



In Search of the Optimal Outcome Measure for Patients with Advanced Cancer and Gastrointestinal Obstruction: A Qualitative Research Study

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ABSTRACT

Background. Gastrointestinal obstruction (GIO) is the most common indication for palliative surgical consultation in patients with advanced cancer. The purpose of this study is to delineate the symptom burden and experience of these patients.

Patients and Methods. Twenty patients with advanced cancer and GIO described symptoms at time of surgical consultation. We analyzed the content of interview transcripts and ranked symptoms by frequency and according to an assessment of relevance conducted by an expert panel (surgeons, palliative care physicians, nurses, and patients/caregivers).

Results. Among the 20 study patients, malignancy types included colorectal ($n = 9$), gastric ($n = 4$), urothelial/renal ($n = 3$), and other ($n = 4$), whereas sites of obstruction were the small bowel ($n = 11$), gastric outlet ($n = 3$), and large bowel ($n = 6$). Thirteen patients (65%) had received chemotherapy within 6 weeks. Imaging evidence of a primary/recurrent tumor was documented in 13 patients (65%), carcinomatosis in 11 (55%), and ascites in 16 (80%). Thirty patient symptoms were identified on qualitative interviewing. Seven GIO-specific items were identified as relevant by the expert panel and will be added to the core symptom assessment inventory for further testing.

Conclusions. We identified symptoms of importance that can be used to assess outcome after treatment of patients with advanced cancer and GIO. Testing for validity and reliability will be required before formal survey development.

Palliative procedures account for more than 1000 procedures per year at major cancer centers and 21–25% of a surgeon's practice.^{1,2} In addition, up to 40% of all inpatient surgical consultations are palliative in nature.³ Gastrointestinal obstruction (GIO) is the most common indication for palliative surgical consultation.^{3,4} The median survival period for patients with advanced cancer and bowel obstruction is approximately 3 months, yet correction of bowel obstruction may be a patient's only chance to improve quality of life and survival.⁴

Traditional outcome measures for surgery such as morbidity and mortality do not capture the true success of palliative surgery, since the primary goal is to improve quality of life and improve symptoms.⁵ A lack of adequate outcome measures has been recognized for many years, and investigators have attempted to identify the most appropriate outcome measure to determine the optimal study design for the difficult clinical scenario of GIO in patients with advanced cancer.^{6,7}

However, no studies that psychometrically validate an instrument specifically for patients with advanced malignancy and GIO have been reported. Therefore, the purpose of this study is to delineate the symptom burden and experience of patients with advanced malignancy and GIO. In addition, we seek to establish content validity for a GIO-specific survey by expert panel rating.

PATIENTS AND METHODS

The study consisted of two consecutive projects to develop a GIO-specific module of the MD Anderson Symptom Inventory (MDASI), a psychometrically validated instrument measuring symptom burden. The MDASI Core assesses the severity and interference with daily activities of common symptoms of cancer and treatment with 13 symptom severity items and 6 interference items rated on a 0-to-10 scale, with 0 meaning no symptom or interference and 10 meaning severity as bad as can be imagined or complete interference. The symptom interference items consist of two three-item subscales: affective interference [relations with others, enjoyment of life, and mood (REM)] and physical interference [work, general activity, and walking (WAW)]. The MDASI provides a standard format for items to ask patients to rate symptoms at their worst or according to their degree of interference in the last 24 h. The MDASI Core was validated in a sample of 527 patients with a variety of cancers who were receiving different treatments. The symptom and interference items of the MDASI Core are broadly applicable to all patients with cancer.⁸ Modules of the MDASI then add symptom items to the MDASI Core that are specific for a particular disease and/or treatment.

Project 1 of this study generated potential symptom items specific to patients with advanced cancer and GIO from qualitative interviews. Project 2 reduced the number of potential symptom items to be added to the MDASI Core on the basis of an expert panel review to identify items most relevant to patients, caregivers, and healthcare professionals. The study was approved by the MD Anderson Cancer Center Institutional Review Board, and written informed consent was obtained from each participant.

Eligibility criteria included age 18 years or older, ability to read and speak English, clinical diagnosis of GIO, and consultation requested for surgical evaluation for GIO. Sociodemographic data collected from patients included age, gender, race, marital status, years of education, and employment status. Disease-related and treatment-related data included information about the patients' underlying disease, previous cancer treatment, occurrence of GIO, treatment for GIO, and comorbidities.

Project 1

The initial sample size was set at 20 patients with advanced cancer who were admitted to MD Anderson Cancer Center for surgical evaluation of cancer-related GIO. The final sample size was determined by saturation, with interviews continuing until no new symptom information was found in three consecutive participants.⁹ The

interview transcripts were reviewed, and quotes from the participants that described symptoms and symptom experience were identified by an expert in qualitative research (L.W.). The symptom items were reviewed by two researchers (B.B. and L.W.) to determine final symptoms and symptom names. A list of symptom items was developed for expert panel review. Themes were developed to describe aspects of the symptom experience.¹⁰ Synthesis was carried out to separate and group the themes to address the core elements of GIO symptom burden. The core elements were used to construct a unified description of the symptom burden of GIO, which will serve as the content domain for the MDASI-GIO questionnaire.

Project 2

A panel of 18 experts (4 surgeons, 4 palliative care physicians, 4 nurses experienced in the care of patients with GIO, 3 patients with GIO, and 3 caregivers) were identified to rate the relevance of the list of symptom items to GIO.¹¹ Eligibility criteria for expert panel participants included healthcare professionals with at least 5 years of experience caring for patients with advanced cancer and GIO, patients with a clinical diagnosis of advanced cancer and GIO, or primary family caregivers of these patients. A questionnaire, modeled after other MDASI module development procedures, was used to rate each item on a four-point ordinal scale.¹² Items were ranked from 1 (the item is irrelevant to patients with GIO) to 4 (the item is extremely relevant to patients with GIO). Mean ratings of the entire panel as well as mean ratings for each group of experts were calculated. Items receiving a mean rating of ≥ 3 (relevant to very relevant) were retained for psychometric testing. Symptoms mentioned by $\geq 20\%$ of participants in qualitative interviews, as well as the 13 MDASI Core symptoms, were also retained for testing.

RESULTS

Project 1

Saturation was reached with the first 20 interviews. Demographic and clinical data for the interview participants are presented in Table 1. Among the 20 studied patients, malignancy types included colorectal ($n = 9$), gastric ($n = 4$), urothelial/renal ($n = 3$), and other ($n = 4$), whereas sites of obstruction were the small bowel ($n = 11$), gastric outlet ($n = 3$), and large bowel ($n = 6$). Thirteen patients had received chemotherapy within 6 weeks. Imaging evidence of a primary/recurrent tumor was documented in 13 patients, carcinomatosis in 11, and ascites in 16.

TABLE 1 Clinicodemographic variables for 20 patients included in qualitative interviews to identify potential symptom items for a gastrointestinal obstruction-specific module

Variable	N (%)
Median age (range)	58 (41–77) years
Gender	
Male	11 (58%)
Female	9 (42%)
Race/ethnicity	
White	16 (80%)
Black	1 (5%)
Hispanic	0
Asian	2 (10%)
Native American	1 (5%)
Highest grade of education	
≤ 12	3 (15%)
13–16	9 (45%)
≥ 17	8 (40%)
Tumor histology	
Colorectal	9 (45%)
Other	11 (55%)
Obstruction site	
Gastric outlet	3 (15%)
Small bowel	11 (55%)
Large bowel	6 (30%)
Chemotherapy within 6 weeks	13 (65%)
Imaging evidence of primary/recurrent tumor	13 (65%)
Imaging evidence of ascites	16 (80%)
Imaging evidence of carcinomatosis	11 (55%)
Imaging evidence of liver/lung metastases	7 (35%)
ECOG performance status	
0–2	9 (45%)
3–4	11 (55%)
White blood cell count	
≤ 11	16 (80%)
> 11	4 (20%)
Hemoglobin	
< 10	4 (20%)
≥ 10	16 (80%)
Albumin	
< 3	3 (15%)
≥ 3	17 (85%)

Twenty-seven symptoms, mostly gastrointestinal related, were identified on the initial analysis. After review, some symptom names were deemed the same symptom and combined, such as pain and abdominal pain. Other symptoms were deemed to be signs (can be known objectively) rather than symptoms, such as weight loss. Nine symptoms

were reported by more than 20% of patients: 4 MDASI Core symptoms and 5 GIO-specific symptoms (Table 2). After the symptoms were reviewed by two researchers (L.W. and B.B.), a final symptom list of 13 MDASI Core symptoms and 17 GIO-specific symptoms was selected for expert panel review. In addition, it was found that patients reported symptom interference with life activities, such as general activities, work, walking, relations with others, mood, and enjoyment of life. Patients discussed methods that could be helpful for relieving symptoms (e.g., nasogastric tube placement), as well as advice to other patients (e.g., be alert to symptom development to catch obstruction early).

Project 2

Four MDASI Core symptoms as well as seven GIO-specific symptoms received relevance ratings of ≥ 3 (Table 3). Three of the MDASI Core symptoms that received expert panel relevance ratings of ≥ 3 were also mentioned by $\geq 20\%$ of patients in the qualitative interviews. Fatigue, mentioned in interviews by 25% of patients, received an expert panel relevance rating of 2.85. Lack of appetite, mentioned by only 5% of patients in interviews, received an expert panel rating of 3.10. In addition to the 13 MDASI Core symptom items, 7 GIO-specific items (5 because they were mentioned by $\geq 20\%$ of patients and qualitative interviews and received expert panel mean relevance ratings of ≥ 3.0 and 2 because they received expert panel mean relevance ratings of ≥ 3.0 ; Table 2) were selected for psychometric testing in a draft MDASI-GIO questionnaire (results to be reported in a subsequent publication). Figure 1 shows a concept domain model for a patient-reported outcome (PRO) measure of symptom burden of cancer-related GIO.

DISCUSSION

In the present study, qualitative interviews of patients with cancer-related GIO were performed and subsequent analysis delineated the major symptoms and symptom burden of GIO in advanced malignancy. An expert panel review then identified symptoms suitable for survey validation to continue in our effort to identify a suitable outcome measure for cancer patients with this common, yet complex, condition requiring palliative surgical consultation. The concept of symptom burden—the severity and interference with daily activities of symptoms of disease and treatment—was found to be relevant to patients with cancer-related GIO. Seven of the GIO-

TABLE 2 Symptoms of patients with advanced cancer and gastrointestinal obstruction with, percentage mentioned in qualitative interviews and expert panel ratings

Symptom items	Percent in qualitative interviews (%)	Expert panel rating	Reason for selection
Pain	80	3.70	MDASI Core, interview, expert Panel
Fatigue	25	2.85	MDASI Core, interview
Nausea	45	3.65	MDASI Core, interview, expert panel
Disturbed sleep	5	2.50	MDASI Core
Distress	0	2.65	MDASI Core
Shortness of breath	0	2.10	MDASI Core
Trouble remembering	0	1.40	MDASI Core
Lack of appetite	5	3.10	MDASI Core, expert panel
Feeling drowsy	0	1.95	MDASI Core
Dry mouth	5	2.50	MDASI Core
Feeling sad	0	2.15	MDASI Core
Vomiting	65	3.75	MDASI Core, interview, expert panel
Numbness or tingling	0	1.40	MDASI Core
Abdominal cramping	30	3.75	Interview, expert panel
Unable to have a bowel movement	30	3.55	Interview, expert panel
Feeling bloated	60	3.5	Interview, expert panel
Abdominal discomfort	45	3.45	Interview, expert panel
Being unable to eat	30	3.4	Interview, expert panel
Constipation	15	3.4	Expert panel
Stomach feeling full	5	3.3	Expert panel
Change in your stool	10	2.85	Not selected
Indigestion	5	2.75	Not selected
GI tract feeling dead	5	2.70	Not selected
General weakness	10	2.50	Not selected
Feeling hungry	10	2.45	Not selected
Stomach growling	10	2.40	Not selected
Confusion	5	1.95	Not selected
Dizziness	5	1.80	Not selected
Trouble paying attention	5	1.80	Not selected
Headache	5	1.40	Not selected

specific symptoms will be considered for further psychometric testing in a larger sample of patients with cancer-related GIO.

The data from this study have expanded upon our previous work in investigating patient reasoning behind choosing palliative surgical intervention and identifying PRO measures.^{13,14} Among the 98 patients who participated in palliative surgical consultations in our previous study, most selected their treatment based on a desire to improve symptoms, with less-common reasons including a desire to follow a doctor's recommendation, to improve length of life, and to allow for additional oncologic treatment.¹³ Our following study expanded on this work, seeking to determine whether an open-ended questionnaire administered during palliative surgical consultation

captured the severe symptoms in cancer patients that a structured validated quality-of-life assessment does not capture.¹⁴ The open-ended questionnaire captured 68 instances of severe symptoms in 47 patients that the global quality-of-life measure did not, which formed the basis for our desire to create a new psychometrically validated module. We intentionally limited the length of the interviews and survey administration in these previous studies to minimize the burden on patients with GIO; therefore, these studies were limited in their ability to delineate symptom burden; this limitation is addressed in our current study.

Relatively few qualitative studies of patients undergoing palliative surgical consultation have been conducted. In an early study, Ferrell et al. performed qualitative interviews

TABLE 3 Symptom themes, with example comments, that received relevance ratings of ≥ 3 by expert panel review

Symptom themes	Example comment
Vomiting	“Physically it was distressing because I was not able to keep any—I was not able to keep any food down. As soon as my stomach reached a certain point, I vomited. So the vomiting was distressing.” <i>77-year-old male</i>
Abdominal cramping	“It’s intense cramps, basically with the effect that you don’t eat, which makes you weaker. Most cramps come at night, so you get very tired. ... The whole process wears you out.” <i>55-year-old male</i>
Pain	“The pain probably started here (points to lower abdomen) and just gradually goes along. And it gets to a point that it’s maxed out. So I get sick, and the pain can be very, very, very, very, very painful. It consists of like being stuck with a knife or a pin, and at times it just goes on and on. Sometimes it’s just like electronic pins and everything.” <i>67-year-old male</i>
Nausea	“I just feel very, very uncomfortable with reference to just any second now I’m going to blow up or throw up. The vomit feeling is just constantly there—a horrible experience.” <i>70-year-old male</i>
Bowel movement	“I couldn’t go to the restroom nor could I pass gas. And I wanted to do both, but I could not.” <i>42-year-old female</i>
Feeling bloated	“A very, very full, full feeling. I can only describe it as you feel like you’re pregnant. You swallowed a basketball. ... I feel like I’m going to pop sometimes.” <i>50-year-old female</i>
Discomfort	“There is some sort of mild discomfort, but all in all, it hasn’t been that painful.” <i>51-year-old male</i>
Unable to eat	“I guess not eating, not having the ability to eat. Nothing has stayed in my stomach, although I am starving. I am very, very hungry. The minute I put a bite of hamburger in my mouth, everything freezes. No more ... Although my hunger is there, I’m very hungry, I’m not able to put anything in my stomach for fear of my stomach exploding—with the fear of my stomach just blowing up.” <i>70-year-old male</i>
Constipation	“I’ve had some problems with constipation. ... Actually just a couple of days, because I actually had a bowel movement that day. I had two, but they were very small and loose. But it had only been a couple of days, I think two days, without a bowel movement.” <i>53-year-old female</i>
Stomach feeling full	“I felt like my belly was very full. And it was just juggling around. Like I could hear it gurgling and everything, like I had a bunch of junk in there.” <i>53-year-old female</i>
Lack of appetite	“(I’m having) loss of appetite, loss of energy, loss of weight.” <i>77-year-old male</i>

of patients and surgeons before palliative surgery to identify issues of greatest concern during decision-making.¹⁵ The study findings indicate that the physical impact of uncontrolled symptoms was the primary motivation to consider surgery; in addition, they highlighted the necessity of identifying symptoms of importance in patients with bowel obstruction as a surgical outcome. A more recent qualitative study of patients who had undergone percutaneous venting gastrostomy tube placement for malignant bowel obstruction found a similar experience of high symptom burden that can be challenging to palliate.¹⁶ Although this study did not include patients evaluated for surgery, the patient experience had some overlap with our study regarding frequency of nausea, vomiting, and pain.¹⁶ These previous studies, along with our study, highlight the importance of the patient experience in identifying areas for service improvement, in improving patient selection, and in obtaining the best possible outcome for the patient that is consistent with the patient’s preferences.

Only a few qualitative studies have identified symptoms and issues of importance in malignant bowel obstruction, and even fewer studies have validated quality-of-life metrics. In a large contemporary systematic review of outcomes after palliative surgery for malignant bowel obstruction, validated quality-of-life outcomes and

measures of patient distress were not reported by any studies.¹⁷ For specific conditions such as gastric outlet obstruction and gastric cancer-related symptoms, investigators have used specific European Organization for Research and Treatment of Cancer instruments, although it is unclear whether instruments validated in the general oncology population are appropriate for high symptom burden conditions such as gastrointestinal obstruction.¹⁸ Similarly, the Edmonton Symptom Assessment Scale and Rotterdam Symptom Checklist have been used to describe the natural history of malignant obstructions, with recognition that future studies should address activity and interference with function.¹⁹

With respect to the potential implications of our study results, our study should be best viewed as focusing on the first two steps of a three-step process of validating a PRO measure that can be useful in research and in practice. Patient-reported outcome is a general term applied to outcomes reported by patients based on their perceptions of a disease and its treatments, without interpretation of that perception by clinicians or others.²⁰ The accepted standard for the development of PROs is to begin with qualitative interviews of patients to determine the content domain of the questionnaire and generate items.^{20–22} This is followed by an expert panel that rates the relevance of the findings of

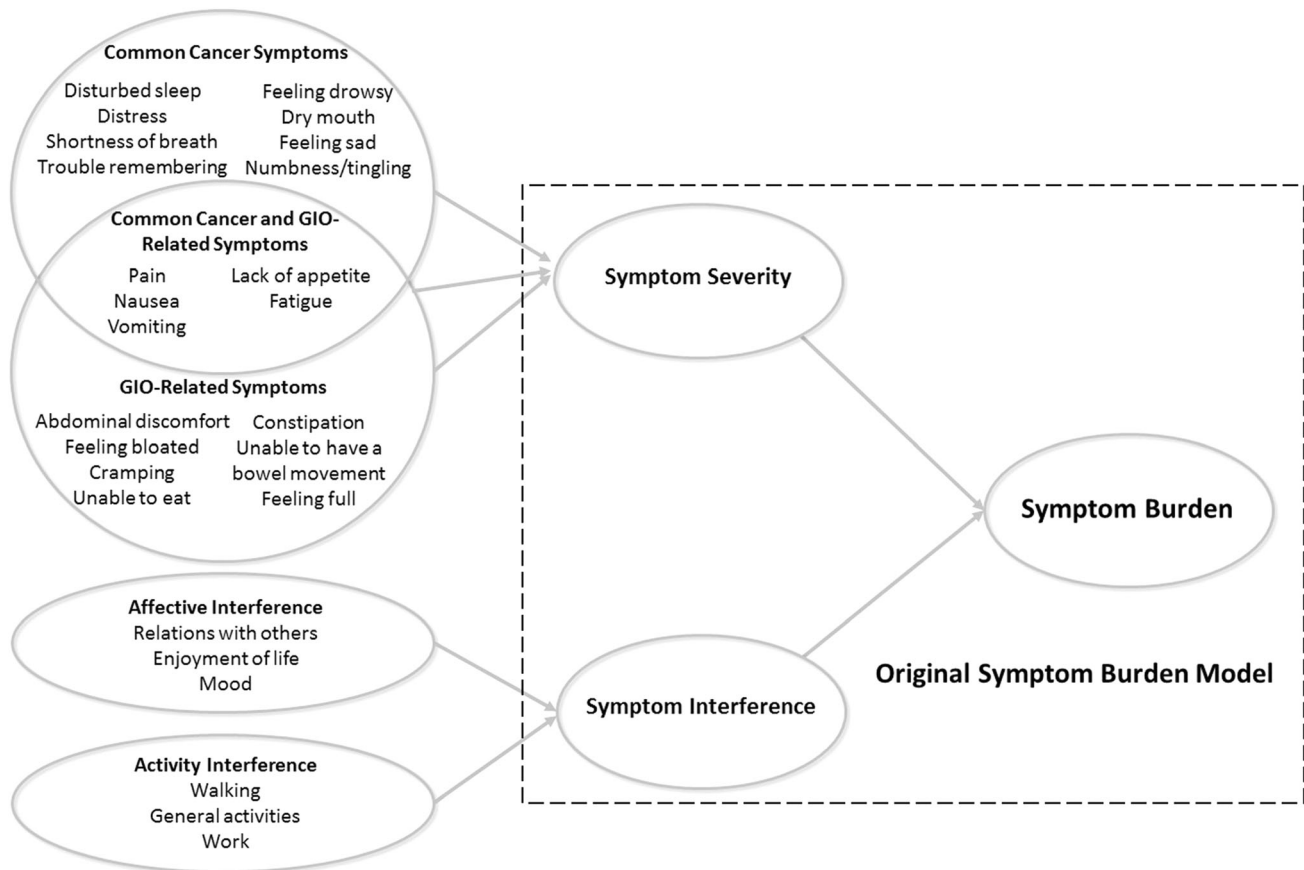


FIG. 1 Concept domain model for a patient-reported outcome measure of symptom burden of cancer-related gastrointestinal obstruction

the qualitative interviews to reduce the content of the questionnaire to what is most significant.^{20,21} The final step in the process is cognitive debriefing and psychometric validation of the questionnaire.^{20,21} Our purpose in the present study is to describe the steps of content domain specification, item generation, and content reduction for the MDASI-GIO questionnaire.

Once a validated tool is available, the next potential step is to identify predictors of outcome and optimal management. The ability of this tool to influence patient and family decisions should proceed naturally once we are able to inform physicians of their outcomes. In addition, the MDASI-GIO could be used for comparative effectiveness studies and quality assessment. Long-term, once armed with a validated symptom assessment survey to determine the success of surgery, we plan to conduct a multidimensional assessment to develop guidelines for the treatment of patients with advanced cancer and GIO. We are also planning a consensus panel exercise to identify an even smaller survey that could be administered in under a minute. For research purposes, the use of a validated questionnaire that allows comparison across groups is

useful, but in a clinical setting, a shorter questionnaire targeting only GIO-specific symptoms may be more beneficial.

In summary, we were motivated to identify the optimal outcome measure in GIO by the almost complete lack of qualitative research in patients with malignant bowel obstruction and the lack of an accepted symptom survey in this challenging, yet frequently encountered, patient population with a high symptom burden. We developed a validated concept domain for a PRO measure of cancer-related GIO. We intend to evaluate this measure psychometrically in a sample of patients with advanced cancer and GIO to develop a brief, valid, and reliable measure of the symptom burden of cancer-related GIO.

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