the 8 were frail. Most patients were discharged home ( $n = 468$ , 88.8%), but 59 (11.2%) experienced non-home discharge including 52 patients to a nursing home or skilled nursing facility and 7 to a sub-acute rehabilitation facility. Of the non-frail patients, 7.0% (28/399) had non-home discharge, while 24.2% (31/128) of frail patients required non-home discharge. On univariate analysis, age, ASA score, and frailty were significantly associated with non-home discharge (Table 4). On multivariate analysis, frailty remained an independent predictor of non-home discharge (OR 2.58, 95% CI: 1.35–4.93), along with age, BMI, and FIGO stage (Table 4). The c-index of the multivariable logistic model that included age, BMI, and FIGO stage was excellent at 0.84 (95% CI, 0.79–0.89); the addition of frailty to the model had minimal impact (0.85; 95% CI, 0.81–0.89).

Median length of stay was 7 days, with an interquartile range (IQR) of 5–10 days. Frail patients had a slightly longer median length of stay of 8 days (IQR 6–11) compared to non-frail patients, whose median length of stay was 7 days (IQR 5–10), however this was not a statistically significant difference ( $p = 0.06$ ). Frailty was not associated with increased length of stay after adjusting for known risk factors including older age, stage IV disease, high surgical complexity, or presence of residual disease.

#### 4. Discussion

This study examines the postoperative care requirements of frail EOC patients following surgery for ovarian cancer. We demonstrate that frail patients 1) are more than three times as likely to require admission to the ICU within 30 days of surgery, independent of other risk factors, 2) are more than twice as likely to need placement outside of the home after surgery, and 3) have a non-statistically significant longer length of stay in the hospital. These outcomes occurred despite the fact that frail patients were less likely to receive high complexity surgery. These data support the need for further frailty assessment in this group of patients to help plan for surgery and postoperative care requirements in all patients, as we find that frailty is an independent risk factor even after factoring in other traditional risk factors such as age and preoperative albumin.

Frailty is an increasingly ubiquitous factor considered in surgical planning [19–21]. While frailty is correlated to age, we have previously shown it is independent of age in predicting poor oncologic and surgical outcomes in EOC [10]. It is therefore not surprising that frail patients in this current cohort also have an increase in healthcare utilization (including ancillary services in the hospital and after discharge), requirement for ICU admission within 30 days of surgery, and non-home discharge to nursing or rehabilitation facilities. These data are consistent with the data in the geriatric general surgery population; in one study, the more frailty characteristics a patient had, the higher the likelihood of post-surgical non-home institutionalization [19,22–24]. Frailty in patients undergoing urologic procedures have similarly been associated with discharge to skilled or assisted living facilities in a large National Surgical Quality Improvement Program (NSQIP) database study [25]. Vascular surgery patients with frailty had a two-fold increased risk of non-home discharge compared to non-frail patients [26]. In ovarian cancer, primary surgery is one treatment avenue for patients with

**Table 4**  
Predictors of non-home discharge.<sup>a</sup>

Characteristic	No. (%) with outcome	Univariate analysis		Multivariable analysis	
		Unadjusted OR (95% CI)	p	Adjusted OR (95% CI)	p
Age (years) <sup>b</sup>	–	3.60 (2.51, 5.15)	<0.001	3.92 (2.63, 5.85)	<0.001
BMI (kg/m <sup>2</sup> ) <sup>b</sup>	–	1.18 (0.98, 1.42)	0.09	1.27 (1.01, 1.60)	0.04
ASA score			<0.001		
<3 (N = 286)	18 (6.3)	Reference			
≥3 (N = 241)	41 (17.0)	3.05 (1.70, 5.47)			
Preoperative albumin			0.06		
≥3.5 g/dL (N = 273)	28 (10.3)	Reference			
<3.5 g/dL (N = 65)	13 (20.0)	2.19 (1.06, 4.51)			
Not available (N = 189)	18 (9.5)	0.92 (0.49, 1.72)			
FIGO grade			0.75		
1 (N = 8)	1 (12.5)	Reference			
2 (N = 18)	1 (5.6)	0.41 (0.02, 7.55)			
3 (N = 496)	56 (11.3)	0.89 (0.11, 7.38)			
FIGO stage			0.15		0.02
IIIC (N = 414)	42 (10.1)	Reference		Reference	
IV (N = 113)	17 (15.0)	1.57 (0.86, 2.88)		2.33 (1.15, 4.72)	
Histology			0.74		
Non-serous (N = 79)	8 (10.1)	Reference			
Serous (N = 448)	51 (11.4)	1.14 (0.52, 2.50)			
Surgical complexity			0.97		
Low (N = 75)	8 (10.7)	Reference			
Intermediate (N = 269)	31 (11.5)	1.09 (0.48, 2.49)			
High (N = 183)	20 (10.9)	1.03 (0.43, 2.45)			
Residual disease			0.07		
Microscopic (N = 234)	18 (7.7)	Reference			
Measurable (≤1 cm) (N = 213)	31 (14.6)	2.04 (1.11, 3.77)			
Suboptimal (>1 cm) (N = 80)	10 (12.5)	1.71 (0.76, 3.89)			
Frailty (deficit index ≥ 0.15)			<0.001		0.004
No (N = 399)	28 (7.0)	Reference		Reference	
Yes (N = 128)	31 (24.2)	4.24 (2.43, 7.40)		2.58 (1.35, 4.93)	

Abbreviations: ASA, American Society of Anesthesiologists; BMI, body mass index; CI, confidence interval; FIGO, International Federation of Gynecology and Obstetrics; OR, odds ratios.

<sup>a</sup> Among the 535 patients, 8 were excluded from this analysis due to death within the initial hospitalization in the post-operative period.

<sup>b</sup> Odds ratio per 10-year increase in age and 5-unit increase in body mass index.

advanced disease, and is associated with high complexity surgery and high rates of complications. Advanced age, ASA score, and higher Ca125 have all been associated with non-home discharge in all stage EOC patients [7]. Other calculators have been utilized to determine surgical risk including age, ASA score, whether surgery is elective, and pre-admission residence [27], and a modified frailty index has been used to predict the need for postoperative intensive care and high grade complications using the NSQIP database [28]. Non-home discharge and 30-day ICU admissions after EOC are important regarding their impact on patients and families and for counseling and planning purposes. There are also associated costs with these outcomes. According to Healthcare Cost Report Information System (HCRIS) in 2005, national estimates for ICU costs were \$82 billion with approximately \$4300 per day of ICU care [29]. Non-home discharge can also be costly with national average in 2016 of \$253 a day for a private room in a nursing home or \$119 per day in an assisted living facility [30].

In order to prepare patients for surgery and in hopes to avoid complications during recovery, the Gynecology Oncology Group (GOG) has issued recommendations for preoperative and intraoperative care for patients with gynecologic malignancies [31]. These recommendations include patient education and counseling, preoperative smoking cessation, alcohol cessation, and addressing anemia and hyperglycemia. However there remains a lack of recommendations regarding frailty evaluation or strengthening programs such as prehabilitation. While excessive preoperative testing is often unnecessary leading to increased healthcare utilization and patient burden, some testing must be completed to evaluate surgical fitness, determine functional status, and establish a baseline of patient health [32].

As demonstrated by our study of the burden of postoperative complications, ICU admission, and non-home discharge for frail patients, this remains an area ripe for examination into process improvement. Frailty may be a modifiable risk factor in EOC patients. In other tumor types and surgical procedures, nutritional and physical medicine rehabilitation have been employed with variable success to decrease patient risk. A review of the literature in 2013 revealed initial evidence that total body prehabilitation for surgical patients likely improves postoperative outcomes and decreases hospital length of stay. Some of these may be applied to EOC patients, particularly in the perioperative time period where physiologic reserve is so important for surgical recovery [33]. Preoperative prehabilitation has been the subject of multiple publications in urologic, orthopedic, and cardiothoracic surgical patients. Prehabilitation has been found to improve frailty scores and decrease hospital stay for patients undergoing major cardiothoracic surgery [34]. A study is currently accruing which is randomizing elderly frail patients with cancer to receive 3 weeks of in-home preoperative prehabilitation before major abdominal or thoracic oncologic surgery [35].

The retrospective nature in which the data collected lends itself to inherent bias of this study design including incomplete data points and patient exclusion when data are limited. The frail and non-frail groups were statistically different at baseline regarding age and BMI, two important risk factors in many published frailty scales. They were not matched in the study design leading to possibility for introduction of other confounders. Only 26 patients (4.9%) in our cohort were frail with albumin < 3.5 g/dL and this may have limited our ability to identify a significant interaction effect between albumin and frailty in the multivariable model ( $p = 0.38$ ) as demonstrated in previous publications [36]. The adjusted odds ratio for the association between low albumin and 30-day ICU admission was 3.22 (95% CI, 1.57–6.64) among non-frail patients and 1.23 (95% CI, 0.45–3.40) among frail patients. However, perhaps more importantly, the data did not support a significant interaction effect on an additive scale in the multivariable model adjusted for the other covariates. The expected odds ratio for the combined effect of frailty and low albumin under the assumption of additivity was 6.17 ( $= 4.09 + 3.08 - 1$ ) and this estimate was contained within the 95% CI for the observed combined effect of these two factors (HR = 5.32, 95% CI 2.14–13.18).

We continue to iterate that patients who undergo extensive and aggressive primary cytoreductive surgery for ovarian cancer who are frail at baseline tend to have poorer surgical outcomes, perioperative outcomes, increased level of care required, and are more likely to have non-home discharge. The benefits of primary debulking surgery must be weighed against the possibility of treatment with neoadjuvant chemotherapy and interval debulking surgery especially in light of recent publications and ongoing trials directly comparing these two approaches. This cohort is the largest in the gynecologic oncology literature and can help move the needle in the direction of examining a patient's frailty status when discussing and determining therapeutic avenues (neoadjuvant chemotherapy versus aggressive upfront cytoreductive surgery) and anticipating postoperative care services that may be required.

Perioperative care in advanced EOC places a large emotional, mental, and economic burden on patients, their families, and the healthcare system in general. As treatments for ovarian cancer continue to evolve, so must our evaluation and treatment strategies in the preoperative period.

### Author contributions

TingTing Yao conceived and designed the analysis, contributed data or analysis tools, and wrote the paper.

Stephanie DeJong collected the data, contributed data analysis tools, and wrote the paper.

Michaela McGree conceived and designed the analysis, contributed data or analysis tools, and performed the analysis.

Amy Weaver conceived and designed the analysis, contributed data or analysis tools, performed the analysis, and wrote the paper.

William Cliby conceived and designed the analysis, contributed data or analysis tools, and wrote the paper.

Amanika Kumar conceived and designed the analysis, collected the data, contributed data or analysis tools, and wrote the paper.

All authors confirmed the final content of the manuscript and take responsibility for its accuracy.

### Conflict of interest statement

The authors have no conflicts to disclose.

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