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Malignant bowel obstruction due to uterine or ovarian cancer: Are there differences in outcome?

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HIGHLIGHTS

- Survival after MBO diagnosis is 105 days.
- MBO associated with uterine cancers have worse prognosis than those from ovarian cancers.
- Surgery may mitigate differences between ovarian and uterine cancer patients with MBO.
- Palliative care consultations are associated with fewer readmissions for MBO
- Discussions at the time of MBO should include expected survival with different interventions for uterine vs ovarian cancer.

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ABSTRACT

Objectives. To describe and compare treatments and outcomes of patients with malignant bowel obstructions (MBO) due to uterine or ovarian cancer.

Methods. Retrospective chart review from two institutions of women admitted 1/1/2005–12/31/2016 with a MBO from recurrent/progressive uterine or ovarian cancer. Data collected includes patient characteristics, cancer-directed treatments before and after MBO, MBO management strategies, and survival after MBO.

Results. Women with MBO from uterine cancer (n = 46) and ovarian cancer (n = 130) underwent similar inpatient interventions such as inpatient chemotherapy and surgery. Median overall survival (OS) after admission for MBO for all patients was 105 days and was shorter for uterine cancer patients (57 vs 131 days, p = 0.0013). Uterine and ovarian cancer patients who had surgery had similar survival (182 vs 210 days, p = 0.6), as did those discharged on hospice from their first admission for MBO (26 vs 38 days, p = 0.1). Uterine and ovarian cancer patients had similar rates of post-discharge chemotherapy (37% vs 50%, p = 0.12), but uterine cancer patients who had chemotherapy still had shorter survival (151 vs 225 days, p = 0.03).

Conclusions. MBO has a relatively poor prognosis. Ovarian and uterine cancer patients whose interventions included surgery or hospice had similar outcomes. Among patients managed medically without hospice, uterine cancer patients experienced worse survival, even when candidates for subsequent chemotherapy. Patient counseling regarding goals of care at this difficult juncture can be informed by these findings and will be enhanced by patient-reported and qualitative data on the patient experience with MBO.

1. Introduction

A malignant bowel obstruction (MBO) occurs when there is blockage of the intestines due to a malignant process causing symptoms of pain, obstipation and/or vomiting. The blockage can result from a single mass or carcinomatosis involving the bowel surfaces. While MBO may occur as the initial presentation in 20% of patients with a gynecologic or gastrointestinal malignancy, in the majority, MBO is a sign of recurrent, incurable disease [1]. The treatment and outcome of patients with MBO who have recurrent, incurable cancer will be the focus of this paper.

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Among gynecologic cancers, MBO is most common in women with cancer of the ovaries, fallopian tube and peritoneum (subsequently referred to as "ovarian cancer"), and ultimately occurs in up to 20% of patients [2,3,4]. MBO has also been described as an end of life condition in 3–11% of uterine cancer patients [1]. Treatments range from hospice care to surgery with bowel resections and/or ostomy placement. However, all treatments remain palliative with a median life expectancy after diagnosis of MBO ranging from 109 to 193 days with surgery, and 33 to 98 days without surgery [3,4,5,6].

Counseling patients and their families on palliative treatments is complex, dependent on individual patient performance status, personal values and physician perspectives. In order to help patients make decisions that are congruent with their wishes in the context of the reality of their disease status, accurate outcome data is necessary. However, there remain large gaps in the data about prognosis and treatment available for patients with ovarian cancer who develop MBO, and even less is known in the setting of uterine cancer.

We sought to describe the presentation, treatments and outcomes of patients with uterine cancer presenting with a MBO and compare them to those with ovarian cancer to provide data that can guide the difficult counseling and decision-making process. We hypothesized that uterine cancer patients presenting with MBO would have poorer overall outcomes compared to their ovarian cancer counterparts.

2. Methods

This is a retrospective chart review of women with a MBO due to recurrent or persistent ovarian and uterine cancers admitted between 1/1/2005 and 6/30/2016 at two urban academic institutions. IRB approval was obtained at each site. The patient list was derived independently at each institution. At the university hospital, the list was developed through two methods. First, an electronic search of radiology reports for attending gynecologic oncology physician names and any of the terms "obstruction," "nausea," "vomiting," "pain," or "bloating" was performed. A single investigator (CH) reviewed the reports to identify eligible patients. Then, the first three billed diagnoses for each patient admitted to the hospital under the section of gynecologic oncology were reviewed for key terms of nausea/vomiting or bowel obstruction (ICD9 codes 560 and ICD10 codes K56.0, K56.6, K56.69 and K56.7) and the resulting list was reviewed for eligible patients. At the academically-affiliated private hospital, an electronic data warehouse was utilized to perform a search for ICD-9 and -10 codes for ovarian, uterine and cervical cancers as well as for bowel obstruction to generate a list of potential patients.

Two investigators (CH and PP) then manually reviewed the appropriate electronic medical records. Inclusion criteria included MBO from recurrent or progressive ovarian or uterine cancer of any histology, clinical and/or radiographic evidence of bowel obstruction, and admission to the hospital for management of bowel obstruction. Exclusion criteria included bowel obstruction deemed to be from benign causes based on surgery, pathology, or subsequent course or from a cancer other than ovarian or uterine cancer, outpatient management only, MBO at initial cancer diagnosis subsequently treated with curative intent, and emergent factors at presentation, such as bowel perforation, regardless of subsequent management.

The investigators abstracted patient and disease characteristics as well as information on hospital course for the first four MBO admissions per patient. Between 2005 and 2012, data was available from the EMR in the form of discharge summaries, pathology reports and radiology reports. After 2012, additional information was available through daily progress and consult notes. All data was entered into an electronic data management system (RedCap) and 10% of charts were spot-checked for accuracy by a single investigator (MC). Follow-up was tracked through outpatient, telephone, and readmission notes. Where dates of death were not available in the medical record, obituary and social security databases were searched and patient date of death confirmed.

The primary outcome of interest was survival after MBO. Exposures of interest included operative and palliative care team involvement in management for MBO. STATA 13 (StataCorps, 2013) was used for statistical analysis to compare variables associated with uterine cancer as compared to ovarian cancer. Student's *t*-test was used for continuous variables and chi-square for categorical variables. A multivariate analysis for survival was performed with a Cox regression model using the Efron method for ties.

3. Results

Patient selection is outlined in Fig. 1. At the university-based institution, over 2000 billed admissions and 1200 radiology reports were retrieved. After initial review of admission diagnoses and radiology reports, 311 charts were reviewed and 86 patients identified as eligible for inclusion. At the academically-affiliated private institution, 215 charts identified by the electronic data warehouse were reviewed and ultimately 90 patients were found to be eligible, for a total of 130 women with ovarian cancer and 46 women with uterine cancer.

The characteristics of the patient population diagnosed with MBO are presented in Table 1. Overall, 62% of patients identified as white and 23% as black. The two institutions had different patient demographics; 43% of the patients at the university hospital identified as white and 37% as black, while at the academically-affiliated private hospital, 79% of the patients identified as white. Cancer histology, age at time of MBO, stage and practice patterns, including rates of surgery were similar between the institutions (data not shown).

At the time of diagnosis with MBO, uterine cancer patients were older than ovarian cancer patients and were more likely to identify as black (Table 1). The majority of ovarian cancer patients had serous histology (82%) while the majority of uterine cancer patients had type 2 endometrial cancer histologies (67%). Both groups presented with similar albumin levels and rates of associated ascites and carcinomatosis, but uterine cancer patients tended to have had fewer previous chemotherapy regimens with a shorter time to development of MBO from diagnosis (16.2 months vs 29.3 months). They were also more likely to have been treated with radiation and to have had earlier stage cancers at original diagnosis than women with MBO from ovarian cancer.

Patients with ovarian and uterine cancers received similar treatments for the management of MBO (Table 2). Forty-eight patients (27% of all patients) had an invasive procedure for MBO within the first 4 admissions; 58% of these at the first admission. Eleven of these procedures were laparotomies performed to place a venting G-tube; these patients were subsequently excluded from the "surgical patient" group, although the outcomes were similar regardless of the group in which these women were included. Compared to nonsurgical and G-tube patients, surgical patients ($n = 37$) had similar median age, race distribution, albumin at MBO diagnosis, time since cancer diagnosis, ovarian versus uterine origin, and active chemotherapy treatment at diagnosis of first MBO, but they were less likely to have known carcinomatosis ($p = 0.03$) or ascites ($p = 0.01$) (Supplementary Table 1). Overall, 41 women (24%) received a venting G-tube, either minimally-invasively placed (endoscopically or IR-guided) or through a laparotomy (Table 2). Chemotherapy was given during any admission in 24% of patients ($n = 41$). Overall, >95% of patients admitted for MBO were tolerating some diet at discharge.

Ovarian cancer patients had a higher overall number of admissions and had a longer cumulative length of stay for their MBO management. Additionally, 54% of ovarian cancer patients as compared to 34% uterine cancer patients were readmitted for recurrent MBO. We also noted a trend towards fewer women with uterine cancer than ovarian cancer ($p = 0.12$) having at least one form of outpatient treatment after MBO diagnosis, whether chemotherapy, PARP inhibitors, or targeted treatments.

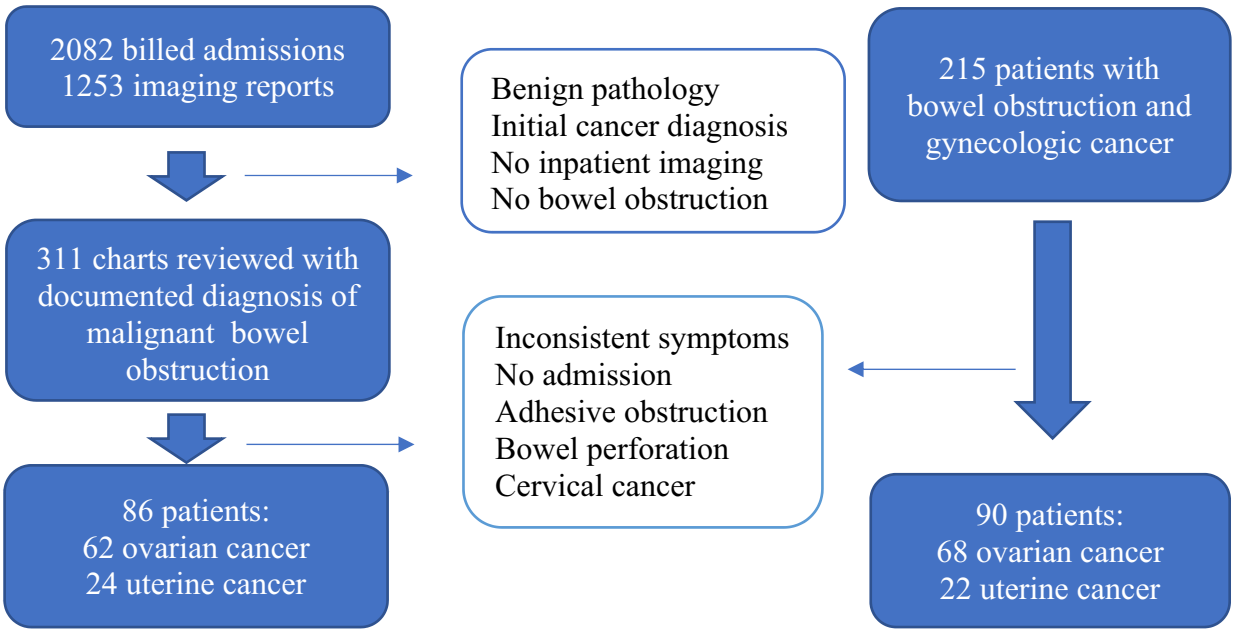

Fig. 1. Diagram outlining patient selection at each institution.

Palliative care was involved at first admission for MBO for 30% of women with either ovarian or uterine cancer. Yet uterine cancer patients were more likely to be discharged to hospice from their first admission for MBO (17 uterine patients (37%) vs 22 ovarian patients (17%), p = 0.005). Patients who had a palliative care consultation during the first admission were less likely to experience a second admission compared to those who did not have an initial palliative care consultation (11/55 (20%) vs 75/126 (59%), p < 0.0001), even after excluding 45 patients discharged on hospice or deceased after first admission (9/25 (36%) vs 75/109 (69%), p = 0.002). There was a trend towards a lower rate of outpatient TPN use as well (7% vs 18%, p = 0.05). Surgical patients had lower rates of palliative care consultation (11% versus 35%, p = 0.004) and a higher rate of readmission (64% versus 45%, p = 0.03). When excluding 43 nonsurgical and 2 surgical patients discharged on hospice or deceased after their first MBO admission, however, readmission rates were similar between surgical and nonsurgical groups (71% vs 62%, p = 0.4).

Table 1
Demographics.

	Ovarian (n = 130)[a]	Uterine (n = 46)[a]	p-Value
Age	63 (41–83)	67 (47–83)	**p = 0.01**
Race: White	89 (70%)	20 (43%)	
Black	20 (15%)	17 (37%)	**p = 0.005**
Asian	5 (4%)	2 (4%)	
Hispanic	9 (7%)	3 (7%)	
Unknown/other	8 (6%)	4 (9%)	
Histology			
Ovary: Serous	106 (82%)		
Other	24 (18%)		
Uterus: Serous/clear cell		17 (37%)	
Carcinosarcoma		10 (22%)	
Endometrioid		15 (33%)	
Sarcoma		4 (8%)	
No previous chemo regimens	3 (1–7)	2 (1–5)	**p = 0.006**
Stage III/IV	123 (95%)	36 (78%)	**p = 0.0001**
Previous radiation	8 (6%)	24 (52%)	**p < 0.0001**
Time from cancer diagnosis to initial MBO (months)	29.3 (3.7–123)	16.2 (7.4–97)	**p = 0.04**
Albumin at MBO[b]	3.4 (2.2–4.4)	3.2 (1.7–4.5)	p = 0.11
Ascites at MBO[c]	67 (52%)	22 (51%)	p = 0.34
Carcinomatosis at MBO	58 (45%)	21 (46%)	p = 0.9

p-values < 0.05 are presented in bold.
[a] Unless otherwise noted, reported as median (95% confidence interval) or number (percentage).
[b] Available for 170 patients.
[c] Available for 168 patients.

Table 2
Interventions.

	Ovarian (n = 130)	Uterine (n = 46)	p-Value
Inpatient chemotherapy	31 (24%)	10 (22%)	p = 0.8
Surgery (laparotomy)[a]	29 (22%)	8 (17%)	p = 0.5
Bowel resection	21	3	
Ostomy	13	4	
Lysis of adhesions only	6	1	
Gastrostomy tube (G-tube)			
Via laparotomy[b]	11 (8%)	1 (2%)	p = 0.1
Minimally-invasive GT[c]	23 (18%)	6 (12%)	p = 0.5
Unsuccessful attempt at G-tube	7 (5.3%)	4 (8%)	p = 0.7
Colonic stent	6 (4.5%)	2 (4.3%)	
Inpatient TPN	44 (34%)	10 (22%)	p = 0.11
Discharge TPN	23 (17%)	4 (8.7%)	p = 0.12
At least one readmission	70 (54%)	16 (34%)	**p = 0.03**
Total # of admissions	2 (1–5)	1 (1–4)	**p = 0.02**
Total inpatient days for MBO across admissions	14 (4–50)	10.5 (3–42)	**p = 0.047**

*Unless otherwise noted, reported as median (95% CI) or number (percentage).
p-values < 0.05 are presented in bold.
[a] Ovarian cancer patients who underwent surgery had more than one procedure. Patients who had an invasive procedure for G-tube placement were excluded.
[b] These patients were excluded from the "surgical" group. G-tube placement during laparotomy was not always the initial intention of the laparotomy. Only 1 patient had a failed minimally-invasive attempt at GT placement prior to laparotomy for a G-tube. 2 patients had a concurrent bowel resection, and 1 patient had a concurrent ostomy.
[c] Endoscopic or interventional radiology placement of gastrostomy tube as opposed to surgically placed gastrostomy tube. One patient had both a laparotomy GT followed by a minimally-invasive GT and was put in the laparotomy GT group.

Of note, as practice patterns changed over the time period included in this study, the rate of palliative care consults during first admission dramatically increased over time, from 7.7% before 2012 to 40% after 2012 ($p < 0.0001$). Other interventions, such as rates of surgery and TPN, remained stable, however, the rate of inpatient chemotherapy dropped from 35% before 2012 to 20% after 2012 ($p = 0.02$).

Mortality within 30 days of first admission was 22% (39 patients) and another 14% (19 patients) died within 30 days of a subsequent discharge for MBO. Median overall survival after initial diagnosis of MBO for the total group was 105 days, but significantly shorter for women with uterine cancer as compared to those with ovarian cancer (57 days vs 131 days, $p = 0.003$) (Table 3).

Eight 8 (17%) uterine cancer patients and 29 (22%) ovarian cancer patients had a surgical intervention for MBO, excluding patients who had procedures only for venting G-tube placement (Table 2). There was no difference in median survival by primary cancer type when surgery was performed (182 days vs 210 days, $p = 0.6$). Among patients who did not have surgery, uterine cancer patients experienced significantly shorter survival (median 46 vs 110 days, $p = 0.001$) (Table 3).

After excluding patients discharged on hospice, a similar proportion of uterine and ovarian cancer patients had subsequent treatment (60% vs 58%); among these patients, those with uterine cancer had shorter survival (151 days vs 225 days, $p = 0.03$) (Table 3). Median survival was similar in subgroups of uterine and ovarian cancer patients who had surgery followed by outpatient chemotherapy (182 days vs 314 days, $p = 0.18$).

Univariate analyses showed that survival was associated with younger age, white versus black race, higher albumin, longer time since diagnosis, absence of ascites, previous platinum sensitivity, undergoing surgery, outpatient chemotherapy after discharge from MBO admission, administration of TPN, and ovarian versus uterine origin of cancer. A multivariate analysis to control for factors that differed between ovarian and uterine cancer patients and other factors associated with survival was performed (Table 4). It showed that uterine cancer origin (as well as age, race, ability to undergo surgery, receiving chemotherapy after MBO, and initial albumin) were independently associated with survival after MBO.

Table 4
Multivariate analysis for survival after MBO.[a]

	Hazard ratio	p-Value	95% CI
Age (continuous)	1.02	0.02	1.004–1.04
Albumin (continuous)	0.65	0.005	0.49–0.88
Race – black (compared to white)	1.94	0.006	1.21–3.11
Patients who underwent surgery[b]	0.56	0.015	0.35 - 0.892
Uterine origin (compared to ovarian)	1.51	0.04	1.01–2.25
Chemotherapy after MBO	0.49	<0.001	0.34–0.69
Ascites	1.14	NS	0.8–1.65
Time from diagnosis to MBO	0.999	NS	0.82–1.00

[a] 159 patients included.
[b] Invasive procedures, excluding patients who had procedures for G-tubes.

4. Discussion

Our study supports previous evidence that a diagnosis of MBO from recurrent/progressive gynecologic cancer is an end-of-life state [3,4,5,6], with overall median survival of 105 days. Women with uterine cancer in our cohort had a median survival after MBO diagnosis that was less than half that of their ovarian cancer counterparts (57 days vs 131 days) despite the fact that a smaller percentage presented with advanced stage disease and they had fewer previous chemotherapy regimens. The poor prognosis of women with uterine cancer who present with MBO corroborates the findings in other small studies and supports our original hypothesis [7].

The novel finding in our study is that for those uterine cancer patients who do undergo surgery, the survival outcome approaches that of ovarian cancer patients (182 days vs 210 days). A similar percentage of patients (37–50%) are able to undergo chemotherapy after MBO but the overall impact on survival is limited with a median 2 -month shorter survival in uterine cancer patients undergoing chemotherapy compared to ovarian cancer patients. The relative resistance of recurrent uterine cancer to subsequent therapy and the lack of effective, sequential therapies in uterine cancer is well known [8,9]. Even in the adjuvant setting, a case-control study of advanced stage uterine and ovarian cancers matched for age and residual disease after cytoreduction showed shorter survival in the uterine cancer patients, including optimally debulked patients [10]. Their findings suggest a difference in tumor biology between the two types of cancer despite a similar disease spread pattern and presentation.

The question of which uterine cancer patients are better suited for surgical intervention of MBO is a difficult one that this study cannot fully address. For both uterine and ovarian cancer patients, women who had surgery had longer survival than those treated medically (182 vs 46 days for uterine cancer patients, 210 vs 110 days for ovarian cancer patients). However, these patients did exclude those who were found to have such extensive disease at laparotomy that they were palliated with a G-tube. In our study, surgical patients had less carcinomatosis and less ascites than nonsurgical patients, but had similar demographic factors such as age, albumin, and treatment status. It is likely that these are patients that had more limited disease and therefore already had a more favorable prognosis. Other studies have found that survival after MBO is inversely correlated with independent factors associated with poor prognosis, such as older age, non-ovarian primary, ascites, carcinomatosis, hypoalbuminemia, and leukocytosis regardless of surgical intervention [6,11].

Recent large database studies have found conflicting results regarding the benefits of surgery for MBO. A study of patients with MBO from

Table 3
Outcomes.

	Ovarian (n = 130)	Uterine (n = 46)	p-Value
Chemo after discharge from first MBO admission	65 (50%)	17 (37%)	p = 0.12
Excluding hospice patients (n = 108)	65 (60%)	17 (58%)	
Survival after MBO (days)	131 (13–1026)	57 (6–623)	**p = 0.0013**
With chemo after first MBO admission (n = 82)	225 (58–1135)	151 (42–652)	**p = 0.03**
With surgery[a] for MBO (n = 37)	210 (26–1368)	182 (28–1341)	p = 0.6
Without surgery for MBO (n = 139)	110 (11–661)	46 (6–555)	**p = 0.001**
Without surgery or chemo (n = 77)	55 (6–758)	25 (4–513)	**p = 0.01**
Discharged on hospice from 1st admission (n = 41)	38 (12–237)	26 (3–554)	p = 0.10
30-day mortality from MBO diagnosis	16 (12%)	15 (32%)	**p = 0.002**
Overall survival (months)	37 (9.1–123)	21 (8.9–110)	**p = 0.003**
Discharge to hospice from 1st MBO admission	22 (17%)	17 (37%)	**p = 0.005**

*Unless otherwise noted, reported as median (95% CI) or number (percentage).
p-values < 0.05 are presented in bold.
[a] Invasive procedures, excluding patients who had the procedure for placement of a G-tube.

ovarian or pancreatic cancer in the SEER database found longer median survival in surgically-managed patients compared to those managed medically or with a G-tube (128 days versus 72 days versus 38 days, respectively) with similar in-hospital mortality and lower readmissions [3]. In contrast, a database study of patients with MBO from any cancer revealed a lower number of hospital-free days and no improvement in survival for those patients who underwent surgery compared to their medically managed counterparts [12]. However, in contrast to our study, these studies did not exclude patients who had emergent surgeries due to MBO and were not limited to gynecologic cancer patients. The differences we found in outcomes with different gynecologic cancers suggests that MBO from different cancers may require individualized approaches. The effect of surgery itself for MBO is being studied in a prospective trial, SWOG S1316. However, to be part of the study, patients with MBO must already be considered surgical candidates, which may bias results and limit generalizability. Our results do provide data on survival after individual interventions that can aid clinicians who are at a crossroads in making treatment recommendations specific to uterine and ovarian cancer patients.

With such a short median survival, using MBO as a trigger for involvement of palliative care, documenting goals of care, and sharing prognosis is appropriate. Unfortunately, we could not collect information on patient-reported outcomes of symptom-free time due to limitations of a chart review. We did find lower readmission rates in women with an inpatient palliative care consultation, which could be due to improved symptom control, better social support or outpatient follow-up. It may also reflect patient and physician directed self-selection of palliative care consultation when less aggressive therapies are better in line with a patient's goals towards the end of life. This is supported by the particularly low rate of surgery and a trend towards lower outpatient TPN use in patients who had palliative care consultations.

From the patient perspective, studies with patient-centered objectives can provide information that is meaningful to patients as they delineate their treatment goals and make end of life choices. This will need to include information not just about length of survival, but quality of life with each intervention. Patients with advanced-stage ovarian cancer have been shown to be willing to trade months of progression-free survival for a less emetogenic chemotherapy regimen or a reduction in abdominal symptoms [13]; patients with MBO are also likely to have priorities to balance against solely length of survival. Societal, family, and personal cost of each option also requires further study. Many of these factors cannot be extracted from charts and will require attention to quantitative patient-reported outcomes and qualitative patient-centered research.

Additionally, a concerning factor associated with decreased survival in our study is black race. The literature has mixed findings on racial disparities in outcomes for black women with gynecologic cancers [14,15,16,17], and the question of causes of disparities requires further study.

This study is subject to potential confounders inherent in retrospective reviews, where patient identification and treatment course may be biased by factors not available in the documentation. We have acquired a breadth of data to attempt to control for confounders such as previous treatments, disease status, and patient characteristics such as age and race, but cannot control for personal and institutional factors missing from the charts. While patient lists were acquired by different methods readily available at each hospital, we assumed that the patient dataset identified through billing diagnoses and the data warehouse would be similar. In addition, we were not able to collect information, including patient reported information on quality of life and symptoms, or detailed information on physician thought process and biases around recommendations that might influence care.

This study's strengths, however, include a thorough manual chart review with accuracy confirmed by a second reviewer for at least 10% of the charts, which allowed us to collect specific data points not available in large database studies such as the specific timing of different interventions throughout the admissions and documentation of conversations. The multi-institutional nature of this study with diverse patient population also helps to increase generalizability.

5. Conclusion

Survival after MBO from recurrent or progressive ovarian or uterine cancer remains short, with a median survival of 105 days. Based on our findings, patients with MBO from uterine cancer can be counseled that their overall survival after an initial MBO diagnosis, when managed medically, is shorter than for those with ovarian cancer, even if receiving chemotherapy afterward. Survival for uterine cancer patients who undergo surgery after MBO is similar to their ovarian cancer counterparts.

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ygyno.2019.04.681.

COI statement

The authors report no conflicts of interest in relation to the information relayed in this manuscript.

Author contribution

SDY and CH contributed to the study design. CH, PP, MC, and EM contributed to the data collection. SDY, NL, JH, and EM provided patients for the study. CH, PP, MC, EM, NL, JH and SDY contributed to the manuscript preparation.

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