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Comparison of patient reported symptom burden on an enhanced recovery after surgery (ERAS) care pathway in patients with ovarian cancer undergoing primary vs. interval tumor reductive surgery☆

Larissa A. Meyer [a,*], Qiuling Shi [b], Javier Lasala [c], Maria D. Iniesta [a], Huei Kai Lin [b], Alpa M. Nick [d], Loretta Williams [b], Charlotte Sun [a], Xin Shelley Wang [b], Karen H. Lu [a], Pedro T. Ramirez [a]

[a] The University of Texas MD Anderson Cancer Center, Department of Gynecologic Oncology, Houston, TX, United States of America
[b] The University of Texas MD Anderson Cancer Center, Department of Symptoms Research, Houston, TX, United States of America
[c] The University of Texas MD Anderson Cancer Center, Department of Anesthesiology and Perioperative Medicine, Houston, TX, United States of America
[d] Tennessee Oncology, Nashville, Tennessee, University of Tennessee Health Sciences Center, Memphis, TN, United States of America

HIGHLIGHTS

- Higher surgical complexity increases patient-reported interference from symptoms after ovarian cancer cytoreductive surgery.
- Patients report higher baseline symptom burden prior to primary cytoreductive surgery compared to interval surgery.
- Patients undergoing primary and interval cytoreductive surgery on ERAS pathways report similar pain levels after surgery.

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ABSTRACT

Objective. To compare symptom burden and functional recovery in women undergoing primary cytoreductive surgery (PCS) or neoadjuvant chemotherapy (NACT) and interval cytoreductive surgery (ICS) within an enhanced recovery after surgery program (ERAS).

Methods. Symptom burden was measured using the MD Anderson Symptom Inventory-Ovarian Cancer, a 27-item validated tool that was administered preoperatively, daily while hospitalized, and weekly for 8 weeks after hospital discharge. Mixed-effect modeling was performed.

Results. 196 patients (71 PCS, 125 ICS) participated. Patients in the PCS group were younger, median age of 59 vs. 63 in ICS group. Median length of stay was 4 days for PCS and 3 days for ICS group. PCS pts had a significantly higher median surgical complexity score (4 vs. 2, $p = 0.002$), and longer median surgical time (257 min vs. 220 min, $p = 0.03$). While patients undergoing PCS had significantly different symptom burden profiles prior to surgery compared to those undergoing ICS, there were no significant differences in symptoms in the immediate in-hospital and extended post-hospital discharge period. Irrespective of the timing of surgery in relation to chemotherapy, patients undergoing intermediate or high complexity surgery had more nausea, fatigue, and higher total interference scores compared to patients undergoing low complexity surgery.

Conclusion. Within a center with a standardized, systematic method for patient selection for PCS and a standardized ERAS care pathway, there were not significant differences in surgery-related symptoms related to recovery between patients undergoing PCS or ICS. However, patient-reported symptom burden and symptom interference did meaningfully differentiate based on surgical complexity score.

1. Introduction

Two major randomized trials of women with advanced ovarian cancer undergoing primary cytoreductive surgery (PCS) or neoadjuvant chemotherapy (NACT) have demonstrated similar overall survival [1,2]. Little is currently known about patient reported outcomes (PROs) in this patient population. PROs are defined as any status report

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* Corresponding author at: The University of Texas MD Anderson Cancer Center, 1155 Herman Pressler, Unit 1362, Houston, TX 77030-1362, United States of America.
E-mail address: lmeyer@mdanderson.org (L.A. Meyer).

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that comes directly from the patient without interpretation from clinicians or other individuals. PRO instruments aim to measure one or more aspects of PROs, which can include topics such as symptom burden to more complex, multi-dimensional concepts such as quality of life (QOL). The randomized trials have largely focused on one aspect of patient reported outcomes, mainly quality of life (QOL). In one trial, there was no difference in QOL [1], and there was a trend towards improvement in QOL in patients who received NACT in the second [2]. However, QOL assessments were performed at intervals of a minimum of 3 cycles of chemotherapy (9 weeks), and then at 6 and 12 months after surgery. The long interval between assessments may not be sensitive to acute differences in postoperative symptom burden or QOL. Data from randomized and observational studies comparing PCS to NACT and interval cytoreductive surgery (ICS), suggests that patients undergoing PCS may be more likely to have bowel surgery [1,3,4], with some studies demonstrating higher risks of infection and other complications in those undergoing PCS [1,2,4,5]. These differences may contribute to differences in how patients' report their symptom burden, QOL and recovery after surgery.

Enhanced recovery after surgery (ERAS) is a multidisciplinary and multi-modal approach to caring for individuals undergoing surgery through implementation of evidence based perioperative practices. ERAS programs have demonstrated improvements in metrics such as length of stay and complication rates [6,7]. Through the implementation of practices such as multimodal analgesia, opioid sparing anesthesia techniques, early feeding and mobilization, use of intraoperative and post-operative opioids have decreased significantly [8,9]. Guidelines for ERAS in gynecologic surgery have been established recently by the ERAS® Society [10,11]. Participation in ERAS for women undergoing gynecologic surgery has been associated with improvements in patient reported outcomes compared to women who had cytoreductive surgery prior to ERAS implementation [9].

Longitudinal collection of patient reported outcomes and analysis of symptom burden is feasible in cancer patients, even women undergoing complex cytoreductive surgery [12–14]. The inclusion of the patient voice is an important component of patient-centered research involving comparative effectiveness, surgical technique and perioperative care [15–17]. In this study, we aimed to compare patient-reported outcomes in women undergoing PCS or ICS after neoadjuvant chemotherapy on an ERAS pathway.

2. Methods

Patients with a diagnosis of ovarian, fallopian tube or primary peritoneal cancer undergoing cytoreductive surgery between 11/6/2014 and 3/31/2018 and consented to participate in collection of patient reported outcomes on a larger ongoing IRB approved protocol of symptom burden (BS99-094) were included in this study. Only patients having surgery for primary therapy were included. Patients with recurrent disease were excluded. Clinical and demographic information was collected from the medical record. Study data were collected and managed using REDCap (Research Electronic Data Capture) electronic data capture tools [18] hosted at MD Anderson. All surgeries were performed by gynecologic oncologists on our ERAS pathway (Supplemental Table 1) with preoperative, intraoperative and postoperative phases, which have been previously reported [19]. Key aspects of this pathway include nutritional counseling, carbohydrate loading, avoidance of mechanical bowel preparation, euvolemia via goal directed fluid therapy, opioid-sparing multi-modal analgesia, and an emphasis on early ambulation and feeding. Patients were triaged to either PCS or ICS by their treating physician, following the Anderson algorithm [20,21], largely based on the Fagotti score, a test that utilizes laparoscopic surgery to assess tumor burden and location in women with advanced ovarian cancer in order to triage them to primary therapy [22].

Comorbidities were assessed using the American Society of Anesthesiologists (ASA) classification of physical health [23] and Charlson

Table 1
Demographic and clinical characteristics (N = 196).

	PCS (n = 71)		ICS (n = 125)		p-Value
	Patient characteristics, mean (SD), median (min–max)				
Age, years	57.79 (13.28)	59 (18–79)	61.92 (11.52)	63 (22–84)	0.02
Length of stay (days)	5.03 (4.45)	4 (2−22)	4.25 (3.71)	3 (2–29)	0.19
Surgical complexity score	3.54 (2.14)	4 (0−10)	2.66 (1.67)	2 (0–8)	0.002
Surgical time (minutes)	263.34 (85.99)	257 (123–544)	239.27 (100.38)	220 (114–840)	0.03
Estimated blood loss	494.37 (439.24)	350 (60–1800)	328.12 (299.80)	230 (25–1750)	0.002
30 day complications	57.25 (15.90)	65 (15–80)	58.28 (17.02)	60 (10–80)	0.68

	PCS (n = 71)	ICS (n = 125)	p-Value
	Patient characteristics, % (no.)		
Education (highest level of education)			0.95
High school	9 (12.68)	16 (12.80)	
College or higher	23 (32.39)	43 (34.40)	
Unknown	39 (54.93)	66 (52.80)	
Race			0.26
White	51 (71.83)	99 (79.20)	
Others	20 (28.17)	26 (20.80)	
Hispanic/Latino			0.05
Yes	13 (18.31)	11 (8.80)	
No	58 (81.69)	114 (91.20)	
Marital status			0.24
Married	57 (80.28)	91 (72.80)	
Unmarried	14 (19.72)	34 (27.20)	
Employment status			0.24
Employed full-time	25 (35.21)	34 (27.20)	
Others	46 (64.79)	91 (72.80)	
ASA physical status			0.001
Unknown	1 (1.41)	2 (1.60)	
II	10 (14.08)	6 (4.80)	
III	57 (80.28)	115 (92.00)	
IV	3 (4.23)	2 (1.60)	
ECOG PS score			<0.0001
Grade 0	42 (59.15)	58 (46.40)	
Grade 1	4 (5.63)	25 (20.00)	
Grade 2	0 (0.00)	2 (1.60)	
Grade 3	0 (0.00)	1 (0.80)	
Unknown	25 (35.21)	39 (31.20)	
Charlson Comorbidity Index			0.07
0	7 (9.86)	4 (3.20)	
1	5 (7.04)	11 (8.80)	
2	20 (28.17)	27 (21.60)	
3	24 (33.80)	36 (28.80)	
4–10	15 (21.13)	47 (37.60)	
Chronic opioid use			0.15
No	71 (100.00)	119 (95.20)	
Yes	0 (0.00)	6 (4.80)	
Surgical complexity			
Low (≤3)	34 (47.2)	93 (74.4)	0.0003
Medium (4–7)	33 (45.8)	30 (24)	
High (≥8)	5 (6.9)	2 (1.6)	
Readmission			0.18
No	61 (85.92)	115 (92.00)	
Yes	10 (14.08)	10 (8.00)	
Reoperation			0.12
No	67 (94.37)	123 (98.40)	
Yes	4 (5.63)	2 (1.60)	
Ovarian histology			0.69
Epithelial	66 (92.96)	119 (95.20)	
Non-epithelial	3 (4.23)	4 (3.20)	
Unknown	2 (2.82)	2 (1.60)	
Ovarian staging			<0.0001
Early (I/II)	29 (40.85)	0 (0.0)	
Advanced (III/IV)	41 (57.75)	122 (97.60)	
Unknown	1 (1.41)	3 (2.40)	

Table 2
Baseline comparison of symptoms in women undergoing primary cytoreductive surgery (PCS) and interval cytoreductive surgery (ICS).

	PCS			ICS			p-Value	Effect size (Cohen's *d*)
Pre-surgery								
Symptom	N	Mean	SD	N	Mean	SD		
1. Your pain at its WORST?	71	3.06	2.86	124	1.33	2.43	<0.0001	0.65
2. Your fatigue (tiredness) at its WORST?	71	3.34	2.76	125	2.61	2.64	0.07	0.27
3. Your nausea at its WORST?	70	1.04	2.13	124	0.70	2.03	0.27	0.16
4. Your disturbed sleep at its WORST?	71	2.72	2.75	125	1.90	2.62	0.04	0.31
5. Your feelings of being distressed (upset) at its WORST?	71	3.30	3.00	125	1.91	2.61	0.0009	0.49
6. Your shortness of breath at its WORST?	71	0.82	1.96	125	0.79	1.55	0.92	0.02
7. Your problem with remembering things at its WORST?	71	1.39	1.97	123	1.48	2.17	0.79	−0.04
8. Your problem with lack of appetite at its WORST?	71	2.46	2.95	124	0.90	2.00	<0.0001	0.62
9. Your feeling drowsy (sleepy) at its WORST?	71	2.14	2.43	124	1.38	2.00	0.02	0.34
10. Your having a dry mouth at its WORST?	71	2.03	2.97	124	1.30	2.27	0.06	0.28
11. Your feeling sad at its WORST?	70	2.80	3.19	124	1.51	2.35	0.002	0.46
12. Your vomiting at its WORST?	71	0.48	1.81	124	0.21	1.15	0.21	0.18
13. Your numbness or tingling at its WORST?	71	0.62	1.68	124	2.64	2.89	<0.0001	−0.85
14. Your pain in the abdomen at its WORST?	71	3.30	3.00	124	0.96	2.06	<0.0001	0.91
15. Your feeling bloated at its WORST?	71	3.35	3.00	124	0.88	1.77	<0.0001	1.00
16. Your constipation at its WORST?	71	2.44	3.13	124	1.14	2.20	0.0009	0.48
17. Your problem with paying attention (concentrating) at its WORST?	71	1.58	1.95	124	0.91	1.65	0.01	0.37
18. Your urinary urgency at its WORST?	71	1.87	2.32	124	1.05	1.90	0.008	0.39
19. Your pain or burning with urination at its WORST?	71	0.38	1.26	124	0.15	0.72	0.11	0.22
20. Your back pain at its WORST?	69	2.13	2.60	119	0.91	1.99	0.0004	0.53
21. Your leg cramps or leg muscle pain at their WORST?	71	1.08	2.12	124	1.10	2.10	0.97	−0.01
22. Your diarrhea at its WORST?	71	1.10	1.99	124	0.48	1.65	0.02	0.34
23. Your indigestion (heartburn) at its WORST?	71	1.69	2.52	124	0.59	1.33	<0.0001	0.55
Interference questions								
24. General activity?	71	3.46	3.25	124	1.69	2.53	<0.0001	0.61
25. Mood?	71	3.41	3.12	123	1.46	2.14	<0.0001	0.73
26. Work (including work around the house)?	71	3.41	3.32	123	1.91	2.92	0.001	0.48
27. Relations with other people?	71	1.85	2.62	124	0.68	1.47	<0.0001	0.55
28. Walking?	71	2.72	3.05	124	1.66	2.69	0.01	0.37
29. Enjoyment of life?	71	3.58	3.21	124	1.49	2.42	<0.0001	0.74
Total interference	71	3.07	2.35	124	1.49	1.88	<0.0001	0.74
Physical interference subscale	71	3.20	2.88	124	1.76	2.40	0.0003	0.54
Affective interference subscale	71	2.94	2.60	124	1.22	1.71	<0.0001	0.78

Comorbidity Index (CCI) [24]. To more accurately reflect pre-cancer comorbid conditions, the current malignancy was not included in the calculation of the CCI. A surgical complexity score was assigned based on procedures documented in the operative report [25]. The Dindo-Clavien grading system was used to characterize the 30-day complication rates [26].

The standard postoperative pain regimen included scheduled acetaminophen and ibuprofen with oxycodone as needed. For additional breakthrough pain, intravenous hydromorphone was available as needed. Pain medication data were collected on the day of surgery, postoperative day (POD) 0 and on the first three days after surgery and subsequently converted into morphine equivalent daily doses (MEDD).

2.1. Patient-reported outcome measures

Perioperative patient-reported symptom burden was evaluated with the MD Anderson Symptom Inventory-Ovarian Cancer module (MDASI-OC), a 27-item validated tool with two additional questions on diarrhea and heartburn [27]. For each symptom component, individuals were asked to rank symptom severity during the previous 24 h on a scale of 0–10, with 0 being "not present" and 10 being "as bad as you can imagine." Symptom interference was also assessed on a 0–10 scale, with 0 being "did not interfere" and 10 being "interfered completely." [27] The total interference score was a composite endpoint of 6 interference questions that asked patients to report how much their symptoms interfere with general activity, mood, work (including work around the house), relations with other people, walking, and enjoyment of life. The MDASI-OC was administered preoperatively, daily while hospitalized after surgery, on days 3 and 7 post discharge and weekly for an additional seven weeks postoperatively. The MDASI-OC was administered on paper, by interactive voice recorded (IVR) telephone system, or electronically via email link. To be included in the analysis, patients had to complete at least three assessments, which had to include the baseline preoperative MDASI with at least two subsequent assessments.

2.2. Statistical methods

The patient cohorts were determined using convenience sampling. However, the minimum sample size was estimated based on patient-reported pain. The standard deviation for the MDASI symptom of pain at its worst is 2.5. Utilizing the criteria of half a standard deviation, the minimally important difference is 1.2 points on the MDASI. Thus, each group was estimated to require a minimum of 67 patients [28]. Descriptive statistics were used to summarize the demographic and clinical characteristics. Categorical variables were compared between the PCS and ICS groups with Fisher's exact test. The Wilcoxon rank-sum test was used to compare medians between continuous variables.

Linear mixed-effects modeling was used to examine the longitudinal change of symptom burden and symptom interference during hospitalization (from day of surgery to day 5 post-surgery), as well as longitudinally after hospital discharge. To control for other factors that might influence patient reported symptom burden between women undergoing PCS and ICS, age, race, length of stay, surgical time, and surgical complexity score were included in all models. The Wilcoxon rank-sum test was used to compare the PCS and ICS groups with respect to the median time to return to mild or no symptom burden, defined as a score < 4 at two consecutive assessments. Kaplan-Meier curves were used to illustrate the time to return to mild or no symptom burden for the two groups.

Linear mixed-effects modeling was also used to examine symptom burden based on the level of surgical complexity both in the hospital

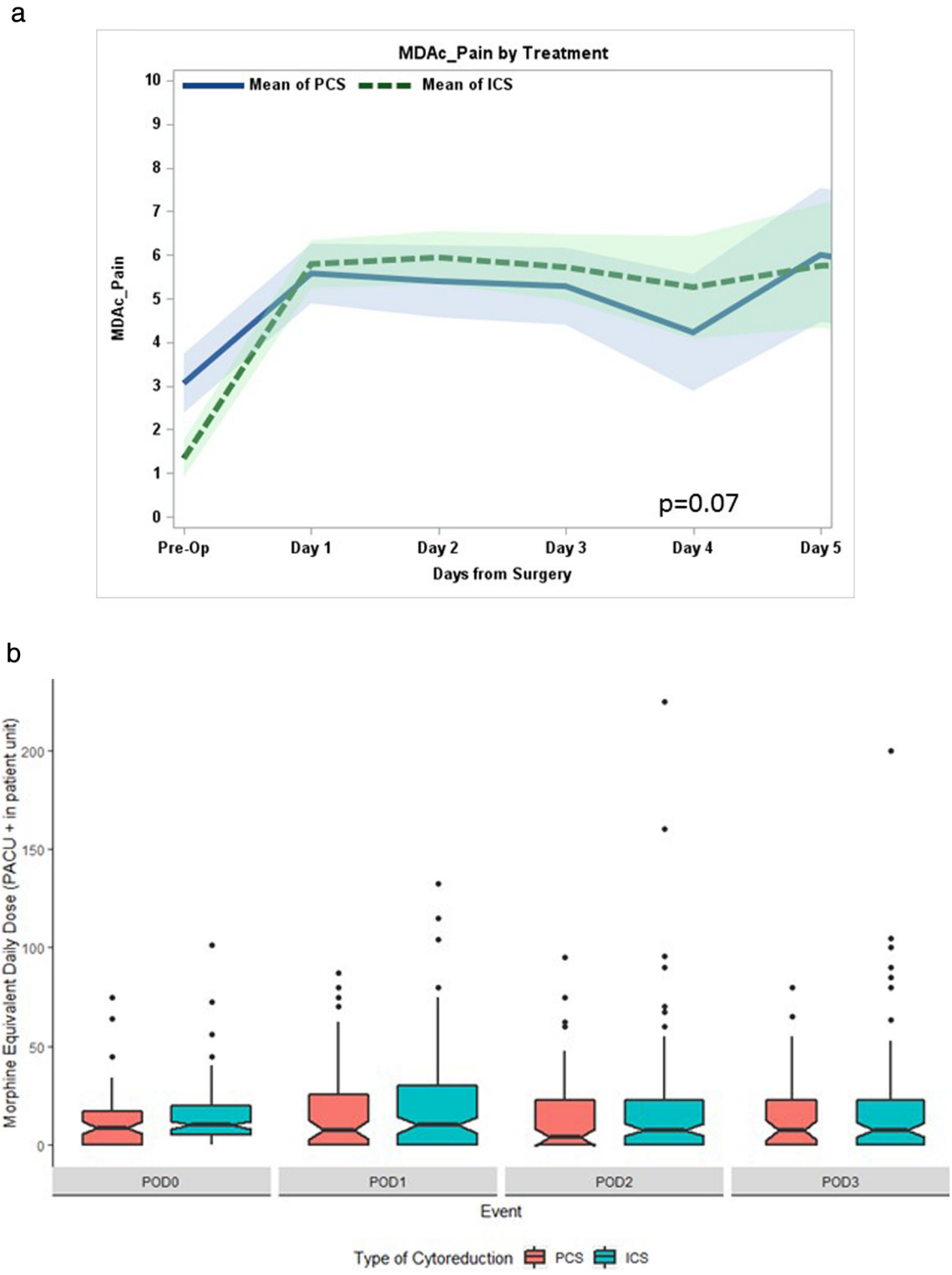

Fig. 1. a. Longitudinal assessment of daily worst pain during hospital stay (shaded area representing 95% CI). p-Value calculated from mixed effect model. b. Morphine Equivalent Dose (PACU + inpatient unit). The median is shown as a bold horizontal bar across the "waist" of the box, while the top of the box represents the third quartile of the distribution and the bottom of the box represents the first quartile of the distribution. The notches on the box represent the 95% confidence interval for the median. The "whiskers" for each box extend to 1.5 × IQR (interquartile range) above and below the box, with a lower limit of 0. Outliers are represented by small circles beyond the whiskers. For aesthetic reasons the extreme outliers beyond 250 are omitted from the figures. The width of a box is proportional to the sample size of the distribution represented by the box. p-Values: POD 0 $p = 0.27$ and POD 1 $p \leq 0.23$, POD 2 $p = 0.32$, POD 3 $p = 0.49$.

and after hospital discharge. Scores ≤3 were considered low surgical complexity, while intermediate surgical complexity was defined as scores of 4–7, and high surgical complexity defined by scores ≥8 [25]. Days from surgery, and type of cytoreduction were added to the model.

3. Results

A total of 196 patients were included in the analysis, 71 patients who underwent PCS and 125 patients who had neoadjuvant chemotherapy

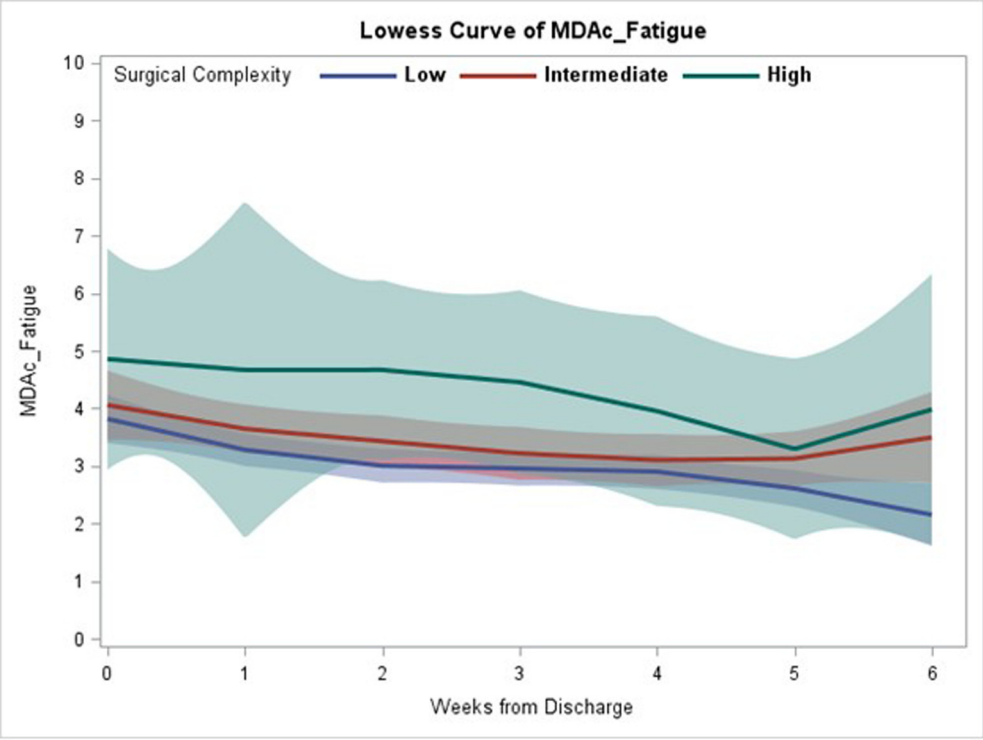

Fig. 2. Lowess curve comparing patient reported fatigue after hospital discharge between patients who underwent low, intermediate and high complexity cytoreductive surgery.

followed by ICS (Table 1). There was a statistically significant difference in age between the two groups, with a median age of 59 years (range 18–79) in the PCS group and 63 years (range 22–84) in the ICS group, $p = 0.02$. There were no significant differences between the two groups in terms of race, ethnicity, marital status, level of education, CCI, or history of chronic opioid use. The distribution of ASA physical status and ECOG performance status were significantly different between the two groups. Estimated blood loss was higher in the PCS group with a median of 350 mL (60 mL–1800 mL) vs. 230 mL (25 mL–1750 mL) in the ICS group, $p = 0.002$. Similarly, surgical time was longer in the PCS group with a median time of 257 min compared to 220 min in the ICS group, $p = 0.03$. There were no significant differences between the two groups related to 30-day postoperative complications, reoperation or readmission. After exclusion of patients with unknown stage or early stage disease, the complete gross resection rate was 90.2% in patients undergoing PCS and 80.3% in patients undergoing ICS.

The two groups had exhibited different baseline symptom burden profiles prior to surgery (Table 2). Women who underwent PCS reported significantly more pain, disturbed sleep, emotional distress, lack of appetite, drowsiness, sadness, abdominal pain, bloating, constipation, difficulty concentrating, urinary urgency, back pain, diarrhea, and indigestion. Additionally, women who underwent PCS reported greater interference from symptom burden, with higher interference scores for general activity, mood, work, relationships with others, walking, and enjoyment of life. In contrast, women who underwent neoadjuvant chemotherapy prior to ICS reported more baseline numbness and tingling.

The overall surgical complexity score of patients in the PCS group was higher than for those in the ICS group (PCS median score = 4 vs. ICS median score = 2, $p = 0.002$, Table 1). Furthermore, surgical complexity was significantly associated with whether women received PCS vs. ICS ($p = 0.0002$). A higher percentage of women who underwent PCS received medium and high surgical complexity procedures compared to women in the ICS group (46.5% vs. 24.0%; and 7.0% vs. 1.6%). A higher percentage of women in the ICS group underwent low complexity surgery compared to women undergoing PCS (74.4% vs. 46.2%).

The five most highly rated symptoms during hospitalization after surgery included pain, abdominal pain, fatigue, dry mouth and drowsiness. At the preoperative baseline assessment, patients in the PCS group reported more pain with a mean score of 3.06 vs. 1.33 for those undergoing ICS, $p < 0.0001$. Intraoperative opioid doses (MEDD) were similar with a median of 62.5 mg for those undergoing PCS and 56 mg for those undergoing ICS, $p = 0.28$. Despite differences in preoperative baseline pain, there was no difference between the two groups in terms of postoperative pain over the first 5 days (Fig. 1a). There were no significant differences in the median amount of opioids used on postoperative days zero through three (Fig. 1b). Similarly, during the first five days of hospitalization, there were no significant differences in longitudinal fatigue, drowsiness, nausea, vomiting, or total interference scores observed between the groups of women who underwent PCS versus ICS.

After hospital discharge, fatigue was the complaint with the highest symptom burden, followed by pain, abdominal pain, disturbed sleep, and lack of appetite. Longitudinally post hospital discharge, there were no significant differences between the PCS and ICS groups in relation to pain, abdominal pain, fatigue, nausea, vomiting, and total interference. There were no differences in sleep disturbance or appetite between women in the PCS and ICS group. Similarly, no significant differences were observed in time to return to low or no symptom burden between women undergoing PCS and ICS for pain, abdominal pain, fatigue, dry mouth, drowsiness, nausea, vomiting or total interference. Women undergoing PCS reported a return to low or no interference (composite score of interference with general activity, mood, work (including work around the house), relations with other people, walking, and enjoyment of life in a median of 9 days compared to 6 days for those in the ICS group, $p = 0.32$).

In a secondary analysis, patients were characterized by surgical complexity scores (low, intermediate, high), rather than by whether or not they received chemotherapy prior to surgery. While still hospitalized, compared to low surgical complexity cases, women with intermediate ($p = 0.01$) and high surgical complexity cases ($p = 0.007$) had significantly increased nausea. Additionally, patients undergoing intermediate

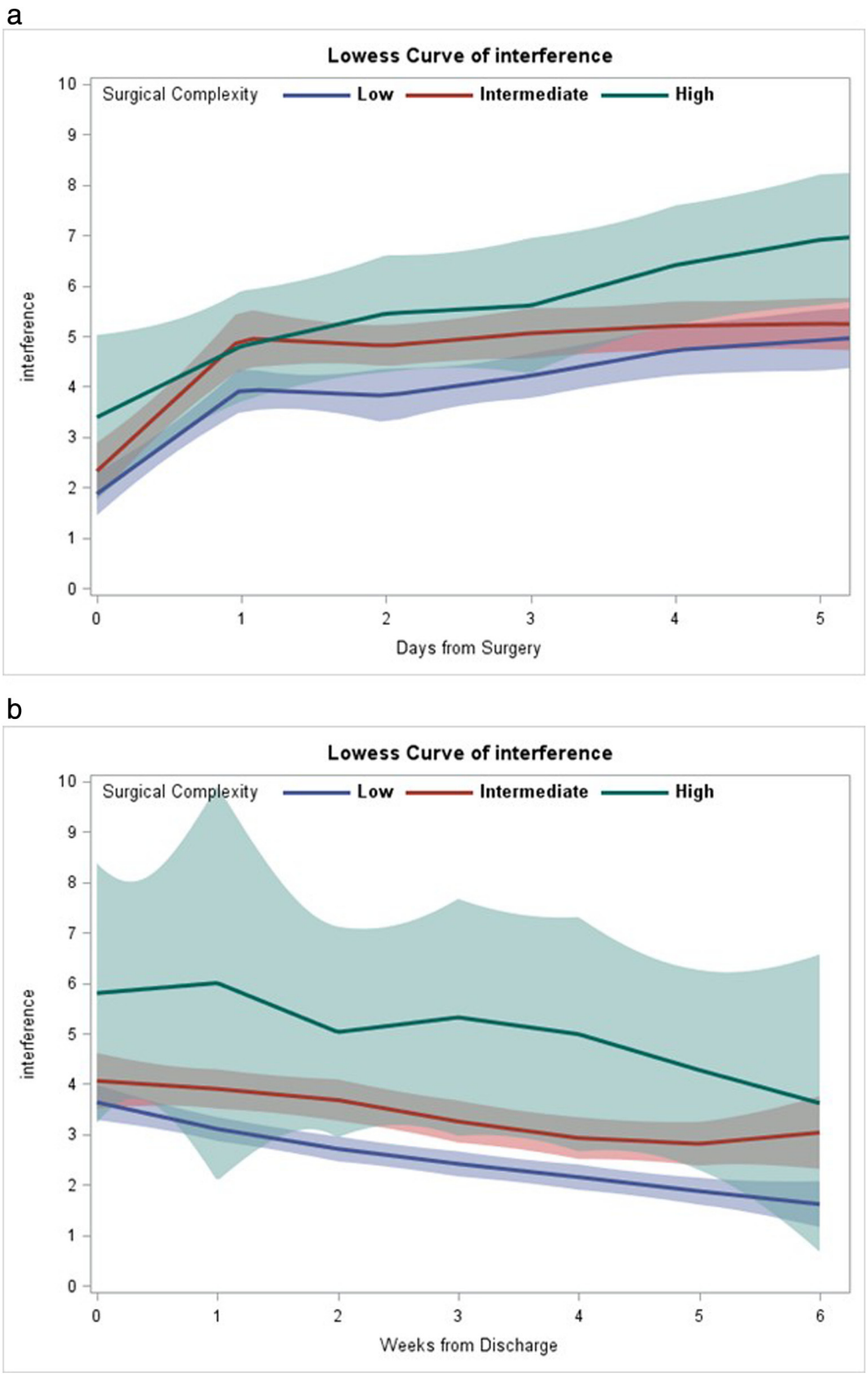

Fig. 3. a. Lowess curve comparing composite endpoint of total interference from symptoms during first five days after surgery between patients who underwent low, intermediate and high complexity cytoreductive surgery. b. Lowess curve comparing composite endpoint of total interference from symptoms after hospital discharge between patients who underwent low, intermediate and high complexity cytoreductive surgery.

complexity cytoreductive surgery longitudinally reported significantly higher pain ($p = 0.02$) and fatigue ($p = 0.005$), compared to those undergoing low surgical complexity cases. Patients undergoing high surgical complexity cases reported even greater fatigue, and while suggestive of a trend, this did not reach statistical significance, ($p = 0.07$).

Patient reported pain and fatigue did not differ significantly between the low, intermediate and high complexity surgery groups in the six weeks after hospital discharge. Although it did not reach a level of statistical significance, the level of fatigue in those who had high surgical complexity surgery trended higher than for those with low or

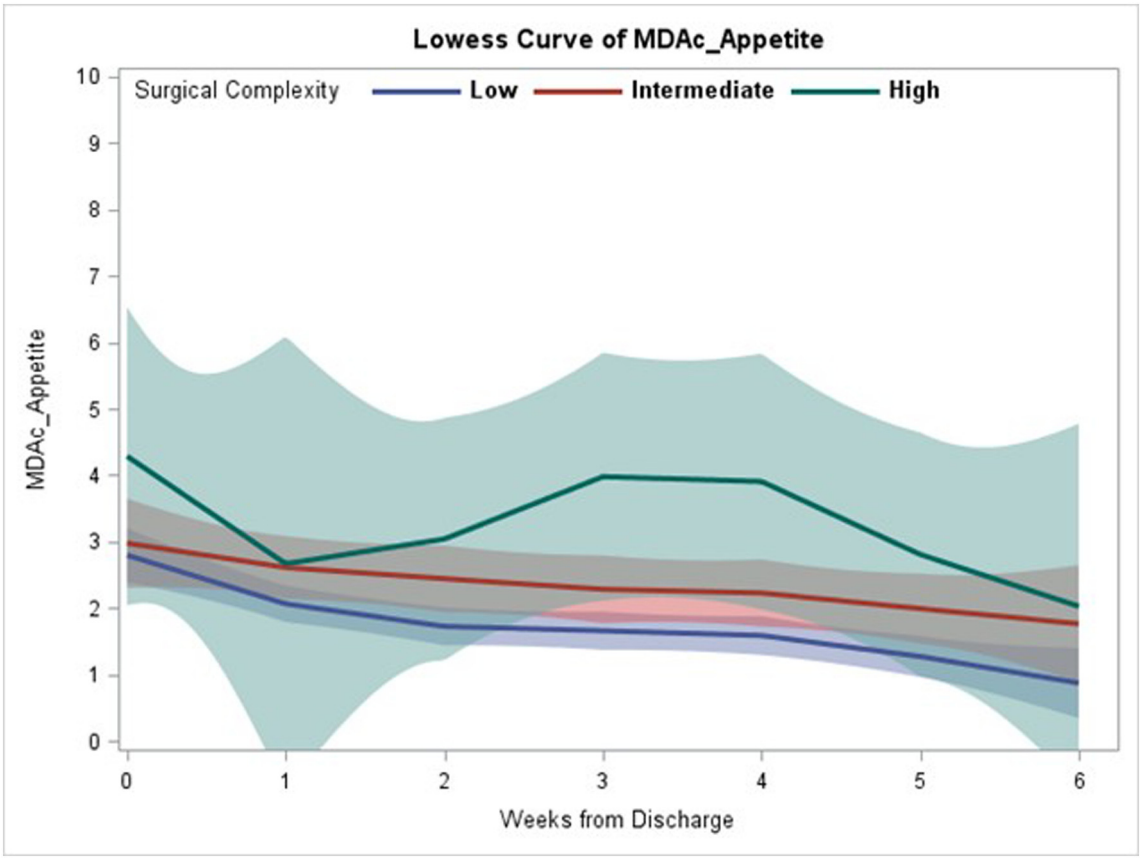

Fig. 4. Lowess curve comparing patient reported loss of appetite after hospital discharge between patients who underwent low, intermediate and high complexity cytoreductive surgery.

intermediate complexity surgery throughout the six week period after discharge (Fig. 2).

Total interference scores, the composite endpoint of the six interference questions (symptom interference with general activity, mood, work (including work around the house), relations with other people, walking, and enjoyment of life) increased with surgical complexity both in the hospital (Fig. 3a) as well as after hospital discharge (Fig. 3b). This difference was statistically different for those in the intermediate surgical complexity ($p = 0.01$), and for those with high surgical complexity ($p = 0.02$). The differences in interference scores after hospital discharge persisted at 6 weeks, with a significant difference between those with low and intermediate complexity surgery ($p = 0.01$) and a trend towards significance for those with high complexity surgery ($p = 0.06$). Symptom burden from nausea after hospital discharge was overall low, however, it was increased in those with intermediate surgical complexity surgery compared to those with low complexity surgery ($p = 0.03$). Similarly, compared to patients undergoing low complexity surgery, those who underwent intermediate ($p = 0.02$) and high complexity surgery ($p = 0.16$) noted a higher degree of lack of appetite longitudinally after hospital discharge (Fig. 4).

4. Discussion

In this study, longitudinal patient reported symptom burden and symptom interference were assessed in women undergoing cytoreductive surgery for ovarian, primary peritoneal and fallopian tube cancer. The significant differences in baseline symptom burden prior to surgery suggest that disease-related symptoms such as (pain, bloating) and emotional symptoms may be related to recent diagnosis and higher tumor burden in patients undergoing PCS while the increased numbness and tingling reflect chemotherapy-related effects in the ICS cohort. Postoperatively, opioid pain medication use and patient reported pain scores did not differ. A secondary analysis comparing women who underwent low, medium and high complexity cytoreductive surgery was performed. While there were no significant differences in PROs noted in the immediate and extended postoperative period when comparing women who underwent PCS and ICS, we did find important differences in PROs and recovery when analyzing by category of surgical complexity. The reasons for this are likely multifactorial. In the primary analysis of PCS vs. ICS, we controlled for surgical complexity. Additionally, patients who underwent PCS were a highly select population. Lastly, the benefits of participation in an ERAS program may provide an equalizing effect that attenuated any potential differences in patient reported symptoms.

It is not clear how generalizable the results of the primary comparison between PCS and ICS is to other practice settings given the variation in clinical decision making. While perioperative care was optimized for both groups through a standardized ERAS pathway, patients were carefully selected for primary cytoreductive surgery through a standardized process that included laparoscopic disease assessment in addition to traditional methods of history, physical exam and radiologic imaging. Additionally the PCS group included patients with earlier stage disease. Those with heavy tumor burden thought to be unresectable at primary cytoreduction and those who were not medically fit for PCS were triaged to neoadjuvant chemotherapy. This strategy aims to select patients most likely to benefit from primary cytoreductive surgery and to minimize surgical morbidity. Not surprisingly, after NACT, there was a higher proportion of patients in the ICS group who had low complexity surgery reflecting the decreased tumor burden immediately prior to surgery.

Our findings demonstrate the trajectory of symptom burden and functional recovery from the perspective of our patients longitudinally during the immediate and extended postoperative recovery period for patients on an ERAS pathway. The contribution of these findings to

the literature is three-fold. It provides an understanding of baseline patient reported symptom burden prior to surgery and how patients undergoing primary vs. interval cytoreductive surgery compare. Our findings suggest that surgical complexity is a more important factor than the categorization of patients by whether or not they had chemotherapy before surgery in terms of recovery and patient symptom burden during the 6 week postoperative period. Lastly, it serves as an example of the MDASI instrument's sensitivity in demonstrating the differences in symptom burden and functional recovery in women undergoing low, medium and high complexity cytoreductive surgery.

In conclusion, with careful patient selection for PCS, after controlling for age, race, length of stay, surgical time, and surgical complexity score, symptom burden and functional recovery are comparable to those of patients undergoing ICS. Surgical complexity appears to be the more important driver of symptom burden after cytoreductive surgery.

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ygyno.2018.10.044.

Conflict of interest

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Author contributions

Each author significantly contributed to the critical aspects of this manuscript, and consequently, preparation of this manuscript would not have been possible without the contributions of each author listed.

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