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ORIGINAL ARTICLE

Indicators of surgery and survival in oncology inpatients requiring surgical evaluation for palliation

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Abstract
Background We sought to determine the clinical presentation, management, and outcomes associated with surgical consultation for symptom palliation in oncology inpatients.
Materials and methods We reviewed the medical records of inpatients for whom surgical consultations were requested (January 2000 to September 2006) at a tertiary referral cancer center to identify those who underwent surgical palliative evaluation (defined as consultation for symptoms attributable to an advanced or incurable malignancy). We used the Cox proportional hazards model to identify prognostic factors associated with overall survival (OS) and logistic regression to identify factors associated with surgical intervention.
Results Surgical consultation was requested for 1,102 inpatients; 442 (40%) met the criteria for surgical palliative evaluation. Gastrointestinal obstruction was the most common complaint (43%), while wound complications/infection and gastrointestinal bleeding accounted for 10% and 8%, respectively. The median OS was 2.9 months. Adverse prognostic factors for OS included ≥2 radiologically evident disease sites (HR=1.4; 95% CI, 1.1–1.8) and carcinomatosis/sarcomatosis (HR=1.4; 95% CI, 1.1–1.7). Palliative surgical procedures were performed in 119 (27%) patients, with a 90-day morbidity and mortality rate of 40% and 7% respectively. Patients with wound complications (OR=3.3; 95% CI, 1.4–7.6), intestinal obstruction (OR=1.9; 95% CI, 1.1–3.2), or an intact primary/recurrent tumor (OR=3.6; 95% CI, 2.2–6.0) were more likely to undergo surgical intervention. Patients with ascites were less likely to undergo surgery (OR=0.4; 95% CI, 0.2–0.8).
Conclusions Surgical palliative evaluations accounted for 40% of inpatient surgical consultations. Given that OS in this population is short and surgery is associated with considerable morbidity and mortality, non-operative management is desirable.

Keywords Palliative care · Surgery · Surgical oncology · Morbidity · Mortality

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Introduction

The 5-year survival for all cancers diagnosed in the USA is only 66%, making cancer the second most common cause of death [2]. With the number of patients diagnosed with incurable malignancies increasing each year, the demand for palliative care is greater than ever. Surgeons are often called upon to evaluate patients with advanced or incurable malignancies for operative interventions. Studies not only show that palliative surgery can relieve symptoms and

improve quality of life but also report associated morbidity rates of 30–40% and mortality rates of 10% [16, 18, 20]. The definition of palliative surgery varies slightly among these studies but is generally considered to be any procedure that is performed to reduce symptoms or improve quality of life in a patient with an advanced or incurable malignancy [13, 17, 18].

Additional studies have examined the frequency with which palliative surgical procedures are performed. Palliative surgical procedures have been reported to account for 13% of all operations and over 1,000 procedures per year at major US cancer centers [10, 18]. A recent report by McCahill et al. [14] demonstrated that up to 21% of all operations performed by surgical oncologists meet the criteria for palliative procedures. Most of the studies of surgical palliation have focused exclusively on patients who underwent surgery and have not included patients who did not undergo surgery; thus, predictors of surgical intervention were not identified. In addition, the inclusion of non-operative patients exemplifies the highly selective nature of palliative surgery. No studies have described an overall inpatient population requiring palliative surgical evaluation. A study of both operative and non-operative palliative care patients would provide surgical oncologists with an analysis of a study population that they can expect to face on a regular basis.

The percentage of acute, inpatient surgical oncology consultations that meet the criteria for palliative care, the frequency with which palliative surgical interventions are selected, and the corresponding outcomes for patients treated with and without surgery are unknown. The purpose of this study was to determine the clinical presentation, management, and outcomes associated with surgical consultation for symptom palliation in oncology inpatients with advanced or incurable disease. In addition, we sought to identify any predictors for surgical intervention and factors associated with decreased overall survival.

Materials and methods

Patients

We reviewed the medical records of inpatients for whom a surgical oncology consultation was requested between January 2000 and September 2006 at The University of Texas M. D. Anderson Cancer Center. The study population consisted of all patients undergoing palliative evaluation by the general surgical oncology consultation service. Surgical palliative evaluation was defined as a consultation with patients who had symptoms attributable to an advanced or incurable malignancy, including patients who were evaluated for symptoms attributable to complications or toxicity of the treatment of their advanced or incurable malignancy. Similarly, we defined palliative surgery as surgery for symptoms attributable to an advanced or incurable malignancy with the sole intent of improving quality of life and symptom burden. Patients who were evaluated for potentially curative surgery, in addition to the relief of their symptoms, were excluded from this study. The study was approved by The M. D. Anderson Institutional Review Board.

Clinicopathologic variables

The clinicopathologic variables extracted from each patient's medical records included age, sex, tumor histology, systemic therapy (chemotherapy or biologic therapy) within the 6 weeks before the consultation, and the presence of neutropenia (absolute neutrophil count <1,000 cells/μl) at the time of consultation. For the purposes of analysis, malignancy type was broadly categorized into solid tumor malignancy, hematologic malignancy, or both. Each patient's malignancy was classified as incurable or advanced on the basis of disease status by a two-physician review panel (BB and JC) and not on the presence of comorbidities that precluded resection or cure. Patients with unequivocal evidence of unresectable or incurable disease were classified as incurable. Patients with an advanced or aggressive malignancy who were potentially curable were classified as having an advanced stage of malignancy.

The reasons for surgical palliative evaluation were classified using the following symptom clusters: (1) obstruction (including gastric outlet and small bowel or large bowel obstruction); (2) gastrointestinal bleeding (bleeding from any source within the gastrointestinal tract); (3) wound complications (infections or complications related to an intact primary tumor or metastasis, including chemotherapy-related wound infections); and (4) "other" (biliary complaints, symptomatic hernias, fistulas of any type, non-specific gastrointestinal complaints, and consultations for feeding tube placement).

To identify radiologically evident sites of disease, we reviewed the pertinent imaging studies—computed tomography or magnetic resonance imaging of the brain, chest, and abdomen/pelvis, positron emission tomography, and bone scans—for each patient. We then classified the radiographic extent of disease into the following categories: intact primary tumor/local recurrence of primary tumor, abdominal visceral metastases, abdominal/chest lymphadenopathy, ascites, bone metastases, brain metastases, lung metastases, carcinomatosis/sarcomatosis, and subcutaneous/muscle/other soft tissue metastases.

The medical records of patients who underwent surgery were reviewed to identify the operative procedures, perioperative complications, and 90-day postoperative

mortality rates. We stratified perioperative complications according to the severity classification system of Dindo et al. [5]. Grade I complications were any deviation from the normal postoperative course requiring only minor pharmacological intervention. Grade II complications required pharmacological treatment with drugs other than the minor pharmacological interventions allowed for grade I complications. Grade III complications required surgical, endoscopic, or radiologic intervention; these complications were further stratified into grade IIIa, signifying no requirement for general anesthesia, and grade IIIb, signifying a requirement for general anesthesia. Grade IVa complications were life-threatening and required intensive care unit management for single organ dysfunction, and grade IVb complications were life-threatening and required intensive care unit management for multiorgan dysfunction. Grade V indicated patient death. The suffix "d" (for disability) was added to the patient's complication grade if he or she continued to suffer from the complication at the time of discharge from the hospital.

Statistical analysis

Overall survival (OS) was defined as the time from surgical evaluation to death from any cause. Patients were censored on the date of their last follow-up. Median OS was estimated using the methods of Kaplan and Meier [8]. Logistic regression analysis was performed to identify clinicopathologic variables associated with surgical intervention. We used the Cox proportional hazards model to examine the relationship between clinicopathologic variables and OS [4]. Computations were carried out using SAS software (version 8.0; SAS Institute, Cary, NC, USA). A P value of less than or equal to 0.05 was considered statistically significant.

Results

Surgical consultation was requested for 1,102 patients; of these, 442 (40%) met our criteria for surgical palliative evaluation and thus formed the study cohort. The demographics and clinicopathologic variables for these patients are summarized in Table 1. The median age was 58, and the gender was more often male (58%). The majority of patients had a solid organ malignancy (81%). Most patients (79%) were deemed to have incurable disease. The specific tumor types were colorectal cancer (n=71), hepatobiliary cancer (n=64), genitourinary cancer (n=51), sarcoma (n=38), leukemia (n=34), lymphoma (n=31), gastroesophageal cancer (n=27), lung cancer (n=22), breast cancer (n=21), miscellaneous solid organ cancer (n=21), unknown primary tumor (n=12), melanoma (n=11), multiple malignancies of any type (n=11), other hematologic malignancies (n=9), head and neck cancer (n=8), gynecologic cancer (n=6), and brain cancer (n=5).

Common symptom groups for which surgical evaluation was requested were gastrointestinal obstruction (43%), wound infections/complications (10%), and gastrointestinal bleeding (8%). The wound infections/complications group included abscess formation (n=17), tumor-associated bleeding (n=3), infection without abscess (n=8), and open or non-healing wound/tumor invasion (n=14). Nearly half of the patients (47%) had received chemotherapy or biologic therapy within the 6 weeks prior to evaluation. Few patients (9%) displayed neutropenia at the time of their

Table 1 Demographic and clinicopathologic variables for 442 patients who met study criteria for surgical palliative evaluation

Variable	Number	Percent
Median age–years (range)	58 (18–88)	
Sex		
Male	256	58
Female	186	42
Malignancy type		
Hematologic	74	17
Solid	360	81
Both	8	2
Disease stage		
Advanced	95	21
Incurable	347	79
Symptom complex		
Wound complications/infections	42	10
Gastrointestinal bleeding	35	8
Bowel obstruction	191	43
Other	174	39
Chemo/biotherapy within 6 weeks		
Yes	209	47
No	233	53
Neutropenia		
Yes	38	9
No	404	91
Imaging extent of disease		
Intact primary/recurrent tumor	124	28
Abdominal visceral metastases	152	34
Abdominal/chest lymphadenopathy	84	19
Ascites	79	18
Bone metastases	48	11
Brain metastases	18	4
Lung metastases	98	22
Carcinomatosis/sarcomatosis	146	33
Subcutaneous/muscle/soft tissue metastases	16	4
Number of disease sites on imaging		
1	126	29
2	162	37
≥3	97	22
N/A	57	13

Table 2 Morbidity and mortality within 90 days following palliative surgery in 119 patients

	Number	Percent
Variable		
Mortality	8	7
Morbidity (48 patients)[a]	67	56
Respiratory distress/failure	14	12
Wound infection/non-healing wound	13	11
Bowel obstruction	6	5
Ileus	5	4
Bacteremia/line sepsis	5	4
Intra-abdominal abscess	4	3
Pulmonary embolus/venous thrombosis	3	3
Biliary obstruction/cholecystitis	3	3
Fascial dehiscence	2	2
Severe sepsis	1	1
Symptomatic pleural effusion	1	1
Ascitic leak	1	1
Miscellaneous[b]	9	8
Severity classification[c]		
I—any deviation from normal post-operative course, minor pharmacologic intervention	3	3
II—major pharmacologic intervention (IId)	36 (12)	30 (10)
IIIa—requiring surgery, endoscopy, or IR without general anesthesia (IIIad)	13 (8)	11 (7)
IIIb—requiring surgery, endoscopy, or IR with general anesthesia (IIIbd)	5 (1)	4 (1)
IVa—life threatening single organ dysfunction (IVad)	7 (0)	6 (0)
IVb—life threatening multiorgan dysfunction (IVbd)	3 (1)	3 (1)
V—death	8	7

d indicates the number of patients suffering from the complication at the time of hospital discharge

[a] Some patients experienced more than one complication.

[b] Including C. difficile colitis, urinary tract infection, delirium, fever, arrhythmia, high ostomy output, or readmission to a hospital for uncontrolled pain.

[c] As put forth by Dindo et al. [7]

evaluation. Radiologic findings included abdominal visceral metastases (34%), carcinomatosis/sarcomatosis (33%), intact primary/recurrent tumor (28%), and ascites (18%). The majority of patients (59%) had ≥2 disease sites present on imaging.

One hundred nineteen patients (27%) underwent palliative surgery. Of these, 21 patients (18%) required bowel resection (three with concomitant stoma formation and two with concomitant feeding tube placement); 28 patients (24%) underwent intestinal bypass (three with stoma formation, 13 with feeding tube placement alone, and one with both); 14 patients (12%) required wound debridement or incision and drainage (one with stoma formation and one with feeding tube placement); 18 patients (15%) underwent stoma formation (two with concomitant feeding tube placement); nine patients (8%) underwent organ resection; and 16 patients (13%) underwent feeding tube placement only. Thirteen patients (11%) underwent a variety of miscellaneous procedures.

Operative procedures were grouped according to the symptom complex at presentation. Among the 42 patients who presented with wound complications or infections, 16 (38%) underwent surgery, which consisted of incision and drainage in 13, wide excision in two, and mastectomy in one. Of the 35 patients who presented with gastrointestinal bleeding, five (14%) required surgery: four required bowel resection, and one required splenic artery ligation. Of the 191 patients who presented with bowel obstruction, 64 (34%) required surgery: 12 required bowel resection, 27 required bypass, 15 required stoma placement, seven required decompressive gastrostomy tube placement, and three required lysis of adhesions. Of the 174 patients who presented with complaints and categorized as "other," 34 (20%) required surgery.

Ninety-day morbidity and mortality rates are outlined in Table 2. Forty-eight patients (40%) developed a total of 67 complications. To grade the severity of patients' complications, we stratified the morbidity according to a commonly accepted surgical complication classification system [5]. Most complications were grade II (i.e., required only pharmacologic intervention), although 15% required further interventions/surgery and 9% were life-threatening. The 90-day mortality rate was 7% (n=8). The median OS for all patients was 2.9 months (95% confidence interval [CI], 2.4–3.3) (Fig. 1). Median OS for those patients treated without surgery was 2.1 months (95% CI, 1.8–2.4) compared to 6.9 months (95% CI, 4.9–10.5) for those patients who underwent surgery.

The results of the univariate and multivariate analyses that were performed to identify clinicopathologic variables associated with patients having undergone surgical inter-

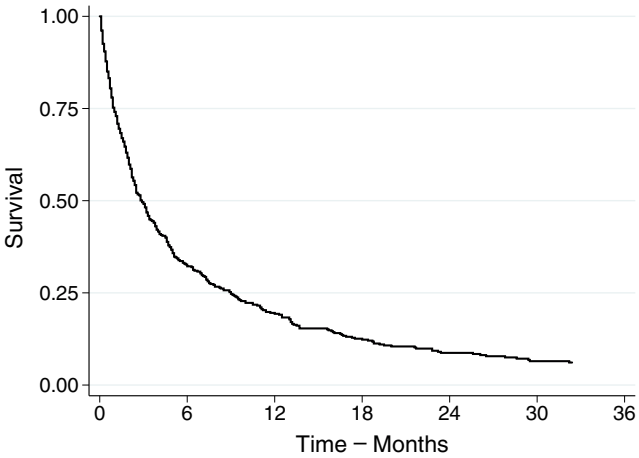

Fig. 1 Kaplan–Meier estimate of overall survival probability for the 442 patients who met our criteria for surgical palliative evaluation

Table 3 Univariate analysis of variables associated with palliative surgery

Variable	OR	95% CI	*P* value
Age	0.98	0.97–0.99	0.02
Male sex	0.91	0.60–1.40	0.68
Hematologic malignancy	0.28	0.14–0.58	<0.001
Solid organ malignancy	3.56	1.66–7.67	0.001
Incurable malignancy	1.29	0.76–2.19	0.35
Symptom complex			
Wound complication/infection	2.91	1.41–5.99	0.004
Gastrointestinal bleeding	0.71	0.26–1.97	0.51
Bowel obstruction	2.15	1.33–3.49	0.002
Other	Referent	Referent	Referent
Chemo/biotherapy within 6 weeks	0.62	0.40–0.95	0.03
Neutropenia	0.30	0.10–0.85	0.02
Imaging extent of disease			
Intact primary/recurrent tumor	3.51	2.21–5.57	<0.001
Abdominal visceral metastases	0.75	0.48–1.18	0.22
Abdominal/chest lymphadenopathy	1.07	0.63–1.80	0.81
Ascites	0.28	0.14–0.56	<0.001
Bone metastases	1.08	0.56–2.07	0.82
Brain metastases	1.18	0.43–3.23	0.74
Lung metastases	0.92	0.56–1.52	0.75
Carcinomatosis/sarcomatosis	0.44	0.27–0.72	0.001
Subcutaneous/muscle/soft tissue metastases	1.07	0.36–3.15	0.90
Number of disease sites on imaging			
1	Referent	Referent	Referent
2	0.79	0.48–1.30	0.35
≥ 3	0.67	0.37–1.20	0.18

OR odds ratio, *CI* confidence interval

vention are shown in Tables 3 and 4, respectively. Univariate analysis revealed that patients with solid organ malignancies, wound complications/infections, bowel obstruction, or an intact primary or recurrent tumor on imaging were more likely to be treated with a surgical procedure. Older patients and patients with hematologic malignancies, recent administration of chemotherapy or biologic therapy, neutropenia, ascites, or carcinomatosis/sarcomatosis on imaging were less likely to be treated with surgical intervention. On multivariate analysis, wound complications/infection, bowel obstruction, and an intact primary or locally recurrent tumor remained significant predictors of surgical intervention. Increasing age and presence of ascites remained predictors of no surgical intervention.

The results of the univariate and multivariate analyses that were performed to identify factors associated with OS are shown in Tables 5 and 6, respectively. Univariate analysis revealed that patients with hematologic malignancies, neutropenia, ascites, carcinomatosis/sarcomatosis, and with ≥2 disease sites on imaging were likely to have shorter OS, while patients with solid organ malignancies were likely to have relatively longer OS. On multivariate analysis, carcinomatosis/sarcomatosis and having ≥2 disease sites on imaging remained significant predictors of shorter OS.

Discussion

In this study, 40% of all inpatient surgical oncology evaluations were requested for symptom palliation in patients with advanced or incurable malignancies. Bowel obstruction was the most common reason for consultation in this patient population. Not unexpectedly, almost half of the patients had received systemic therapy within 6 weeks

Table 4 Multivariate analysis of variables associated with palliative surgery

Variable[a]	OR	95% CI	*P* value
Age	0.97	0.95–0.99	0.002
Symptom complex			
Wound complications/infections	3.26	1.40–7.59	0.006
Gastrointestinal bleeding	0.83	0.28–2.47	0.73
Bowel obstruction	1.88	1.10–3.22	0.02
Other	Referent	Referent	Referent
Imaging extent of disease			
Intact primary/recurrent tumor	3.64	2.20–6.03	<0.001
Ascites	0.39	0.19–0.82	0.01

OR odds ratio, *CI* confidence interval

[a] Solid organ and hematologic malignancy, chemo- or biotherapy within 6 weeks, neutropenia, and carcinomatosis/sarcomatosis on imaging were not significant on multivariate analysis

Table 5 Univariate analysis of variables associated with overall survival

Variable	HR	95% CI	*P* value
Age	1.00	0.99–1.01	0.38
Male sex	1.05	0.86–1.28	0.62
Hematologic malignancy	1.51	1.17–1.94	0.001
Solid organ malignancy	0.67	0.51–0.87	0.002
Symptom complex			
Wound complication/infection	0.71	0.50–1.02	0.06
Gastrointestinal bleeding	0.98	0.67–1.43	0.92
Bowel obstruction	0.91	0.73–1.12	0.36
Other	Referent	Referent	Referent
Chemo/biotherapy within 6 weeks	0.96	0.79–1.17	0.70
Neutropenia	1.42	1.01–2.00	0.05
Imaging extent of disease			
Intact primary/recurrent tumor	0.99	0.79–1.24	0.91
Abdominal visceral metastases	1.15	0.93–1.43	0.20
Abdominal/chest lymphadenopathy	0.84	0.65–1.09	0.18
Ascites	1.44	1.11–1.86	0.006
Bone metastases	1.01	0.74–1.40	0.93
Brain metastases	0.99	0.61–1.63	0.99
Lung metastases	0.91	0.71–1.16	0.43
Carcinomatosis/sarcomatosis	1.42	1.15–1.77	0.001
Subcutaneous/muscle/soft tissue metastases	1.19	0.72–1.96	0.50
Number of disease sites on imaging			
1	Referent	Referent	Referent
2	1.49	1.16–1.91	0.002
≥ 3	1.44	1.08–1.91	0.01

HR indicates hazard ratio, *CI* confidence interval

preceding the request for surgical palliative evaluation. In addition to demographic and clinicopathologic factors, we included the extent of disease present on radiologic imaging in the patient assessment because it often influences clinical decisions at the time of consultation. As anticipated, several radiologic findings were associated with non-surgical management or shorter OS on multivariate analysis.

The definition of surgical palliation varies [12, 15, 19]. Most recent studies have included patients with advanced or incurable cancer for whom the goal is symptom improvement [17, 18]. Determining whether cancers are advanced or incurable is subjective and a limitation of all palliative surgical studies. Even more difficult is determining whether a hematologic malignancy is advanced or incurable. In lymphoma classification, for example, most clinicians use the revised International Prognostication Index, which is often not documented, seldom used by non-hematologists, and does not facilitate comparisons to solid-organ malignancy staging [1]. Some studies [20, 21] use the World Health Organization's broader definition of palliation, which includes approaches to improving quality of life for patients and their families and includes treating both physical and spiritual problems. [3] As ours is one of the few studies that included palliative consultations for patients managed with and without surgery, we had to create our own definition of surgical palliative evaluation based on commonly accepted definitions [17, 18].

Recent studies have recognized the importance of quality of life and symptom improvement in palliative surgery, however, these studies focused only on patients who underwent surgery [11, 18, 20, 21]. The largest study of palliative procedures for advanced cancer found short-term symptom improvement in 80% of patients, recurrence of the symptoms in 25%, and development of new symptoms requiring treatment within 2 months postoperatively in 29% [18]. A smaller study of patients who underwent palliative surgery reported considerable symptom improvement but little change in quality of life [20]. These studies' findings emphasize the importance of patient selection for palliative

Table 6 Multivariate analysis of variables associated with overall survival

Variable[a]	HR	95% CI	*P* value
Imaging extent of disease			
Carcinomatosis/sarcomatosis	1.35	1.09–1.68	0.007
Number of disease sites on imaging			
1	Referent	Referent	Referent
2	1.43	1.11–1.84	0.005
≥3	1.35	1.01–1.80	0.04

HR hazard ratio, *CI* confidence interval

[a] Solid organ and hematologic malignancy, symptom complex, neutropenia, and ascites on imaging were not significant on multivariate analysis

surgery and the need to identify factors predicting a poor surgical outcome and short survival in this challenging patient population. Although our study did not examine symptom relief and durability of palliation, it is one of the few studies that examines outcomes for operative and non-operative patients by utilizing the common denominator of patients requiring inpatient surgical oncology evaluation. In this regard, we examined the factors associated with undergoing surgical intervention as well as predictors of OS. Prognostication is a difficult but critical aspect of the risk–benefit analysis for palliative surgery [7, 17].

Perioperative mortality rates associated with palliative surgical interventions have ranged from 0% in smaller studies of select patient subgroups to as high as 21% for patients who underwent surgery for malignant bowel obstruction [11, 21]. The largest study [18] reported in 2004 found a mortality rate of 11%, which is consistent with many other reports of palliative surgery [6, 9, 18, 22]. Although a higher mortality rate might be expected for an inpatient population, we found a 90-day surgical mortality rate (7%) similar to those of the aforementioned studies. Morbidity rates remain significant, and our study is similar to other studies in this regard as well [16, 18]. We have included a severity scale similar to the scale used in other reports to allow for more accurate comparison [18]. Although much of the consideration for palliative surgery centers on expected symptom improvement, the morbidity and mortality rates remain important in consideration of surgical intervention.

Limitations of the current study included the heterogeneity of the patient population, although this largely reflects the wide spectrum of patients and diverse symptoms requiring surgical evaluation at our institution. Specific management recommendations for each clinical presentation would require subset analysis beyond the scope of this study. Future studies will be required to provide more clinically relevant indicators of management for specific symptom clusters such as malignant bowel obstruction and gastrointestinal bleeding. Furthermore, criteria for operative intervention are difficult to define retrospectively, as this was performed at the attending physician's discretion after multidisciplinary input and family/patient discussions. Future studies would also be strengthened by inclusion of a comorbidity index and performance status data. Owing to our study's retrospective design, we may not have captured all consultations and complications from surgery; however, this is a limitation of all retrospective evaluations. The next step in our research is to prospectively follow patients requiring surgical palliative evaluation with inclusion of quality of life and symptom improvement data.

In summary, this study provides data on the frequency with which inpatient surgical evaluation at a tertiary cancer hospital met the criteria for palliative care. Overall survival in this population was short; in particular, carcinomatosis/sarcomatosis and ≥2 disease sites on imaging were associated with shorter survival. The incidence rate of surgical intervention in this study reflects a multifactorial, selective approach, and many of these factors are not measurable on retrospective analysis. However, we have demonstrated that younger patients with wound complications, bowel obstruction, and an intact primary or recurrent tumor on imaging were more likely to be treated with surgical intervention. Patients with ascites were the least likely to undergo surgical intervention. On the basis of these results, we conclude that surgery can be performed with acceptable mortality in highly selected inpatients, although with considerable associated morbidity. Given that OS in this population is short, non-operative management is desirable and should be considered for patients with carcinomatosis or sarcomatosis and multiple disease sites.

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