SYMPTOM EXPERIENCE OF OLDER ONCOLOGY PATIENTS WITH LOW VERSUS HIGH LEVELS OF MULTIMORBIDITY PRIOR TO CHEMOTHERAPY

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ABSTRACT

Purpose: Evaluate for differences in demographic and clinical characteristics between older oncology patients with low multimorbidity (<2 multimorbidities) and high multimorbidity (≥2 multimorbidities) and evaluate for differences in symptom occurrence, severity, and distress ratings between the two groups.

Methods: Symptoms of older oncology patients (n=125) were assessed using the Memorial Symptom Assessment Scale prior to chemotherapy administration. Data were analyzed using t-tests for continuous variables and Chi-square or Fisher's exact tests for categorical variables.

Results: For the total sample, lack of energy and pain were the two most common symptoms. Compared to the low multimorbidity group, the high multimorbidity group had a higher number of symptoms and significantly higher occurrence rates for feeling nervous, difficulty sleeping, dry mouth, and pain. Compared to the low multimorbidity group, the high multimorbidity group had significantly higher severity ratings for pain, feeling sad, lack of energy, feeling drowsy, and worrying. For distress, the high multimorbidity group reported significantly higher ratings for pain, worrying, feeling sad, feeling nervous, and "I don't look like myself". No differences were found in any demographic or clinical characteristics between the two multimorbidity groups.

Conclusions: Multimorbidity is associated with higher symptom occurrence, severity, and distress in older oncology patients. Our findings suggest that the symptoms with the highest severity ratings were not the most distressing. Clinicians should identify multimorbidities and assess symptoms prior to chemotherapy to identify patients at increased risk and initiate referrals for interventions.

Key words: older adults; cancer; symptoms; multimorbidity; comorbidity; chemotherapy

INTRODUCTION

The number of older adults with cancer is increasing dramatically. By 2035, more than 60% of all new cancer cases worldwide will occur in adults ≥65 years of age (Pilleron et al., 2019; Smith et al., 2009). Of note, between 55% and 98% of older adults (i.e., ≥60 years) experience multimorbidity (Marengoni et al., 2011; Vetrano et al., 2020). In addition, compared to patients without cancer, older adults with cancer experience a higher multimorbidity burden (Jørgensen et al., 2012; Williams et al., 2016). Multimorbidity is defined by the World Health Organization as the coexistence of two or more chronic conditions (WHO, 2016). As noted in the geriatric literature (Agustini et al., 2020; Eckerblad et al., 2015; Jones et al., 2016; Portz et al., 2017; Sasseville et al., 2019), multimorbidity is associated with a significantly higher symptom burden in older adults. In addition, multimorbidity and a higher symptom burden are associated with decreased quality of life and increased mortality (Willadsen et al., 2016). Findings from a recent study suggest that compared to patients without comorbid conditions, those individuals with ≥5 multimorbidities were significantly more bothered by these conditions (Ritchie et al., 2017). Nonetheless, current clinical practice guidelines on multimorbidity assessment do not include a recommendation to assess symptoms in older adults with multiple comorbid conditions (Tripp-Reimer et al., 2020).

While chemotherapy is a common and effective treatment for numerous cancer types, it causes multiple side effects (Hurria et al., 2016). For older patients, chemotherapy may worsen other age-related conditions (e.g., depression) (Leach et al., 2016). In addition, as noted in a recent review (Mohile et al., 2018), older oncology patients may experience overtreatment, related to the higher likelihood of chemotherapy-related complications and toxicities. On the other hand, older adults may be at increased risk for undertreatment, because they may be excluded from standard, evidence-based chemotherapy regimens based on assessments of their general condition (Mohile et al., 2018). Careful assessment of older oncology patients´ levels of multimorbidity and symptom experiences prior to chemotherapy may help to prevent overtreatment or undertreatment, as well as provide

guidance to clinicians to initiate pre-emptive symptom management interventions (Hurria et al., 2016).

Traditional oncology performance measures (e.g., Karnofsky Performance Status (KPS) scale (Verger et al., 1992) Eastern Cooperative Oncology Group score (Zubrod et al., 1960)), may not be sensitive enough to identify older adults who are at the highest risk for adverse outcomes from chemotherapy. These tools were validated in younger adults and do not address the diversity in health status among older oncology patients (Hurria et al., 2005; Hurria et al., 2016; Mohile et al., 2018). Therefore, more detailed assessments of multimorbidity are warranted in older adults receiving chemotherapy. Multimorbidity can be measured in several ways (Johnston et al., 2019). Commonly used measures include the clinician-rated Charlson Comorbidity Index (Barbera et al., 2010; Portz et al., 2017), patient-reported Older Americans Resources and Services Comorbidity Scale,(Williams et al., 2018) and the Self-Administered Comorbidity Questionnaire (SCQ) (Mazor et al., 2019; Röhrl et al., 2019; Utne et al., 2019). As noted in one systematic review (Johnston et al., 2019), no recommendations exist regarding the most appropriate instrument to use to measure multimorbidity.

Previous studies of older oncology patients found that depression, anxiety, lack of energy, pain, and worrying were the most commonly reported symptoms (Cohen, 2014a; Ritchie et al., 2014). Symptoms are often evaluated using the Edmonton Symptom Assessment Scale (Portz et al., 2017), the Brief Symptom Inventory (Cohen, 2014a), and the Memorial Symptom Assessment Scale (MSAS) (Cataldo et al., 2013; Ritchie et al., 2014). The Edmonton Symptom Assessment scale only measures symptom occurrence and severity, and is primarily used in palliative care (Chang et al., 2000). In contrast, the MSAS provides a more comprehensive assessment of patients' symptom experiences, because it evaluates symptom occurrence, frequency, severity, and distress (Portenoy et al., 1994).

In three studies of oncology patients that evaluated for associations between multimorbidity and MSAS symptoms (Deshields et al., 2014; Mazor et al., 2019; Röhrl et al., 2019), the findings were inconsistent. While in one study (Mazor et al., 2019), a higher level

of multimorbidity was associated with a significantly higher symptom burden, in the other two studies (Deshields et al., 2014; Röhrl et al., 2019) no associations were found. Reasons for these inconsistencies include: heterogeneity in the age of the patients who were assessed and the timing of the assessments (i.e., during (Röhrl et al., 2019), after (Mazor et al., 2019), or both during and after (Deshields et al., 2014) chemotherapy). To our knowledge, only one study evaluated for associations between multimorbidity and symptoms in older oncology patients receiving chemotherapy (n=326) (Van Cleave et al., 2013). In this study, symptoms were evaluated using the Symptom Distress Scale and multimorbidity was defined as one or more preexisting diseases or health conditions in addition to the index cancer. Those patients with $\geq$3 multimorbidities reported significantly higher symptom distress (total score ranged from 13 to 65) compared to patients with $\leq$2 multimorbidities. While patients who were not receiving chemotherapy were included in this sample, types of cancer treatment (i.e., surgery plus chemotherapy, surgery plus chemotherapy and radiation therapy) were not associated with symptom distress. However, in contrast to an assessment of multiple dimensions of a patient's symptom experience (i.e., occurrence, severity, distress) provided by the MSAS, this study evaluated only symptom distress. In addition, the symptoms were evaluated at variable time points (i.e., during or after chemotherapy).

The limitations of the previous studies (Deshields et al., 2014; Mazor et al., 2019; Röhrl et al., 2019; Van Cleave et al., 2013) and the paucity of information on associations between multimorbidity and the symptom experience of older oncology patients prior to chemotherapy suggests that additional research is warranted. Therefore, the purpose of this study was to evaluate for differences in demographics and clinical characteristics between older oncology patients with lower (n=62) versus higher (n=63) levels of multimorbidity, who were assessed prior to the initiation of chemotherapy. In addition, between group differences in occurrence, severity, and distress ratings for 32 symptoms were evaluated prior to the administration of chemotherapy.

METHODS

Patients and settings

This analysis is part of a larger longitudinal study of changes in cognitive and physical function in older oncology patients receiving chemotherapy. The methods for this study are published in detail elsewhere (Torstveit et al., 2021). Patients were recruited from one community and two university hospitals in Norway. Inclusion criteria were: age ≥60 years; diagnosis of gynecological or colorectal cancer; scheduled to receive primary or adjuvant chemotherapy; had a Montreal Cognitive Assessment (MoCA) score of ≥23 (Nasreddine et al., 2005); and had a KPS score of ≥60 (Schag et al., 1984). A total of 208 patients were approached and 149 consented to participate (71.6% response rate). Of these 149 patients, one withdrew and nine were excluded because they had a low MoCA score (<23). For this analysis, of the 139 patients recruited, 14 patients did not complete the MSAS. Therefore, 125 patients were included in this analysis.

Instruments

Demographic and clinical characteristics - Patients completed a demographic questionnaire that obtained information on age, gender, living arrangements, marital status, education, height and weight, and employment status. In addition, they completed the KPS scale that ranged from 40 (disabled; requires special care and assistance) to 100 (normal no complaints; no evidence of disease) (Ando et al., 2001; Schnadig et al., 2008) and the Self-Administered Comorbidity Questionnaire (SCQ-16) (Sangha et al., 2003). The SCQ-16 includes 16 common medical conditions and evaluates the occurrence of, treatment for, and functional impact of each of the comorbid conditions (e.g., heart disease, arthritis). Total SCQ scores can range from 0 to 48. The SCQ-16 has well established validity and reliability (Sangha et al., 2003).

Memorial Symptom Assessment Scale (MSAS) -The MSAS was used to evaluate the occurrence, severity, and distress of 32 symptoms commonly associated with cancer and its treatment. The MSAS is a self-report questionnaire designed to measure the multidimensional experience of symptoms. Using the MSAS, patients were asked to indicate whether they had experienced each symptom in the past week (i.e., symptom occurrence). If

they had experienced the symptom, they were asked to rate its severity and distress using a 0 to 10 numeric rating scale. The validity and reliability of the MSAS are well established in studies of oncology inpatients and outpatients (Portenoy et al., 1994).

Study procedures

The Regional Committee for Medical and Research Ethics, Norway and the institutional review board at each of the study sites approved the longitudinal study (reference No. 2015/1277/REK southeast). Oncologists or nurses approached patients prior to the initiation of chemotherapy to assess their interest in study participation. Then, patients were introduced to the research staff who explained the study, obtained written informed consent, and scheduled an appointment to perform the measures. The questionnaires were administered in the clinic or in the patient's home prior to the initiation of chemotherapy. Research staff reviewed patients' medical records for disease and treatment information.

Statistical analyses

Data were analyzed using the Statistical Package for the Social Sciences (SPSS) version 27 (SPSS, 2020). Using the conditions listed in the SCQ, patients were divided into low multimorbidity (LM; i.e., patients who had <2 chronic conditions in addition to their cancer) and high multimorbidity (HM; i.e., patients who had $\geq$2 chronic conditions in addition to their cancer) groups. To evaluate for between group differences in demographic and clinical characteristics, and symptom occurrence, severity and distress ratings, we used t-tests for continuous variables and Chi-square or Fisher's exact tests for categorical variables. To evaluate for clinically meaningful differences in symptom severity and distress scores between the two multimorbidity groups, effect size calculations were done (i.e., Cohen`s d) and were evaluated with cut-offs for small (from 0.2 to 0.5), medium (from 0.5 to 0.8), and large (>0.8) effects (Cohen, 2013; Osoba, 2002; Sloan et al., 2006). A p-value of <0.05 was considered statistically significant.

RESULTS

Differences in demographic and clinical characteristics

As shown in Table 1, of the 125 older oncology patients, 49.6% were in the LM group with a mean number of 0.5 (±0.5) multimorbidities and 50.4% were in the HM group with a mean number of 3.3 (±1.5) multimorbidities. Overall, the sample was predominately female (93.6%), married or partnered (62.1%), and 35.9% had a college degree. The mean age of the sample was 70.7 (±6.5) years. In addition, the total sample reported 10.2 (±5.4) MSAS symptoms, had a body mass index (BMI) of 26.0 (±6.1), a KPS score of 86.7 (±10.9), and were diagnosed with cancer for 1.4 (±3.8) years. Of the total sample, 88.8% had a diagnosis of gynecological cancer and 53.6% had surgery prior to chemotherapy.

No between group differences were found in any demographic characteristics. In terms of clinical characteristics, compared to the LM group, the HM group reported a higher total number of MSAS symptoms. In addition, a higher percentage of patients in the HM group reported the occurrence of heart disease, high blood pressure, lung disease, diabetes, ulcer or stomach disease, headache, depression, arthritis, back/neck pain, and disease of the connective tissue.

Differences in symptom occurrence rates

The occurrence rates for each of the MSAS symptoms for the total sample and within each of the multimorbidity groups are listed in Table 2. For the total sample, the five symptoms with the highest occurrence rates were: lack of energy (78.5%), pain (61.7%), worrying (61.3%), feeling drowsy (59.3%), and dry mouth (52.1%). Compared to the LM group, the HM group reported significantly higher occurrence rates for pain (51.7% vs. 71.7%), dry mouth (41.7% vs. 62.3%), difficulty sleeping (32.8% vs. 59.0%), and feeling nervous (18.3% vs. 45.2%), respectively.

Differences in symptom severity ratings

As shown in Table 3, the five symptoms with the highest mean severity ratings for the total sample were problems with sexual interest/activity (5.92 ±3.58), changes in skin (5.58 ±2.98), hair loss (5.58 ±3.48), constipation (5.06 ±2.56), and feeling bloated (4.96 ±2.28). Significant between group differences in severity ratings were found for five (15.6%) of the 32 MSAS symptoms. Compared to the LM group, the HM group reported significantly higher

severity scores for: lack of energy (3.96 ±1.90 vs. 5.52 ±2.41), pain (3.45 ±1.65 vs. 5.47 ±2.35), worrying (3.65 ±2.23 vs. 5.02 ±2.42), feeling sad (3.05 ±1.93 vs. 4.94 ±2.22), and feeling drowsy (3.38 ±1.99 vs. 4.86 ±1.93), respectively.

Differences in symptom distress ratings

As shown in Table 4, the five symptoms with the highest mean distress ratings for the total sample were: changes in skin (5.14 ±3.61), feeling nervous (4.92 ±2.60), problems with urination (4.68 ±3.68), constipation (4.65 ±3.20), and worrying (4.43 ±2.83). Significant between group differences in distress ratings were found for five (15.6%) of the 32 MSAS symptoms. Compared to the LM group, the HM group reported significantly higher distress ratings for: feeling nervous (3.30 ±1.64 vs. 5.54 ±2.66), worrying (3.36 ±2.36 vs. 5.32 ±2.90), "I don´t look like myself" (2.14 ±2.16 vs. 6.13 ±3.98), pain (2.96 ±2.17 vs. 4.90 ±3.24), and feeling sad (2.65 ±2.03 vs. 4.57 ±2.81), respectively.

DISCUSSION

To our knowledge, this study is the first to comprehensively evaluate for differences in multiple dimensions of the symptom experience in older oncology patients with lower and higher levels of multimorbidity prior to chemotherapy. Using the MSAS, our findings suggest that older adults with higher levels of multimorbidity report a higher number of MSAS symptoms, as well as higher occurrence, severity, and distress ratings for a number of different symptoms. Of note, except for the higher rates of several specific comorbidities and a higher overall comorbidity burden, that was expected, no between group differences were found in any other demographic or clinical characteristics. This finding is in contrast to other studies (Calderón-Larrañaga et al., 2019; Martin, 2017), and may be explained by the fact that patients with lower KPS and MoCA scores were excluded from this study.

Symptom experience of the total sample

In terms of the total sample, consistent with a previous study of older oncology patients (Ritchie et al., 2014), our patients reported an average of 10.2 (±5.4) symptoms. In terms of the five most common MSAS symptoms in our study, lack of energy, pain, and feeling drowsy were among the top five most common symptoms in two previous studies

(Cataldo et al., 2013; Ritchie et al., 2014). While difficulty concentrating was among the top five most common symptoms in these previous studies (Cataldo et al., 2013; Ritchie et al., 2014), this symptom was twelfth in its occurrence in our sample. This difference may be explained by the timing of the assessments, because difficulty concentrating is a common symptom that occurs during and following chemotherapy administration (Vardy et al., 2015). While our patients were assessed prior to chemotherapy, in the previous two studies (Cataldo et al., 2013; Ritchie et al., 2014), the older oncology patients were assessed following the receipt of chemotherapy.

In contrast to previous studies (Cataldo et al., 2013; Ritchie et al., 2014), worrying and dry mouth were among the top five most common symptoms in our sample. One possible explanation for these findings is that some of the specific comorbidities that the patients reported are associated with these two symptoms (e.g., a clinical diagnosis of depression may be associated with worrying, diabetes may be associated with dry mouth). Equally plausible is the fact that these older adults were worried about receiving a new treatment. In addition, dry mouth is a common problem in older adults and may be related to a variety of medications, including medications for depression (Tan et al., 2018).

Consistent with several studies of oncology patients (Cataldo et al., 2013; Mazor et al., 2019; Ritchie et al., 2014; Röhrl et al., 2019), lack of energy (i.e., fatigue) was reported by 80% of our older oncology patients. In addition, both the severity (4.75 $\pm$2.29) and distress (3.90 $\pm$3.13) ratings for fatigue were in the moderate range. Given that fatigue is one of the most common symptoms during chemotherapy (Escalante et al., 2020), it is interesting to note that the majority of our sample, regardless of multimorbidity levels, reported moderate levels of this symptom prior to chemotherapy. One possible explanation for this finding is that the majority of older patients in the LM (51.6%) and HM (55.6%) groups were enrolled soon after surgery. Additional explanations for the high occurrence rates include that 78.3% of our patients had metastatic disease and/or the synergetic effects of fatigue associated with other chronic conditions. Our findings suggest that fatigue needs to be monitored and addressed in older adults during and following chemotherapy.

Pain was the second most common symptom reported by 61.7% of our sample of older adults. This percentage is consistent with previous reports of pain in older adults in the general population (Eckerblad et al., 2015; Patel et al., 2013). In addition, this finding is consistent with a study of oncology patients (Posternak et al., 2016), that found that pain was associated with multimorbidity. While the causes of pain were not assessed in our study, the relatively high rates of back and neck pain (32.5%) and arthritis (41.0%), as well as the high rate of metastatic disease (78.3%) may explain the high occurrence rates of pain. While the severity and distress ratings for pain in the total sample, were not in the top five, older adults in our study who had pain reported severity (4.62 $\pm$2.30) and distress (4.09 $\pm$2.98) ratings in the moderate to severe range. Clinicians need to assess patients for causes of both cancer and non-cancer pain and initiate appropriate pain management interventions.

Symptom experience between the multimorbidity groups

While the total sample reported a relatively high number of symptoms (10.2 $\pm$5.4), compared to the LM group (8.9 $\pm$4.8), the HM group reported a significantly higher number of symptoms (11.5 $\pm$6.0). These findings suggest that higher levels of multimorbidity are associated with an increased symptom burden in older oncology patients. Of the 32 symptoms, pain was the only one that was significantly different between the two multimorbidity groups across all three symptom dimensions (i.e., occurrence, severity, distress). As noted above, while pain is a significant problem in older oncology patients in general (Goudas et al., 2005), our findings support previous reports in the geriatric literature(Nicholson et al., 2018; Sharpe et al., 2017), that older adults with higher levels of multimorbidity report higher rates of pain and more severe pain.

While we did not perform a detailed evaluation of the causes of pain in our sample, our findings may be partially explained by the relatively high comorbidity burden in the HM group as well as the higher occurrence rates for several comorbidities that are associated with pain (e.g., diabetes, ulcer or stomach disease, headache, arthritis, back/neck pain). Of note, the higher pain severity and distress ratings in the HM group represent not only statistically significant, but clinically meaningful differences in these scores, with large (d=-

0.88) and medium (d=-0.65) effect sizes, respectively. These findings suggest that clinicians should integrate nonpharmacological pain treatments into geriatric oncology care. Especially vulnerable patients are those with cardiac conditions and kidney and gastrointestinal diseases, because of the increased risk for adverse effects associated with nonopiods analgesics. Therefore, thoughtful and proactive pharmacological management is warranted.

While no between group differences were found in the occurrence rates for fatigue, the HM group reported not only statistically significant but clinically meaningfully higher fatigue severity scores (d=-0.68). Given that fatigue was not in the top five most severe symptoms in the LM group, this finding suggests that multimorbidity may be contributing to moderate to high levels of fatigue in the HM group (i.e., 5.52 $\pm$2.41). This association is supported by studies of fatigue in geriatric patients with multimorbidity (Eckerblad et al., 2015; Wijeratne et al., 2007).

For worrying and feeling sad, significant between group differences were found for both severity and distress ratings. In addition, occurrence and distress ratings for feeling nervous were higher in the HM group. Our study's findings are consistent with previous studies of older oncology patients (Cohen, 2014b; Van Cleave et al., 2013). In addition, it is interesting to note that in previous studies of oncology patients that used the MSAS (Deshields et al., 2014; Molassiotis et al., 2010), worrying, feeling sad, and feeling nervous are often related to each other in a psychological symptom cluster. In addition, in our study, a clinical diagnosis of depression was one of the self-reported comorbidities that had a significantly higher occurrence rate in the HM group (20.3%) compared to the LM group (0%). Additional evidence in support of our findings comes from a study that evaluated associations between somatic multimorbidity and somatic symptoms and mental distress in a sample of older oncology patients (age $\geq$65 years) (Grov et al., 2009). Compared to patients without somatic multimorbidity, patients who reported one or more disease(s) from a list of somatic comorbidities (e.g., asthma, rheumatoid arthritis, diabetes) experienced higher levels of mental distress. In addition, as noted in another study of oncology patients with multimorbidity (Irwin, 2013), depression is associated with poorer health-related quality of

life. Taken together, these findings support the use of an assesment tool, to identify older adults with high rates of psychological symptoms. In addition, oncology clinicians need to refer older adults for counseling or other mental health services.

While no between group differences were found in severity and distress ratings, a higher percentage of patients in the HM group reported difficulty sleeping (i.e., 59% vs. 32.8%). Of note, previous reports in the geriatric literature found that almost 50% of older adults report sleep disturbance or insomnia (Foley et al., 1995; Monane, 1992) and that multimorbidity in older adults is associated with higher rates of sleep disturbance (Crowley, 2011). While the high rates of psychological symptoms may contribute to the sleep disturbance in our sample, future studies need to determine the underlying cause(s) for this symptom so that appropriate interventions can be initiated.

Dry mouth was another symptom where between group differences were found only for symptom occurrence (i.e., LM group = 41.7% vs. HM group = 62.3%). While a number of specific comorbidities that were more common in the HM group (e.g., rheumatoid arthritis, disease in connective tissue) may cause dry mouth (Guggenheimer and Moore, 2003), in a systematic review of adverse effects of medications in older adults (aged $\geq$60 years) (Tan et al., 2018), a higher number of medications and several medication classes were associated with the occurrence of xerostomia and salivary gland hypofunction. While information on medications was not collected in our study, given the higher comorbidity burden in the HM group, as assessed by the SCQ, it is reasonable to hypothesize that these patients' medications contributed to the occurrence of this symptom.

In terms of "I don't look like myself", patients in the HM group reported higher distress ratings (6.13 $\pm$3.98) for this symptom compared to the LM group (2.14 $\pm$2.16). As described in previous reports (de Souto Barreto et al., 2011; Reboussin et al., 2000), several demographic and clinical characteristics (e.g., age, gender, functional limitations, chronic diseases) may be associated with older adults' perceptions of their body image and body satisfaction. In terms of specific clinical characteristics that may be associated with body satisfaction, in a previous study of older adults (de Souto Barreto et al., 2011), body mass

index, (which was measured for our sample and not found significantly different between the multimorbidity groups), was the strongest predictor of satisfaction with appearance for both men and women. Of note, given that only multimorbidity related characteristics (i.e., number of multimorbidities, overall comorbidity burden, the occurrence of ten specific comorbidities) were different between the two groups, this difference in distress ratings for “I don’t look like myself” may be related to body image changes associated with a variety of chronic conditions. Additional research is warranted to explain this finding.

Several study limitations need to be acknowledged. While this study’s sample size was relatively large, the two multimorbidity groups were relatively small. Therefore, findings from this study warrant replication in a larger sample. In addition, the sample is predominantly female and consists of patients with gynecological or colorectal cancer. Therefore, our findings may not be generalized to all oncology patients. In addition, the exclusion of patients with KPS score <60 and MoCA score <23, may have contributed to an under-estimation of the impact of multimorbidities on cancer symptoms. Given that older adults are less likely to enroll in clinical studies (Abbasi, 2019) and because this study was a secondary analysis, it is possible that our patients represent a sample of individuals with lower levels of multimorbidity. Unfortunately, information on the patients who declined participation is not available because of restrictions on data collection imposed by the Regional Committee for Medical and Research Ethics.

Despite these limitations, this study is the first to evaluate for differences in the symptom experience of older oncology patients with low and high levels of multimorbidity prior to chemotherapy. Of note, the number of multimorbidities has a significant impact on the occurrence, severity, and distress of symptoms commonly associated with cancer and its treatments in older oncology patients. Our findings suggest that symptoms with the highest severity ratings are not necessarily the most distressing. Clinicians should assess multimorbidity and symptoms in older oncology patients prior to chemotherapy to identify patients at increased risk and tailor interventions and referrals for those vulnerable individuals.

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Table 1. Differences in Demographic and Clinical Characteristics Between Patients with Low Multimorbidity (LM) and High Multimorbidity (HM)

Characteristics	Total (n=125)	LM (<2) 49.6% (n=62)	HM (≥2) 50.4% (n=63)	Statistics
	Mean (SD)	Mean (SD)	Mean (SD)	
Age (years)	70.7 (6.5)	70.5 (7.0)	70.9 (5.9)	t=-0.36; p=.717
Karnofsky Performance Status score	86.7 (10.9)	88.2 (10.8)	85.1 (10.9)	t=1.61; p=.111
Body mass index (kg/m^2)	26.0 (6.1)	25.0 (6.4)	27.1 (5.7)	t=-1.94; p=.055
Number of multimorbidities	1.9 (1.1)	0.5 (0.5)	3.3 (1.5)	t=-14.17; p<.001
Total number of symptoms (MSAS)	10.2 (5.4)	8.9 (4.8)	11.5 (6.0)	t=-2.71; p=.008
Self-administered Comorbidity Questionniare score	3.7 (2.8)	0.9 (0.9)	6.4 (3.9)	t=-11.06; p<.001
Time since cancer diagnosis (years)	1.4 (3.8)	1.0 (2.1)	1.8 (4.9)	t=-1.17; p=.247
Hemoglobin (g/dl)	12.7 (1.5)	12.5 (1.4)	12.8 (1.6)	t=-0.95; p=.346
	% (n)	% (n)	% (n)	
Gender				
Females	93.6 (117)	91.9 (57)	95.2 (60)	FE; p=.491
Males	6.4 (8)	8.1 (5)	4.8 (3)	
Married or partnered (% yes)	62.1 (77)	60.7 (37)	63.5 (40)	FE; p=.853
Lives alone (% yes)	35.8 (44)	36.7 (22)	34.9 (22)	x^2=1.13; p=.568
Currently employed (% yes)	16.1 (19)	19.0 (11)	13.3 (8)	FE; p=.459
Education				
Primary school	16.2 (19)	19.3 (11)	13.3 (8)	x^2=.04; p=.833
High school	47.9 (56)	40.4 (23)	55.0 (33)	
College	35.9 (42)	40.4 (23)	31.7 (19)	
Specific comorbidities (% yes)				
Heart disease	13.2 (16)	4.9 (3)	21.7 (13)	FE; p=.007
High blood pressure	35.5 (44)	14.5 (9)	56.5 (35)	FE; p<.001
Lung disease	10.7 (13)	0.0 (0)	21.3 (13)	FE; p<.001
Diabetes	7.4 (9)	1.6 (1)	13.1 (8)	FE; p=.032
Ulcer or stomach disease	7.4 (9)	1.6 (1)	13.1 (8)	FE; p=.032
Bowel disease	9.9 (12)	5.0 (3)	14.8 (9)	FE; p=.126
Kidney disease	1.7 (2)	1.7 (1)	1.7 (1)	FE; p=1.000
Liver disease	1.7 (2)	0.0 (0)	3.3 (2)	FE; p=.496
Anemia/ blood disease	3.4 (4)	0.0 (0)	6.9 (4)	FE; p=.057
Headache	8.5 (10)	1.8 (1)	14.8 (9)	FE; p=.017
Depression	10.1 (12)	0.0 (0)	20.3 (12)	FE; p<.001
Artrosis	41.0 (50)	13.6 (8)	66.7 (42)	FE; p<.001
Back/neck pain	32.5 (38)	7.1 (4)	55.7 (34)	FE; p<.001
Rheumatoid arthritis	3.4 (4)	0.0 (0)	6.9 (4)	FE; p=.057
Disease in connective-tissue	6.8 (8)	1.7 (1)	12.1 (7)	FE; p=.032
Skin disease	6.7 (8)	1.7 (1)	11.5 (7)	FE; p=.062

Cancer diagnosis Gynecological Colorectal	 88.8 (111) 11.2 (14)	 83.9 (52) 16.1 (10)	 93.7 (59) 6.3 (4)	x^2=3.01; p=.096
Surgery prior to chemotherapy (% yes)	53.6 (67)	51.6 (32)	55.6 (35)	FE; p=.721
Metastasis (% yes)	78.3 (94)	74.1 (43)	82.3 (51)	FE; p=.376

Abbreviations: dl = deciliters, FE = Fisher's Exact, g = grams, kg = kilograms, m^2 = meters squared, SD = standard deviation

Table 2 – Differences in Symptom Occurrence Prior to the Initiation of Chemotherapy Between Patients with Low Multimorbidity (LM) and High Multimorbidity (HM)

Symptoms	Total (n=125) % (n)	LM (<2) 49.6% (n=62) % (n)	HM (≥2) 50.4% (n=63) % (n)	Statistics
Lack of energy	78.5 (95)	78.3 (47)	78.7 (48)	FE; p=1.000
Pain	61.7 (74)	51.7 (31)	71.7 (43)	FE; p=.038
Worrying	61.3 (76)	54.8 (34)	67.7 (42)	FE; p=.197
Feeling drowsy	59.3 (73)	59.7 (37)	59.0 (36)	FE; p=1.000
Dry mouth	52.1 (63)	41.7 (25)	62.3 (38)	FE; p=.029
Difficulty sleeping	45.9 (56)	32.8 (20)	59.0 (36)	FE; p=.006
Feeling bloated	44.6 (54)	45.0 (27)	44.3 (27)	FE; p=1.000
Constipation	44.3 (54)	36.1 (22)	52.5 (32)	FE; p=.101
Lack of appetite	44.3 (54)	40.0 (24)	48.4 (30)	FE; p=.368
Feeling sad	41.5 (51)	32.8 (20)	50.0 (31)	FE; p=.068
Numbness/tingling in hands/feet	38.5 (47)	41.0 (25)	36.1 (22)	FE; p=.710
Difficulty concentrating	38.5 (45)	36.8 (21)	40.0 (24)	FE; p=.849
Sweats	38.0 (46)	32.8 (20)	43.3 (26)	FE; p=.264
Weight loss	36.4 (44)	40.0 (24)	32.8 (20)	FE; p=.453
Dizziness	34.4 (42)	27.9 (17)	41.0 (25)	FE; p=.182
Shortness of breath	33.9 (41)	35.0 (21)	32.8 (20)	FE; p=.849
Feeling nervous	32.0 (39)	18.3 (11)	45.2 (28)	FE; p=.002
Nausea	31.4 (38)	23.3 (14)	39.3 (24)	FE; p=.078
Change in the way food tastes	28.9 (35)	23.0 (14)	35.0 (21)	FE; p=.164
Problems with sexual interest/activity	23.6 (26)	18.9 (10)	28.1 (16)	FE; p=.272
Cough	23.0 (28)	20.0 (12)	25.8 (16)	FE; p=.521
Feeling irritable	22.0 (27)	16.4 (10)	27.4 (17)	FE; p=.191
Diarrhea	18.7 (23)	19.7 (12)	17.7 (11)	FE; p=.821
Problems with urination	16.0 (19)	10.2 (6)	21.7 (13)	FE; p=.132
Swelling of arms or legs	14.6 (18)	8.2 (5)	21.0 (13)	FE; p=.072
Changes in skin	13.8 (17)	9.8 (6)	17.7 (11)	FE; p=.296
“I don`t look like myself”	13.2 (16)	11.5 (7)	15.0 (9)	FE; p=.602
Mouth sores	13.2 (16)	16.7 (10)	9.8 (6)	FE; p=.296
Itching	13.1 (16)	10.0 (6)	16.1 (10)	FE; p=.423
Difficulty swallowing	10.7 (13)	9.8 (6)	11.5 (7)	FE; p=1.000
Hair loss	10.7 (13)	6.7 (4)	14.5 (9)	FE; p=.241
Vomiting	6.6 (8)	6.7 (4)	6.6 (4)	FE; p=1.000

Abbreviation: FE = Fisher’s Exact

Table 3 – Differences in Symptom Severity Ratings[1] Prior to the Initiation of Chemotherapy Between Patients with Low Multimorbidity (LM) and High Multimorbidity (HM)

Symptoms	Total Mean (SD) n=125	LM (<2) Mean (SD) 49.6% (n=62)	HM (≥2) Mean (SD) 50.4% (n=63)	Statistics
Problems with sexual interest/activity	5.92 (3.58)	5.30 (3.68)	6.31 (3.57)	t=-0.70; p=.494
Changes in skin	5.58 (2.98)	3.83 (2.93)	6.55 (2.66)	t=-1.94; p=.071
Hair loss	5.58 (3.48)	3.00 (2.45)	6.88 (3.27)	t=-2.08; p=.065
Constipation	5.06 (2.56)	4.36 (2.57)	5.55 (2.47)	t=-1.69; p=.097
Feeling bloated	4.96 (2.28)	4.85 (2.03)	5.07 (2.54)	t=-0.36; p=.724
“I don`t look like myself”	4.93 (2.96)	3.67 (1.37)	5.78 (3.49)	t=-1.40; p=.186
Swelling of arms or legs	4.89 (3.27)	3.00 (2.45)	5.62 (3.33)	t=-1.59; p=.132
Problems with urination	4.84 (3.40)	4.00 (3.41)	5.23 (3.47)	t=-0.72; p=.480
Lack of energy	4.75 (2.29)	3.96 (1.90)	5.52 (2.41)	t=-3.52; p=.001
Pain	4.62 (2.30)	3.45 (1.65)	5.47 (2.35)	t=-4.09; p<.001
Dry mouth	4.61 (2.45)	4.38 (4.45)	4.76 (2.48)	t=-0.60; p=.548
Lack of appetite	4.59 (2.15)	4.21 (1.86)	4.90 (2.34)	t=-1.18; p=.244
Shortness of breath	4.59 (2.79)	4.10 (2.55)	5.10 (3.01)	t=-1.16; p=.255
Sweats	4.47 (3.04)	4.30 (3.06)	4.60 (3.08)	t=-0.33; p=.746
Feeling nervous	4.45 (2.36)	3.45 (1.63)	4.85 (2.51)	t=-1.70; p=.098
Diarrhea	4.43 (3.06)	3.50 (2.61)	5.45 (3.30)	t=-1.58; p=.128
Worrying	4.41 (2.42)	3.65 (2.23)	5.02 (2.42)	t=-2.55; p=.013
Numbness/tingling in hands/feet	4.40 (2.77)	3.76 (2.24)	5.14 (3.17)	t=-1.74; p=.089
Difficulty sleeping	4.34 (2.35)	3.60 (2.33)	4.75 (2.30)	t=-1.79; p=.080
Mouth sores	4.25 (2.49)	4.30 (2.58)	4.17 (2.56)	t=0.10; p=.922
Feeling sad	4.20 (2.29)	3.05 (1.93)	4.94 (2.22)	t= -3.11; p=.003
Change in the way food tastes	4.17 (1.98)	3.71 (2.23)	4.48 (1.78)	t=-1.12; p=.270
Feeling drowsy	4.11 (2.09)	3.38 (1.99)	4.86 (1.93)	t=-3.23; p=.002
Dizziness	3.93 (2.62)	3.41 (2.15)	4.29 (2.90)	t=-1.06; p=.295

Feeling irritable	3.63 (2.40)	3.40 (2.27)	3.76 (2.54)	t=-0.37; p=.711
Difficulty concentrating	3.45 (2.18)	2.85 (1.73)	3.96 (2.42)	t=-1.77; p=.085
Nausea	3.32 (2.11)	2.77 (1.83)	3.63 (2.22)	t=-1.19; p=.244
Difficulty swallowing	3.31 (2.10)	2.67 (1.86)	3.86 (2.27)	t=-1.02; p=.329
Weight loss	3.27 (1.98)	3.00 (1.87)	3.60 (2.11)	t=-1.00; p=.323
Itching	3.13 (2.36)	2.50 (1.87)	3.56 (2.65)	t=-0.84; p=.416
Vomiting	2.75 (2.60)	2.00 (2.45)	3.50 (2.89)	t=-0.79; p=.458
Cough	2.63 (2.11)	3.17 (2.17)	2.20 (2.04)	t=1.19; p=.245

[1] Severity ratings were done on a 0 (none) to 10 (intolerable) numeric rating scale.

Abbreviation: SD = standard deviation

Table 4 – Differences in Symptom Distress Ratings[1] Prior to the Initiation of Chemotherapy Between Patients with Low Multimorbidity (LM) and High Multimorbidity (HM)

Symptoms	Total Mean (SD) n=125	LM (<2) Mean (SD) 49.6% (n=62)	HM (≥2) Mean (SD) 50.4% (n=63)	Statistics
Changes in skin	5.14 (3.61)	3.40 (3.78)	6.11 (3.33)	t=-1.39; p=.189
Feeling nervous	4.92 (2.60)	3.30 (1.64)	5.54 (2.66)	t=-2.48; p=.018
Problems with urination	4.68 (3.68)	4.33 (3.33)	4.85 (3.96)	t=-0.28; p=.787
Constipation	4.65 (3.20)	4.10 (3.15)	5.03 (3.24)	t=-1.04; p=.306
Worrying	4.43 (2.83)	3.36 (2.36)	5.32 (2.90)	t=-3.04; p=.003
Swelling of arms or legs	4.38 (3.99)	2.50 (2.65)	5.22 (4.32)	t=-1.15; p=.274
“I don`t look like myself”	4.27 (3.75)	2.14 (2.16)	6.13 (3.98)	t=-2.36; p=.034
Shortness of breath	4.21 (3.30)	3.86 (3.00)	4.65 (3.67)	t=-0.73; p=.470
Feeling bloated	4.20 (3.10)	4.46 (2.85)	3.92 (3.39)	t=0.62; p=.540
Pain	4.09 (2.98)	2.96 (2.17)	4.90 (3.24)	t=-2.92; p=.005
Lack of energy	3.90 (3.13)	3.49 (2.71)	4.27 (3.45)	t=-1.17; p=.246
Feeling sad	3.80 (2.68)	2.65 (2.03)	4.57 (2.81)	t=-2.62; p=.012
Lack of appetite	3.76 (2.50)	3.57 (1.89)	3.89 (2.91)	t=-0.44; p=.661
Mouth sores	3.73 (2.71)	4.30 (2.67)	2.60 (2.70)	t=1.16; p=.267
Problems with sexual interest/activity	3.68 (3.76)	2.75 (3.41)	4.21 (3.97)	t=-0.87; p=.393
Hair loss	3.62 (4.37)	3.00 (3.56)	3.89 (4.86)	t=-0.33; p=.751
Diarrhea	3.55 (4.17)	3.40 (3.69)	3.70 (4.81)	t=-0.16; p=.877
Difficulty concentrating	3.32 (2.91)	2.85 (2.11)	3.76 (3.51)	t=-1.02; p=.318
Difficulty sleeping	3.24 (2.67)	2.63 (2.36)	3.59 (2.80)	t=-1.25; p=.216
Dizziness	3.23 (2.76)	2.81 (1.72)	3.52 (3.30)	t=-0.87; p=.388
Sweats	3.20 (3.11)	3.30 (3.03)	3.10 (3.26)	t=0.21; p=.836
Dry mouth	3.02 (2.95)	3.00 (2.94)	3.03 (3.00)	t=-0.04; p=.972
Numbness/tingling in hands/feet	3.02 (3.35)	2.52 (2.84)	3.60 (3.84)	t=-1.03; p=.309
Nausea	2.97 (2.42)	2.69 (2.02)	3.13 (2.66)	t=-0.52; p=.609
Difficulty swallowing	2.92 (3.04)	2.00 (3.03)	3.71 (3.04)	t=-1.02; p=.332
Weight loss	2.75 (2.80)	2.24 (2.26)	3.32 (3.27)	t=-1.20; p=.238
Vomiting	2.60 (3.58)	2.33 (4.04)	3.00 (4.24)	t=-0.18; p=.870
Change in the way food tastes	2.58 (2.17)	2.42 (2.43)	2.67 (2.06)	t=-0.32; p=.755
Feeling irritable	2.58 (2.18)	3.10 (2.08)	2.25 (2.24)	t=0.97; p=.344
Feeling drowsy	2.38 (2.64)	1.94 (2.40)	2.82 (2.82)	t=-1.35; p=.180
Cough	1.76 (2.54)	2.09 (2.88)	1.50 (2.31)	t=0.57; p=.574
Itching	1.38 (2.06)	1.25 (1.89)	1.44 (2.24)	t=-0.15; p=.883

[1] Distress ratings were done on a 0 (not at all distressing) to 10 (most distressing) numeric rating scale.

Abbreviation: SD = standard deviation