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Perioperative trajectory of patient reported symptoms: A pilot study in gynecologic oncology patients

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Abstract

Objective—With the growing focus on patient-centered care, patient reported outcomes (PROs) are becoming an important component to clinical trials and quality metrics. The objective of this study was to pilot the collection of patient reported symptom burden in women undergoing surgery in a gynecologic oncology practice.

Methods—Perioperative patient reported symptom burden was measured for women undergoing laparotomy on the gynecologic oncology service at the University of Texas MD Anderson Cancer Center. Symptoms were assessed using the M.D. Anderson Symptom Inventory (MDASI-OC), a 27 item tool validated for use in patients with ovarian cancer. The MDASI-OC was administered as a preoperative baseline, daily while admitted to the hospital after surgery, twice a week on the first week after discharge and then weekly until 8 weeks postoperatively.

Results—29 patients were evaluable. Seventy-five percent of patients had a diagnosis of ovarian cancer. Of those patients, half underwent a primary debulking surgery and the other half had neoadjuvant chemotherapy prior to interval cytoreductive surgery. In the postoperative inpatient setting, the five symptoms with the highest overall burden were fatigue, pain, abdominal pain, dry mouth and drowsiness. Longitudinal change of the top 5 symptoms during hospitalization did not show any significant difference between those who had neoadjuvant chemotherapy and those who did not.

Conclusion—The collection of longitudinal PROs to assess symptom burden is feasible in patients undergoing gynecologic oncology surgery. Patient reported outcomes are a crucial component of patient-centered research and the longitudinal collection and analysis of symptom burden can allow for more meaningful comparisons of surgical technique and perioperative care.

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Introduction

Traditional metrics to assess surgical quality include hospital length of stay, readmission rates, and surgical site infection among other measures of event-related or clinician judgment of morbidity. However, patient-reported outcomes (PROs) which currently represent the gold standard in the related research areas of assessment of symptom burden, health-related quality of life, treatment preferences, and patient satisfaction, have also become an area of increasing focus in comparative effectiveness research, health care quality assessments, as well as endpoints in clinical trials. [1, 2] Additionally, there is a burgeoning interest in incorporating PROs into routine surgical clinical care and as a tool to measure providers' performance.[3] The Center for Medical Technology Policy (CMTP) recommends that prospective clinical comparative effectiveness research (CER) capture the subjective patient experience. [4]

Historically, the majority of trials that incorporated PROs were solid tumor treatment trials. The use of PROs in surgical trials has lagged behind. There have been relatively few trials in gynecologic oncology with patient reported outcomes as a primary outcome measure. [5] Two notable trials utilizing PROs as a secondary outcome in gynecologic oncology include the EORTC trial comparison of quality of life in advanced ovarian cancer patients who were randomized to neoadjuvant chemotherapy or primary debulking surgery [6] and the Gynecologic Oncology Group LAP2 trial in which the quality of life was compared between women with endometrial cancer undergoing open or laparoscopic surgery. [7] Despite the inclusion of quality of life in these landmark trials, there continues to be a lack of consensus on the optimal methodology to collect PROs in a surgical population and which outcome measures are most relevant to the patient.[3] Additionally, a more thorough understanding of the clinical sensitivity of specific PRO tools can help establish the role of patient reported outcomes in routine clinical care.

While patient satisfaction with perioperative care and quality of life (QOL) assessments have been previously reported, patient reported symptom burden has not previously been systematically evaluated perioperatively in women undergoing surgery for gynecologic oncology indications. A high proportion of patients undergoing laparotomy for gynecologic oncology indications will also receive chemotherapy, either in a neoadjuvant or adjuvant setting. Moreover, many patients, especially those with ovarian cancer, carry a significant disease-specific preoperative symptom burden. For these reasons, we elected to use an instrument that was tailored to the symptom burden in this oncology population. The M.D. Anderson Symptom Inventory (MDASI) is a validated tool comprised of a core of 13 questions that aims to capture common symptoms experienced by the patient from the patient's own point of view over the previous 24 hours. [8, 9] The MDASI is a recognized, widely validated and recommended tool for measuring patient reported outcomes (PROs) and symptom burden in cancer patients. [4] The sensitivity of the MDASI has previously been established on the basis of previous data comparing symptoms in patients with different stages of disease, before, during and after aggressive cancer treatment as well as unaffected populations. [8, 10, 11] Although the disease specific module of MDASI in ovarian cancer (MDASI-OC) [10, 12] was developed and validated, there is still a lack of clinical data of how a patient's perspective of their symptom burden corresponds with

clinical outcomes in an accurate and timely fashion. The objective of our study was to pilot the collection of patient-reported symptoms in the perioperative setting and to quantify symptom burden of women undergoing open surgical procedures for a known or presumed gynecologic malignancy.

Methods

Subjects

Women age 18 and older undergoing exploratory laparotomy at the University of Texas MD Anderson Cancer Center with known or suspected gynecologic cancer were enrolled prospectively. All patients signed consent to participate in this institutional review board approved study. Exclusion criteria included non-English speaking patients, and patients who did not undergo an open abdominal surgical procedure.

Assessment Measures

Symptoms were assessed using the M.D. Anderson Symptom Inventory (MDASI-OC), a 27 item tool previously validated for use in patients with ovarian cancer (MDASI-OC) [10]. Two additional questions to address diarrhea and gastrointestinal reflux were added based on clinician impression of their prevalence in the post-operative period. Each symptom was rated on an 11-point scale, with 0 being “not present” and 10 being “as bad as you can imagine” with the rating to reflect the symptom at its most severe in the preceding 24 hours. Patients also rated the degree to which their symptoms interfered in the previous 24 hours with six common functional domains, including walking, work (including work around the house), general activity, mood, enjoyment of life, and relations with others. Relevant demographic and clinical information was abstracted from the medical record.

The MDASI-OC was administered at the following time points: preoperatively, daily while in the hospital, twice a week on the first week after discharge and then weekly until 8 weeks postoperatively. For the subset of patients undergoing chemotherapy, the MDASI-OC was administered every 2 weeks while receiving chemotherapy after the completion of the 8 week perioperative period. The preoperative and inpatient MDASI-OC was administered via a paper form. After hospital discharge, the MDASI-OC was administered using a telephone based, interactive voice response (IVR) system. Study staff attempted to contact the patients by phone to administer the MDASI-OC when the IVR system failed to record a scheduled time point. Clinical and demographic information was abstracted from the medical record.

Statistical Analysis

The top 5 symptoms were defined as the most severe symptoms during hospitalization after surgery. A composite top 5 symptom score was obtained by averaging severity levels of those 5 symptoms. Major clinical and demographic factors were demonstrated as percent (for categorical variables) and mean (for continuous variables). For patients with ovarian cancer, we compared baseline levels of the top 5 symptoms between those who underwent a primary debulking surgery and those who underwent an interval cytoreduction after neoadjuvant chemotherapy (NACT) using the Wilcoxon rank test. Linear mixed models were used to examine whether symptoms developed differently between those who did not

and who did receive NACT during hospitalization. SAS version 9.2 statistical software (SAS Institute, Cary, NC) was used to perform all analyses. All statistical tests were 2-sided, and P values < .05 were considered statistically significant.

Results

29 women were enrolled and included in this analysis. Demographic and clinical variables are illustrated in Table 1. The median age was 57 years (range 38-77 years). The median surgical time was 221 minutes (range 98-523) and median length of stay was 4 days (range 2-27). Seventy-five percent of patients had ovarian cancer. Of the ovarian cancer patients, eleven patients (50%) were undergoing an interval cytoreductive surgery after neoadjuvant chemotherapy.

There was 100% compliance with preoperative evaluation and 68% compliance with completion of the MDASI-GYN during hospitalization (108/159 instruments returned). Reasons for not completing the MDASI-OC during hospitalization included patient factors such as intubation and altered mental status as well as system issues such as failure to administer on the weekend. During the first week post discharge, only 50% compliance was achieved using the IVR system.

The five symptoms with the highest overall burden post-operatively in the hospital were pain (mean score 5.75, SD 3.68), abdominal pain (mean score 5.58, SD 3.63), fatigue (mean score 5.52, SD 3.10), dry mouth (mean score 5.50, SD 3.85), and drowsiness (mean score 5.05, SD 3.18). The mean composite score from 119 observations was 5.48 with a standard deviation of 2.74. The daily trend of the top five symptoms demonstrates a double peak, with the highest symptom burden on post-operative day 1 and for those who remained hospitalized, on postoperative day 6 (Figure 1). Figure 2 compares the symptom burden in patients who were discharged before and after the mean hospital stay of five days. The individual symptoms (fatigue, pain, abdominal pain, drowsiness and dry mouth) as well as the composite mean of the top 5 rated symptoms are compared. The secondary rise in symptoms in patients with prolonged hospital stay is most notable for the symptoms of fatigue, pain, abdominal pain, and dry mouth.

Among the 22 ovarian cancer patients, 11 had prior NACT. Compared with those without prior chemotherapy, patients with prior NACT reported lower levels of pain, abdominal pain, drowsiness and dry mouth and a higher level of fatigue. However, all differences are statistically insignificant. (Table 2) Longitudinal change of the top 5 symptoms during hospitalization did not show any significant difference between those who had prior neoadjuvant chemotherapy and those who did not.

Tracking symptom change over time may be predictive of patients at high risk for perioperative morbidity. For example, one patient was diagnosed with an anastomotic leak from a colon resection on postoperative day 6. A review of corresponding medical records that day demonstrates a clinical examination of a non-tender, non-distended abdomen, mild tachycardia and low grade fevers. The initial clinical work up was focused on a pulmonary etiology as elicited and documented symptoms were not indicative of an intra-abdominal

process. However, review of the patient's self-reported individual abdominal pain symptom curve demonstrates a sharp increase from postoperative day 5 to 6 with an absolute change in SCORE of 4 (5 vs 9). (figure 3) Interestingly, the patient-reported abdominal pain score correlated tightly with significant clinical events, including diagnosis of anastomotic leak with subsequent drain placement by interventional radiology and a second spike in abdominal pain correlating with the day the patient was taken back to the operating room for failed conservative management of the leak.

The post-hospital symptom trajectory is illustrated in figure 4. In this figure, day 0 represents day of discharge. After hospital discharge, the mean of the composite score top 5 symptoms peaking on the third day post hospital discharge (4.45), followed by a continuing decline in symptom burden with a low score of 1.73 after 3 weeks after discharge from the hospital.

Discussion

In routine clinical hospital practice, minimal time during the focused postoperative patient-provider interaction is spent reviewing and documenting symptoms. In this pilot study, we have demonstrated that structured and detailed symptom assessment via a validated instrument is feasible in a busy gynecologic oncology practice. To our knowledge, this is the first report to demonstrate the clinical sensitivity of the MDASI instrument to correlate with a surgical complication through assessment of patient reported symptoms collected in a longitudinal fashion and suggests that the MDASI-OC may be an added tool to determine perioperative outcomes earlier than what might be detected through routine clinical evaluation.

An additional strength of this study includes the prospective longitudinal collection of patient reported outcomes with sufficient frequency to detect differences in acute postoperative symptoms in the hospital setting as well as after hospital discharge. In our pilot study, we found that the MDASI-OC was sensitive and dynamic, with examples of symptom burden mirroring clinical events and decreasing postoperatively with time. Figure 1 demonstrated a second peak in patients who were discharged after the mean hospital stay suggesting a correlation of patient reported symptom burden with postoperative length of stay and potential surgical morbidity.

The time period between hospital discharge and the postoperative evaluation is not well studied. Regular collection of symptoms after discharge may provide a more robust understanding of the continued symptom burden in the perioperative setting as well as how symptoms interfere with daily living. Additionally, repetitive measurement of symptoms longitudinally and comparison to a preoperative baseline allows for a more quantifiable definition of functional recovery after surgery that is constructed solely from the patient's perspective.

A weakness of this study is the small sample size. We did not identify a statistically different symptom burden profile between women with ovarian cancer who underwent neoadjuvant chemotherapy and those who underwent a primary tumor debulking surgery. However, this

was a pilot study and not powered to detect such differences. Additionally, the MDASI-GYN, while validated for women with ovarian cancer, has not been specifically validated in the perioperative setting. However, the core instrument the MDASI has been found to be an effective means of differentiating symptom burden after cancer surgery in a thoracic surgery population.[13] Our patient population had lower compliance with the out of hospital IVR system compared to other studied oncologic patient populations [13, 14]Hypotheses include medical reasons such as a higher degree of functional limitations after gynecologic oncology surgery than other studied populations, as well as generational differences with our patient population favoring other modes of communication compared to other populations and challenges with the IVR system. Next steps for this study include a formal patient satisfaction evaluation with the IVR system, improved education and IVR training with patients to improve compliance and piloting the use of different techniques of distribution such as a web-based application or distribution via an email platform.

Recent evidence suggests that quality of life measures may be predictive of surgical outcomes.[15] However, QOL measures may lack the specificity for more robust clinical application. In contrast, the opportunities for integration of PROs focusing specifically on the assessment of symptom burden are wide and varied. Clinically, routine automated symptom assessment can serve as a screening tool or as a triage strategy to improve symptom control after major surgery[13, 16] The addition of patient reported outcomes has the potential to increase the meaningfulness of comparative effectiveness research and may allow the results of such studies to have a greater impact on shared medical decision making and application of findings. The increasing focus on patient-centered research is leading to the adoption of patient reported outcomes more systematically into the reporting of adverse events in clinical research.[1] Other exciting horizons include the development of PRO tools specifically validated to capture symptom burden in a surgical population, integration of PROs into clinical cancer registry data, incorporation of PROs into value assessments of health care delivery and as an adjunct to routine clinical care.[17]

Conclusion

Patient reported outcomes are a crucial component of patient-centered research and can allow for more meaningful comparisons of surgical technique and perioperative care. The routine systematic collection and interpretation of symptom burden also have the potential to be incorporated in innovative ways to transform clinical practice.

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Highlights

- It is feasible to collect patient- reported symptoms in the postoperative setting.
- We demonstrate an example of the clinical sensitivity of the MDASI tool.
- Prolonged hospital stay correlates with increased symptom burden postoperatively.

Figure 1.
Symptom curve of the most highly ranked symptoms by postoperative patients during their hospitalization.

Figure 2.
Comparison of the top 5 ranked postoperative symptoms by women discharged before or after the mean length of stay.

Figure 3.
Trajectory of patient report of abdominal pain and correlation with significant clinical events.

Figure 4.
Trajectory of top 5 postoperative symptom composite score after hospital discharge.

Table 1
Demographic and clinical factors (n=29)

	Mean (SD)	Median (min-max)
Age	56.9 (10.1)	57.2 (38.1 – 76.9)
BMI	29.4 (7.3)	28.7 (17.7-51.4)
Surgical time (min)	244.6 (115.5)	221.0 (98 – 523)
Days of hospitalization	5.6 (4.6)	4 (2 - 27)
	N	%
Race/Ethnicity		
Hispanic	5	17.2
White	24	82.8
Marital status		
Married	19	65.5
Unmarried	10	34.5
Employment status		
Employed	11	37.9
Unemployed	6	20.7
Retired	6	20.7
Unknown	6	20.7
Diagnosis		
Ovarian cancer	22	75.86
Other	7	24.14
Surgery type group		
Hysterectomy+/- salpingo-oophorectomy	6	20.69
Hysterectomy +/- salpingo-oophorectomy and lymphadenectomy	5	17.24
Tumor debulking surgery or other bowel surgery	18	62.07
ASA		
2	2	6.9
3	17	58.7
Unknown	10	34.4
Prior Treatment		
Primary surgery	18	62.1
Neoadjuvant chemotherapy	11	37.9

Table 2

Baseline preoperative symptom burden for the five most highly ranked postoperative symptoms in women with ovarian cancer.

	Primary Debulking (n=11)					Neoadjuvant Chemotherapy (n=11)					P*
	Mean	SD	Median	Min	Max	Mean	SD	Median	Min	Max	
Pain	3.91	3.42	4	0	10	1.82	2.27	0	0	5	0.116
Fatigue	3.55	2.46	3	0	7	4.73	2.53	5	0	9	0.305
Drowsiness	3.36	3.80	2	0	10	2.27	2.72	2	0	9	0.617
Dry Mouth	2.82	4.00	0	0	10	1.82	2.36	1	0	8	0.945
Abdominal pain	3.64	3.14	3	0	10	2.00	2.49	0	0	6	0.177
Top 5	3.45	2.65	3	0	9	2.53	1.29	3	0	4	0.439

* Wilcoxon rank test