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ORIGINAL ARTICLE – HEALTH SERVICES RESEARCH AND GLOBAL ONCOLOGY

Palliative Care and Symptom Burden in the Last Year of Life: A Population-Based Study of Patients with Gastrointestinal Cancer

Shaila J. Merchant, MSc, MHSc, MD, FRCSC, FACS[1,8], Susan B. Brogly, PhD[1], Christopher M. Booth, MD[2], Craig Goldie, MD[3], Sulaiman Nanji, MD, PhD[1,8], Sunil V. Patel, MSc, MD[1,8], Katherine Lajkosz, MSc[4], and Nancy N. Baxter, MD, PhD[5,6,7]

[1]Department of Surgery, Queen's University, Kingston, ON, Canada; [2]Division of Cancer Care and Epidemiology, Queen's Cancer Research Institute, Kingston, ON, Canada; [3]Division of Palliative Care, Queen's University, Kingston, ON, Canada; [4]Institute for Clinical Evaluative Sciences, Queen's University, Kingston, ON, Canada; [5]Department of Surgery, Li Ka Shing Knowledge Institute, St. Michael's Hospital, Toronto, ON, Canada; [6]Department of Surgery, University of Toronto, Toronto, ON, Canada; [7]Institute for Clinical Evaluative Sciences, University of Toronto, Toronto, ON, Canada; [8]Division of General Surgery and Surgical Oncology, Kingston Health Sciences Centre, Kingston, ON, Canada

ABSTRACT

Introduction. The symptom profile in cancer patients and the association between palliative care (PC) and symptoms has not been studied in the general population. We addressed these gaps in gastrointestinal (GI) cancer patients in the final year of life.

Methods. Patients dying of esophageal, gastric, colon, and anorectal cancers during 2003–2015 were identified. Symptom scores were recorded in the year before death using the Edmonton Symptom Assessment System (ESAS), which includes scores from 0 to 10 in nine domains. Symptom severity was categorized as none–mild ($\leq$ 3) or moderate–severe ($\geq$ 4–10). Adjusted associations between outpatient PC and moderate–severe ESAS scores were determined, and the effect of PC initiation on ESAS scores was estimated.

Results. The cohort included 11,242 patients who died (esophageal [17%], gastric [20%], colon [38%], and anorectal [26%] cancers). Fifty percent experienced moderate–severe scores in tiredness, lack of well-being, and lack of appetite earlier (weeks 18 to 12 before death), whereas 50% experienced moderate–severe scores in drowsiness, pain, and shortness of breath later (weeks 5 to 2 before death) in the disease course. Outpatient PC was associated with an increased likelihood of moderate–severe scores in all domains, with the highest score in pain (odds ratio [OR] 1.86, 95% confidence interval [CI] 1.68–2.05). In PC-naïve patients with moderate–severe scores, initiation of outpatient PC was associated with a 1- to 3-point decrease in subsequent scores, with the greatest reductions in pain (OR − 1.91, 95% CI − 2.11 to − 1.70) and nausea (OR − 3.01, 95% CI − 3.31 to − 2.71).

Conclusion. GI cancer patients experience high symptom burden in the final year of life. Outpatient PC initiation is associated with a decrease in symptoms.

Managing symptoms during the cancer disease trajectory is critical, particularly near the end of life when symptom burden escalates.[1] Patients with cancer report a variety of symptoms throughout the disease process, with the nature and severity of symptoms depending on type of cancer[2,3] and proximity to death.[1] Uncontrolled symptoms

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S. J. Merchant, MSc, MHSc, MD, FRCSC, FACS
e-mail: merchant.shaila@gmail.com;
shaila.merchant@kingstonhsc.ca

often lead to patient and caregiver distress[4,5] and contribute to increased healthcare utilization, such as inpatient hospitalization[6] and emergency department visits.[7]

To address cancer-related symptoms, care providers require accurate and reliable methods to identify such symptoms. The Edmonton Symptom Assessment System (ESAS) is a reliable and validated symptom screening tool that is available in several languages[8] and has been used widely in cancer patients.[9,10] In Ontario, Canada's most populous province, the ESAS was implemented at all regional cancer centers in 2006 as part of the Provincial Palliative Care Integration Project.[11] This tool allows patient reporting of symptoms directly to clinicians while in hospitals, clinics, or from home.[11] Despite these initiatives, whether clinical action reduces symptom scores is unknown.[12]

Patients with gastrointestinal (GI) cancer have high symptom burden[6] and health care utilization at the end of life, including hospitalization and subsequent death in hospital.[13] We previously reported a high incidence of hospitalization and emergency department visits in patients with GI cancer,[14] and that palliative care (PC) was associated with a reduction in these elements of potentially aggressive care;[15] however, patient symptomatology as a contributing factor to such trends in potentially aggressive end-of-life care has not been studied. Furthermore, the symptom profile in patients with cancer at the end of life is not well defined. We therefore sought to (1) describe the symptom profile and (2) determine the effect of outpatient PC initiation on symptom burden in patients with GI cancer in the final year of life.

METHODS

Patient Cohort

We conducted a population-based study of patients in Ontario, Canada, who died of an alimentary canal GI cancer between 1 January 2003 and 31 December 2015, and who also had at least one ESAS score recorded in the final year of life. Ontario has a population of approximately 14 million and a universal health care system, which covers most health care services (i.e. physician visits, inpatient hospitalizations and procedures), but does not comprehensively cover all medications and supportive services such as home care. Cases with a primary cause of death from esophageal, gastric, colon, and anorectal cancer recorded in the Ontario Cancer Registry (OCR) were included in the study cohort. Diagnoses of esophageal (C15, C150–155, C158–159), gastric (C16, C160–166, C168–169), colon (C18, C180–190), and anorectal (C20, C21, C210–212, C218) cancers were derived from the International Classification of Diseases, Tenth Revision (ICD-10) codes.

Patients were excluded if they had multiple cancer diagnoses, non-GI cancer diagnoses, died within 30 days of cancer diagnosis, were younger than 18 years of age at death, were not residents of Ontario at the time of death, did not have a valid Ontario provincial health card number, or did not have an ESAS assessment recorded in the last year of life (Fig. 1). This study was approved by the Health Sciences Research Ethics Board, Queen's University, Kingston, ON, Canada.

Administrative Health Care Databases

We used the linked administrative healthcare databases for Ontario, available through the Institute for Clinical Evaluative Sciences (ICES). The Canadian Institute for Health Information (CIHI) Discharge Abstract Database (DAD) contains information on Ontario patients discharged from hospital, and the Ontario Health Insurance Plan (OHIP) database holds physician billing claims for services, including procedure and consultation visits. The OCR includes information on all incident cancers diagnosed since 1964.[16] The Vital Statistics Registry (VSR) provides information regarding the date and cause of death. All data sets were held securely at the ICES.

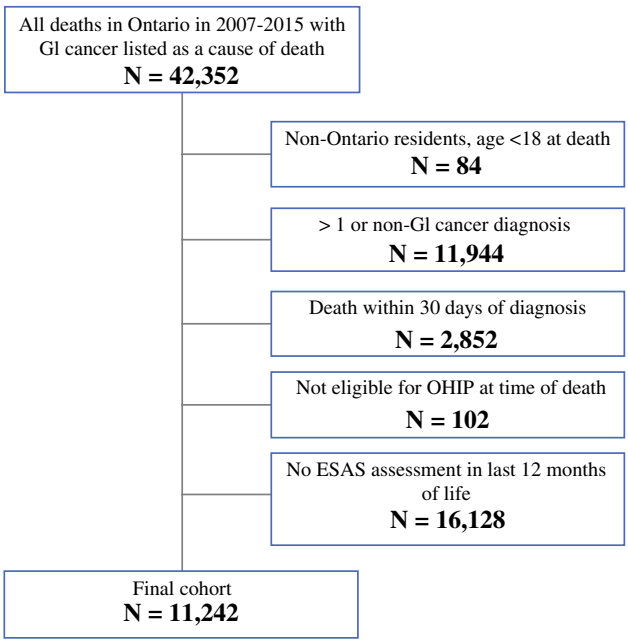

FIG. 1 Selection of the study cohort. *GI* gastrointestinal, *OHIP* Ontario health insurance plan, *ESAS* edmonton symptom assessment system

Edmonton Symptom Assessment System (ESAS)

The ESAS is a validated symptom screening tool[10] that was developed to assist health care providers in the assessment of nine symptoms that are common in PC patients, including pain, tiredness, drowsiness, nausea, lack of appetite, depression, anxiety, shortness of breath, and lack of well-being. Symptoms are measured on a scale from 0 (lowest) to 10 (highest).[9] Scores are commonly assigned to the following categories: no symptoms (score 0), mild symptoms (score 1–3), moderate symptoms (score 4–6), and severe symptoms (score 7–10)[17,18] and may be combined to determine a total symptom distress (TSD) score.[9,19] We followed this approach in our study.

ESAS data are available in ICES from January 2007 onwards as Cancer Care Ontario launched the Provincial Palliative Care Integration Project in 2006.[11] Most assessments occur in ambulatory patients presenting to a regional cancer center. All patients with GI cancer with at least one record of an ESAS assessment in the final year of life were included. When patients had multiple assessments performed in 1 week, the assessment with the highest score in any individual domain was included. Because of the opportunistic nature of the screening tool, some patients were counted multiple times. Individual domain scores and TSD scores were recorded. Individual domain scores were largely complete ($> 99.5\%$). Those with missing data were excluded.

Outpatient Palliative Care (PC)

The primary exposure was outpatient PC as most patients with ESAS assessments were seen in an outpatient setting. Outpatient PC services were identified with OHIP codes A945 and K023 (outpatient location). These codes were extensively discussed and vetted by two physician authors (CG and SM). All outpatient PC records from the time of cancer diagnosis were included.

Covariates

Patient and clinical factors at the time of first recorded ESAS assessment were used as covariates. These included patient age, sex, cancer site, comorbidity, socioeconomic marginalization, and location of residence. Other variables measured were time between cancer diagnosis and death, receipt of chemotherapy and radiotherapy in the final year of life, and location and number of ESAS assessments.

Age was categorized (< 50, 50–64, 65–80, > 81 years). Comorbidity was determined using the Charlson Comorbidity Index with Deyo modification, with a 12-month look-back period.[20] Socioeconomic deprivation was measured in quintiles using the Ontario Marginalization Index (ON-Marg), a tool derived from census data that illustrates levels of marginalization across geographic units in the province.[21] Patients in the highest quintile represent the most deprived. Residence was defined as either rural (community size $< 10{,}000$) or urban. Time from cancer diagnosis to death was categorized (< 6 months, 6 months–1 year, >1 year–3 years, > 3–5 years, > 5 years). Receipt of chemotherapy (G075, G281, G381, G345, G359, G382, G388, G390) and radiotherapy (X310, X311, X312, X313) in the final year of life was identified from OHIP codes. The location (clinic vs. other location) and number of ESAS assessments were recorded.

Statistical Analyses

Descriptive frequencies and symptom profiles are reported. In a cross-sectional study, logistic regression[22] was used to determine associations between PC (exposure) and moderate–severe symptom scores (outcome) in unadjusted and covariate-adjusted models. Univariate associations were reported for each ESAS score dichotomized as none–mild or moderate–severe, and models were then adjusted for patient and clinical factors (receipt of PC, age, sex, cancer site, comorbidity, socioeconomic marginalization, location of residence, time between cancer diagnosis and death, receipt of chemotherapy and radiotherapy in the final year of life).

PC-naïve patients who had ESAS scores prior to and following PC initiation were included in a prospective cohort to estimate the effect of PC initiation on symptom scores. The pre-PC ESAS score was the closest score immediately preceding the PC visit, while the post-PC ESAS score was the first score immediately following the PC visit. We excluded post-PC ESAS scores occurring < 7 days after the date of the PC visit, with the assumption that the intervention would require a week or more to influence symptom scores. Generalized estimating equation (GEE) analyses[23] accounting for repeated measures were used to estimate the effect of PC initiation on symptom scores. Models were stratified on pre-PC ESAS severity (none–mild or moderate–severe). In addition to the aforementioned covariates adjusted for in the logistic models, we also adjusted for year of first PC record, week of ESAS assessment prior to death, and receipt of chemotherapy and or radiotherapy (up to and including 30 days prior to pre-PC ESAS, and up to and including the day of post-PC ESAS). Because the number and timing of ESAS assessments varied among patients, we adjusted for the number of days between ESAS assessment and PC initiation, and between PC initiation and the subsequent ESAS assessment.

In sensitivity analyses, we repeated the GEE analyses excluding patients in the last 8 weeks of life since

symptom scores escalated dramatically near the end of life. We also performed the analyses stratifying the pre-PC symptom severity into low, moderate, and severe categories. All statistical analyses were completed using SAS version 9.3 (SAS Institute, Inc., Cary, NC, USA) at the ICES, Queen's University.

RESULTS

Characteristics of the Cohort

The cohort included 11,242 patients who died (esophageal [17%], gastric [20%], colon [38%], and anorectal [26%] cancers). Mean age was 67.0 years, 63% were male, and 86% resided in an urban location. Sixty-five percent and 43% received chemotherapy and radiotherapy, respectively, in the last year of life. The majority (98%) of ESAS assessments were performed in an outpatient clinic setting, with the remainder occurring at home (1%) and over the telephone (0.6%). Almost one-quarter (24%) of patients had 10 or more assessments.

Patients with at least one ESAS score in the final year of life were compared with those with no recorded ESAS score (n = 16,128) [Table 1]. Patients with an ESAS score were younger (67 vs. 74 years, $p < 0.001$) and had a significantly higher Charlson Comorbidity Index (43% vs. 18% with 2 +, $p < 0.001$). Fewer patients with an ESAS score died within 6 months of diagnosis (19% vs. 32%, $p < 0.001$). More patients with an ESAS score received chemotherapy (65% vs. 28%, $p < 0.001$) and radiotherapy (43% vs. 17%, $p < 0.001$) in the final year of life compared with those without an ESAS score.

Individual Domain and Total Symptom Distress Scores

A total of 68,590 ESAS assessments were performed on 11,242 patients in the final year of life. The ESAS assessment was 48 weeks before death for 25% of patients, 33 weeks for 50% of patients, 16 weeks for 75% of patients, and 8 weeks for 90% of patients. The symptom profile of the cohort by individual domain and TSD score is shown in Fig. 2a, b, respectively. Individual domain and TSD scores escalated near the end of life. There were no statistically significant differences in the mean TSD scores between males and females.

The proportion of patients with at least one moderate–severe score ($\geq$ 4) in any individual domain was examined (electronic supplementary Fig. 1). Fifty percent experienced moderate–severe scores in tiredness, well-being, and appetite earlier (weeks 18 to 12 before death), whereas 50% experienced moderate–severe scores in drowsiness, pain, and shortness of breath later (weeks 5 to 2 before death) in the disease course. Moderate–severe scores in anxiety, depression, and nausea were experienced by fewer patients.

Outpatient PC

Most patients received outpatient PC after cancer diagnosis (n = 8725, 78%), while the remainder (n = 2517, 22%) had no recorded outpatient PC. Of those who received PC, 5827 (52%) received their first PC in the final year of life.

Association between PC and Moderate–Severe ESAS Scores

Associations between PC and moderate–severe scores in any domain in the last year of life were examined in unadjusted and adjusted models (Table 2). Receipt of PC was associated with higher odds of having moderate–severe scores in all ESAS domains, with the greatest scores in pain (odds ratio [OR] 1.86, 95% confidence interval [CI] 1.68–2.05).

Effect of Outpatient PC Initiation on ESAS Scores

The effect of outpatient PC on ESAS scores stratified by score severity is summarized in Fig. 3. Those with post-PC ESAS scores occurring < 7 days after the PC visit were excluded from the analyses (n = 135). In adjusted analysis, all patients experienced statistically significant decreased scores in anxiety (OR − 0.24, 95% CI − 0.37 to − 0.12), nausea (OR − 0.24, 95% CI − 0.36 to − 0.11), pain (OR − 0.26, 95% CI − 0.40 to − 0.12), and lack of well-being (OR − 0.16, 95% CI − 0.30 to − 0.03) after first PC. When examined by severity, patients with a low pre-PC domain score experienced a statistically significant increase in all score domains after first PC. Those with moderate–severe pre-PC domain scores experienced a statistically significant decrease of from 1 to 3 points in all score domains after first PC. The greatest reductions in score were in pain (OR − 1.91, 95% CI − 2.11 to − 1.70) and nausea (OR − 3.01, 95% CI − 3.31 to − 2.71).

Sensitivity Analysis

An adjusted GEE analysis estimating the effect of outpatient PC on symptom scores was performed, excluding patients with post-PC ESAS scores in the last 8 weeks of life. In this cohort (n = 1423) results were similar to those of our primary analysis in that PC significantly decreased symptom scores in all domains by 1–3 points in patients with moderate–severe scores (data not shown). When pre-

TABLE 1 Demographic, clinical, and disease characteristics of the cohort

Characteristic	ESAS assessment [n = 11,242]	No ESAS assessment [n = 16,128]	p-value
Age (years)			
Mean ± SD	67.03 ± 12.58	74.27 ± 12.90	< 0.001
Median (IQR)	68 (58–77)	77 (66–84)	< 0.001
< 50	1001 (8.9)	725 (4.5)	< 0.001
50–64	3679 (32.7)	2907 (18.0)	
65–80	4860 (43.2)	6474 (40.1)	
> 81	1702 (15.1)	6022 (37.3)	
Sex			
Female	4114 (36.6)	6938 (43.0)	< 0.001
Male	7128 (63.4)	9190 (57.0)	
Cancer site			
Colon	4263 (37.9)	7426 (46.0)	< 0.001
Esophageal	1875 (16.7)	1516 (9.4)	
Gastric	2230 (19.8)	3058 (19.0)	
Anorectal	2874 (25.6)	4128 (25.6)	
Charlson comorbidity index			
0–1	6410 (57.0)	13,236 (82.1)	< 0.001
2+	4832 (43.0%)	2892 (17.9)	
Marginalization quintile			
Unknown	73 (0.6)	215 (1.3)	< 0.001
1 (least deprived)	2170 (19.3)	2439 (15.1)	
2	2246 (20.0)	2798 (17.3)	
3	2327 (20.7)	3185 (19.7)	
4	2205 (19.6)	3583 (22.2)	
5 (most deprived)	2221 (19.8)	3908 (24.2)	
Patient residence			
Urban	9614 (85.5)	13,903 (86.2)	0.032
Rural	1627 (14.5)	2216 (13.7)	
Time between diagnosis and death			
< 6 months	2095 (18.6)	5232 (32.4)	< 0.001
6 months–1 year	2251 (20.0)	2111 (13.1)	
> 1–3 years	4252 (37.8)	4208 (26.1)	
> 3–5 years	1437 (12.8)	1753 (10.9)	
> 5 years	1207 (10.7)	2824 (17.5)	
Any chemotherapy in the final year of life	7341 (65.3)	4474 (27.7)	< 0.001
Any radiotherapy in the final year of life	4837 (43.0)	2664 (16.5)	< 0.001
ESAS assessment location			
Clinic	11,029 (98.1)		
Clinic–home	11 (0.1)		
Home	135 (1.2)		
Telephone	63 (0.6)		
Number of ESAS assessments in the final year of life			
1	2378 (21.2)		
2	1481 (13.2)		
3	1128 (10.0)		
4	849 (7.6)		
5	703 (6.3)		
6	600 (5.3)		
7	521 (4.6)		

TABLE 1 continued

Characteristic	ESAS assessment [n = 11,242]	No ESAS assessment [n = 16,128]	p-value
8	454 (4.0)		
9	396 (3.5)		
10 +	2732 (24.3)		

For patients with an ESAS assessment [n = 11,242] data are reported at the time of the first assessment in the final year of life. For patients without an ESAS assessment [n = 16,128] data are reported at 1 year before death, unless otherwise specified

Data are expressed as n(%) unless otherwise specified

ESAS edmonton symptom assessment system, *SD* standard deviation, *IQR* interquartile range

PC scores were stratified separately by moderate and severe, those with severe scores experienced the most dramatic score reductions after first PC (by 2–4.5 points, data not shown).

DISCUSSION

Patients with cancer experience escalation in symptomatology at the end of life; however, the type of symptom and timing of escalation relies heavily on cancer type and proximity to death.[1,24] We have defined the symptom profile in the final year of life in patients with GI cancer.

We report that patients with GI cancer with any ESAS assessment in the last year of life were younger, less likely to die within 6 months of cancer diagnosis, and more likely to receive cancer-directed therapies such as chemotherapy and radiation in the final year of life than patients without an ESAS assessment. Overall, these findings support that those who have ESAS assessments are well enough to present for outpatient assessment and be offered cancer-directed therapies compared with those without an ESAS assessment, who are likely sicker. Furthermore, the majority of ESAS assessments captured in administrative databases are performed in an outpatient clinic setting, again supporting that these patients are well enough to present for such an encounter.

The specific features of the cohort symptom profile are important to consider. Although all individual domain symptoms escalated near the end of life, the pattern and timing of symptoms should be noted. For example, while moderate–severe symptoms in the individual domains were experienced by a substantial proportion of the cohort close to death, symptoms related to tiredness, well-being, and appetite became more severe earlier in the disease course, whereas symptoms related to drowsiness, pain and shortness of breath became more severe closer to death. Such detailed information on type and timing of symptoms has not previously been available and may allow health care providers to anticipate certain patterns.

Many investigators have reported a lack of[25] or late[26] referrals to PC in cancer patients. Most patients (78%) in our study received outpatient PC after cancer diagnosis, and just over half (52%) of these patients received their first outpatient PC in the final year of life, which is encouraging. Furthermore, the receipt of PC concurrently with cancer-directed therapy is encouraged by major cancer societies.[27,28] Our data suggest that those who received PC had a greater likelihood of moderate–severe symptoms in any domain compared with those who did not receive PC. This may suggest that those with greater symptoms are more likely to be referred to PC, which is encouraging. However, others have shown that despite considerable symptoms, referral to a pain and symptom management team is low in patients with cancer.[12]

While the uptake of the ESAS assessments in Ontario has been promising,[11] the impact of these assessments on targeted interventions remains understudied. Barbera et al.[29] reported that one-third of elderly cancer patients with severe pain reported on an ESAS assessment did not fill an opioid prescription. In an outpatient cancer population, Seow et al.[12] demonstrated that as the ESAS severity category increased, the proportion of pain (i.e. ordering pain-reducing medications) and shortness of breath-related actions (i.e. ordering chest x-rays, computed tomography scans) also increased; however, referrals to a pain and symptom management team remained low. These represent areas where care can be improved. In order to address this gap, we specifically examined whether outpatient PC as an intervention affected symptom scores.

Hui et al.[30] demonstrated that a change in domain score of 1 point reflects the minimal clinically important difference and applies to both improvement and worsening of symptoms in all ESAS domains in cancer patients. This information is directly relevant to our study. We have demonstrated that in those with moderate–severe pre-PC scores, outpatient PC resulted in both a statistically significant and clinically meaningful decrease in symptoms, ranging between 1 and 3 points. The greatest reduction in symptoms was noted in the pain and nausea domains.

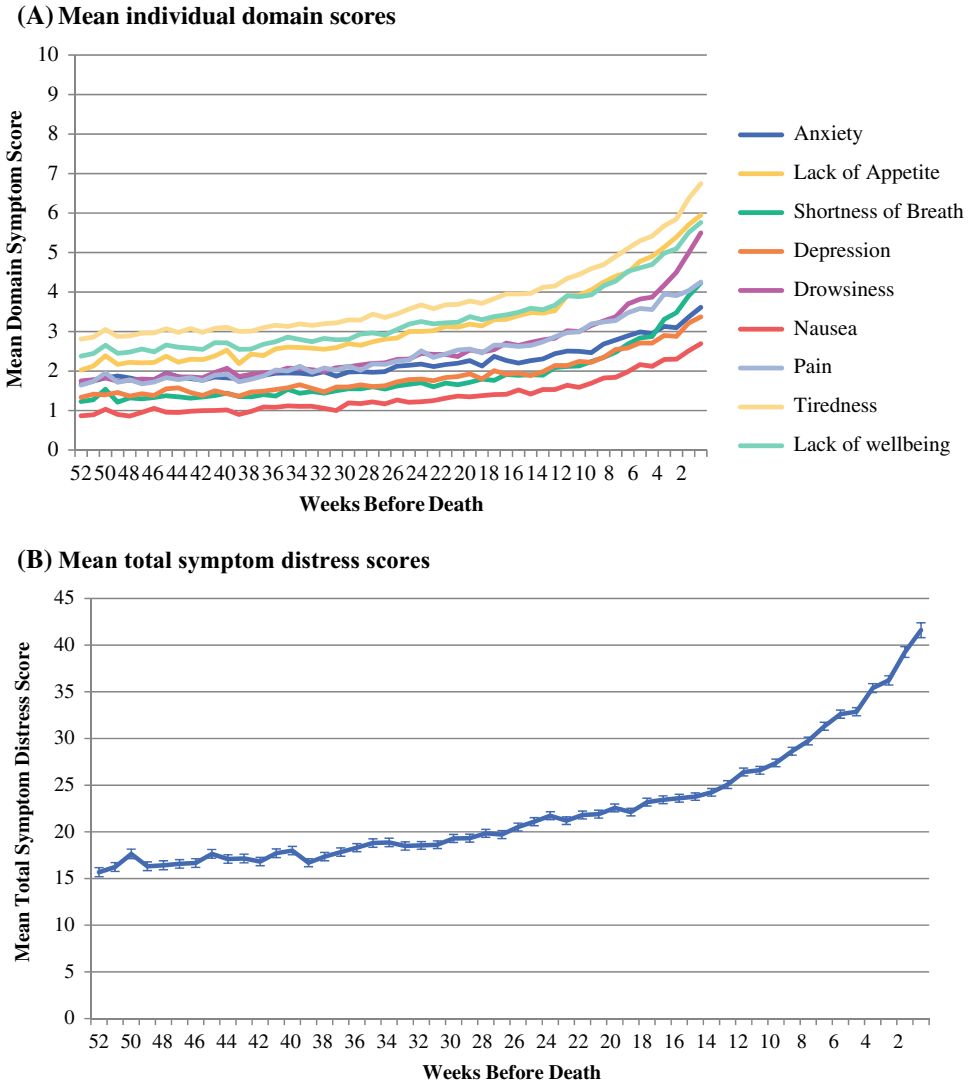

FIG. 2 Symptom profile of the cohort, by week, in the final year of life by **a** mean individual domain score and **b** mean total symptom distress score, with 95% confidence intervals. A total of 68,590 ESAS assessments were performed on 11,242 patients. *ESAS* Edmonton Symptom Assessment System

These symptoms are 'positive' symptoms that may be ameliorated more readily with medications than 'negative' symptoms such as lack of well-being and tiredness, which are more difficult to restore. Our data support other smaller case series of advanced cancer patients where those with the most severe symptoms derived the greatest reduction in score after a PC encounter.[31,32] Patient symptom burden is a major contributing factor to hospitalization,[6] and, if managed effectively in an outpatient setting, may reduce costly health utilization and patient distress related to hospitalization.

In our study, symptom scores increased in those with no–mild symptoms. This increase was statistically significant for all domains, but clinically significant (i.e. change by 1 point) in only a few domains. This is consistent with a report from Kang et al.[33] who showed exacerbation of symptoms in cancer patients with none–mild symptoms after an outpatient PC encounter. This may be because symptom scores in all domains increase closer to death, and/or that an intervention may only be effective when symptoms reach a certain severity level. In addition, we were not able to determine what specific intervention was performed at the PC encounter; for example, whether general counseling was performed or whether a prescription was provided to address a specific symptom. This would be a logical next area of study.

The strengths of this study include the use of a large population-based cohort enabling the study of symptom profile and the effectiveness of PC in a real-word setting. Our sensitivity analyses confirm the robustness of the data.

TABLE 2 Logistic regression model demonstrating the association between receipt of palliative care and moderate–severe ESAS scores in any domain in the final year of life

Domain	Unadjusted			Adjusted[a]		
	OR	95% CI	*p*-value	OR	95% CI	*p*-Value
Anxiety	1.49	(1.36–1.64)	< 0.0001	1.45	(1.31–1.60)	< 0.0001
Lack of appetite	1.54	(1.39–1.71)	< 0.0001	1.5	(1.34–1.67)	< 0.0001
Shortness of breath	1.36	(1.24–1.50)	< 0.0001	1.35	(1.23–1.49)	< 0.0001
Depression	1.69	(1.53–1.86)	< 0.0001	1.63	(1.48–1.80)	< 0.0001
Drowsiness	1.61	(1.46–1.77)	< 0.0001	1.56	(1.42–1.73)	< 0.0001
Nausea	1.69	(1.53–1.87)	< 0.0001	1.58	(1.43–1.75)	< 0.0001
Pain	1.98	(1.80–2.17)	< 0.0001	1.86	(1.68–2.05)	< 0.0001
Tiredness	1.67	(1.49–1.88)	< 0.0001	1.62	(1.44–1.83)	< 0.0001
Lack of wellbeing	1.54	(1.38–1.72)	< 0.0001	1.49	(1.33–1.67)	< 0.0001

Unadjusted and adjusted analyses are presented. Analysis excludes 55 patients with missing residence and/or marginalization data

ESAS edmonton symptom assessment system

[a]Adjusted for receipt of palliative care, age, sex, cancer site, comorbidity, socioeconomic marginalization, location of residence, time between cancer diagnosis and death, receipt of chemotherapy and radiotherapy in the final year of life

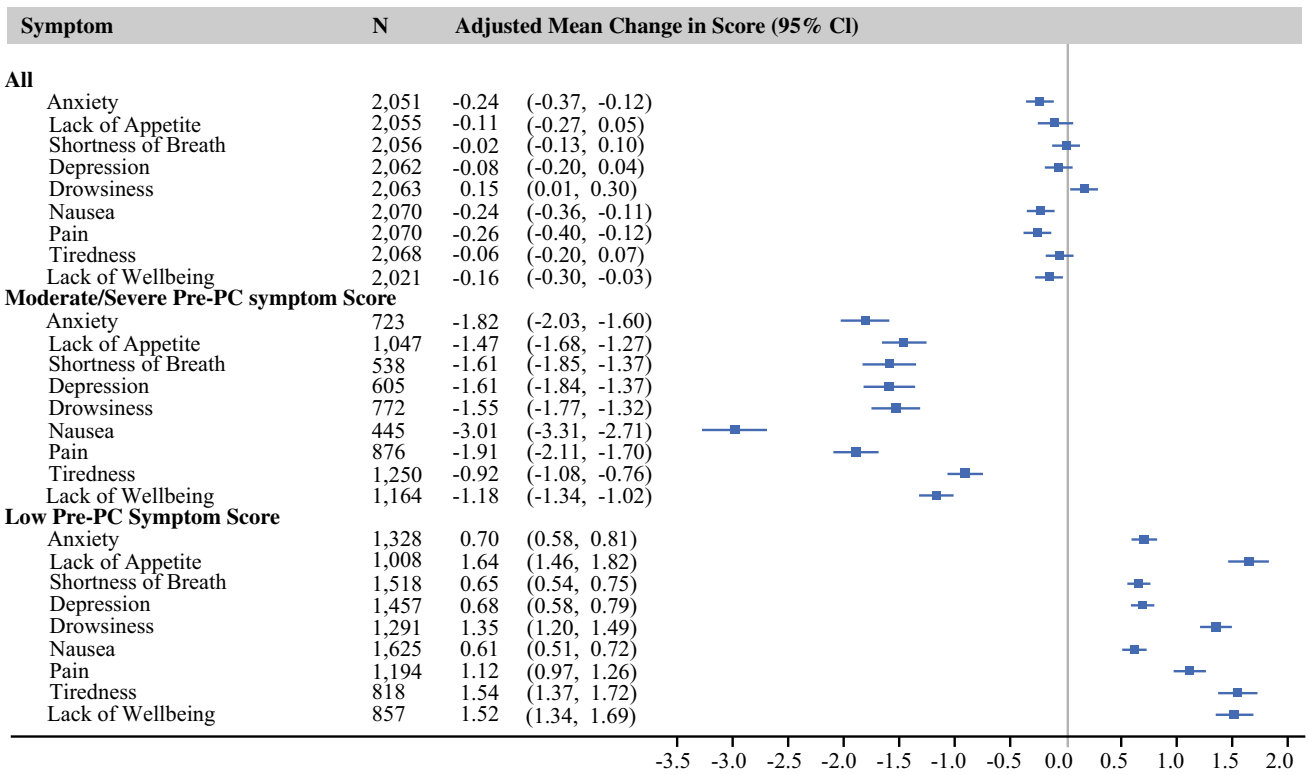

FIG. 3 Forest plot of the generalized estimating equation model estimating the effect of first PC on individual domain scores, stratified by pre-PC symptom severity, in PC-naïve patients. The change in each domain was calculated as the post-PC domain score minus the pre-PC domain score. A negative value reflects a decrease in symptom score, and a positive value reflects an increase in symptom score. Adjusted analysis is shown. Models exclude 12 patients with missing values in marginalization, residence, and pre- or post-PC symptom scores. The model is adjusted for receipt of palliative care, age, sex, cancer site, comorbidity, socioeconomic marginalization, location of residence, time between cancer diagnosis and death, receipt of chemotherapy and radiotherapy in the final year of life, year of first PC record, week of ESAS assessment prior to death, receipt of chemotherapy and or radiotherapy (up to and including 30 days prior to pre-PC ESAS, and up to and including the day of post-PC ESAS), number of days between the ESAS assessment and PC initiation, and between PC initiation and the subsequent ESAS assessment. *PC* palliative care, *CI* confidence interval, *ESAS* edmonton symptom assessment system

However, we acknowledge the limitations. There are inherent limitations in using administrative data for research purposes.[34] While broad trends can be identified, more detailed information pertaining to patient and provider preferences, and views pertaining to PC, was not captured. ESAS is an opportunistic assessment and, as a result, patients are not screened at regular intervals, which may limit the ability to assess, intervene, and reassess symptoms. There is variability in the uptake of this screening tool at cancer centers, which will affect patient symptom capture.[11] Furthermore, the assessment is performed largely in outpatient settings, predominantly cancer centers, therefore sicker patients who may require inpatient assessment are not captured. In addition, PC provided in other outpatient settings (i.e. family physician offices) where ESAS information is not submitted to administrative databases would not be captured. We chose to examine outpatient PC for this study, but recognize that PC services may be administered in a variety of settings (inpatient, convalescent care, telephone calls) and by other health care personnel (nurses). While we demonstrated that a single outpatient PC visit meaningfully reduces ESAS scores in those with greater symptom burden, the effect of multiple PC visits and types of score reductions that may prevent subsequent visits to the Emergency Department and inpatient hospitalizations require further study. Finally, PC is an intervention that is comprised of multiple components[28] and we were not able to determine which specific component of this intervention led to decreased scores.

CONCLUSION

We have defined the symptom profile for GI cancer patients in the last year of life, providing important information on the type and timing of symptoms, which will assist health care providers. We also report that outpatient PC reduces symptom scores in those with greater symptom burden. Further work is needed to determine the impact of score reduction on healthcare utilization and the specific elements of PC that lead to improved symptoms.

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REFERENCES

1. Seow H, Barbera L, Sutradhar R, Howell D, Dudgeon D, Atzema C, et al. Trajectory of performance status and symptom scores for patients with cancer during the last 6 months of life. *J Clin Oncol.* 2011;29(9):1151–8.
2. Barbera L, Seow H, Howell D, Sutradhar R, Earle C, Liu Y, et al. Symptom burden and performance status in a population-based cohort of ambulatory cancer patients. *Cancer.* 2010;116(24):5767–76.
3. Bubis LD, Davis L, Mahar A, Barbera L, Li Q, Moody L, et al. Symptom burden in the first year after cancer diagnosis: an analysis of patient-reported outcomes. *J Clin Oncol.* 2018;36(11):1103–11.
4. Wen FH, Chen JS, Chou WC, Hsieh CH, Chang WC, Shen WC, et al. Quality of life and psychological distress are differentially associated with distinct symptom-functional states in terminally ill cancer patients' last year of life. *Psychooncology.* 2018;27(9):2111–8.
5. Wilson KG, Chochinov HM, Skirko MG, Allard P, Chary S, Gagnon PR, et al. Depression and anxiety disorders in palliative cancer care. *J Pain Symptom Manag.* 2007;33(2):118–29.
6. Brooks GA, Abrams TA, Meyerhardt JA, Enzinger PC, Sommer K, Dalby CK, et al. Identification of potentially avoidable hospitalizations in patients with GI cancer. *J Clin Oncol.* 2014;32(6):496–503.
7. Barbera L, Atzema C, Sutradhar R, Seow H, Howell D, Husain A, et al. Do patient-reported symptoms predict emergency department visits in cancer patients? A population-based analysis. *Ann. Emerg Med.* 2013;61(4):427–37.
8. Hui D, Bruera E. The edmonton symptom assessment system 25 years later: past, present, and future developments. *J Pain Symptom Manag.* 2017;53(3):630–43.
9. Bruera E, Kuehn N, Miller MJ, Selmser P, Macmillan K. The Edmonton Symptom Assessment System (ESAS): a simple method for the assessment of palliative care patients. *J Palliat Care.* 1991;7(2):6–9.
10. Chang VT, Hwang SS, Feuerman M. Validation of the edmonton symptom assessment scale. *Cancer.* 2000;88(9):2164–71.
11. Pereira J, Green E, Molloy S, Dudgeon D, Howell D, Krzyzanowska MK, et al. Population-based standardized symptom screening: cancer care Ontario's edmonton symptom assessment system and performance status initiatives. *J Oncol Pract.* 2014;10(3):212–4.
12. Seow H, Sussman J, Martelli-Reid L, Pond G, Bainbridge D. Do high symptom scores trigger clinical actions? An audit after implementing electronic symptom screening. *J Oncol Pract.* 2012;8(6):e142–8.
13. Okafor PN, Stobaugh DJ, Nnadi AK, Talwalkar JA. Determinants of palliative care utilization among patients hospitalized with metastatic gastrointestinal malignancies. *Am J Hosp Palliat Care.* 2017;34(3):269–274.
14. Merchant SJ, Lajkosz K, Brogly SB, Booth CM, Nanji S, Patel SV, et al. The final 30 days of life: a study of patients with

gastrointestinal cancer in Ontario, Canada. *J Palliat Care*. 2017;32(3–4)92–100.
15. Merchant SJ, Brogly SB, Goldie C, Booth CM, Nanji S, Patel SV, et al. Palliative care is associated with reduced aggressive end-of-life care in patients with gastrointestinal cancer. *Ann Surg Oncol*. 2018;25(6):1478–87.
16. Clarke EA, Marrett LD, Kreiger N. Cancer registration in Ontario: a computer approach. *IARC Sci Publ*. 1991;(95):246–57.
17. Li KK, Harris K, Hadi S, Chow E. What should be the optimal cut points for mild, moderate, and severe pain? *J Palliat Med*. 2007;10(6):1338–46.
18. Selby D, Cascella A, Gardiner K, Do R, Moravan V, Myers J, et al. A single set of numerical cutpoints to define moderate and severe symptoms for the edmonton symptom assessment system. *J Pain Symptom Manag*. 2010;39(2):241–9.
19. Hui D, Kilgore K, Fellman B, Urbauer D, Hall S, Fajardo J, et al. Development and cross-validation of the in-hospital mortality prediction in advanced cancer patients score: a preliminary study. *J Palliat Med*. 2012;15(8):902–9.
20. Deyo RA, Cherkin DC, Ciol MA. Adapting a clinical comorbidity index for use with ICD-9-CM administrative databases. *J Clin Epidemiol*. 1992;45(6):613–9.
21. McMaster University. Ontario Marginalization Index 2012 [cited 1 Nov 2016]. https://crunch.mcmaster.ca/documents/ON-Marg_user_guide_1.0_FINAL_MAY2012.pdf.
22. Spiegelman D, Hertzmark E. Easy SAS calculations for risk or prevalence ratios and differences. *Am J Epidemiol*. 2005;162(3):199–200.
23. Wang M. Generalized estimating equations in longitudinal data analysis: a review and recent developments. *Adv Stat*. 2014; 2014:303728. https://doi.org/10.1155/2014/303728.
24. Spoozak L, Seow H, Liu Y, Wright J, Barbera L. Performance status and symptom scores of women with gynecologic cancer at the end of life. *Int J Gynecol Cancer*. 2013;23(5):971–8.
25. Wong AKY. Referral patterns to palliative care: an inpatient snapshot study. *J Clin Oncol*. 2016;34(26 Suppl):119.
26. Morita T, Akechi T, Ikenaga M, Kizawa Y, Kohara H, Mukaiyama T, et al. Late referrals to specialized palliative care service in Japan. *J Clin Oncol*. 2005;23(12):2637–44.
27. Cherny N, Catane R, Schrijvers D, Kloke M, Strasser F. European society for medical oncology (ESMO) program for the integration of oncology and palliative care: a 5-year review of the designated centers' incentive program. *Ann Oncol*. 2010;21(2):362–9.
28. Ferrell BR, Temel JS, Temin S, Alesi ER, Balboni TA, Basch EM, et al. Integration of palliative care into standard oncology care: American society of clinical oncology clinical practice guideline update. *J Clin Oncol*. 2017;35(1):96–112.
29. Barbera L, Seow H, Husain A, Howell D, Atzema C, Sutradhar R, et al. Opioid prescription after pain assessment: a population-based cohort of elderly patients with cancer. *J Clin Oncol*. 2012;30(10):1095–9.
30. Hui D, Shamieh O, Paiva CE, Perez-Cruz PE, Kwon JH, Muckaden MA, et al. Minimal clinically important differences in the edmonton symptom assessment scale in cancer patients: a prospective, multicenter study. *Cancer*. 2015;121(17):3027–35.
31. Hui D, Park M, Shamieh O, Paiva CE, Perez-Cruz PE, Muckaden MA, et al. Personalized symptom goals and response in patients with advanced cancer. *Cancer*. 2016;122(11):1774–81.
32. Shamieh O, Khamash O, Khraisat M, Jbouri O, Awni M, Al-Hawamdeh A, et al. Impact of outpatient palliative care (PC) on symptom burden in patients with advanced cancer at a tertiary cancer center in Jordan. *Support Care Cancer*. 2017;25(1):177–83.
33. Kang JH, Kwon JH, Hui D, Yennurajalingam S, Bruera E. Changes in symptom intensity among cancer patients receiving outpatient palliative care. *J Pain Symptom Manag*. 2013;46(5):652–60.
34. Nicholls SG, Langan SM, Benchimol EI. Routinely collected data: the importance of high-quality diagnostic coding to research. *CMAJ Can Med Assoc*. 2017;189(33):E1054–E5.