



# Symptom frequency and change of oldest old cancer patients

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## Abstract

**Purpose** The oldest old, described as those aged 85 and older, is a growing cancer population. There are limited studies evaluating the symptoms of the oldest old cancer patient population. Our study aimed to evaluate symptom frequency and clinical symptom change as assessed by the Edmonton Symptom Assessment System (ESAS) of the oldest old ( $\geq 85$ ) compared to older adult (65–84) and general adult (18–64) outpatient cancer patients on initial consult and follow-up visit.

**Methods** Retrospective review of a total of 441 patients, 200 randomly sampled patients in the general and older adult group and 41 consecutive patients in the oldest old group. Chart review was performed for demographic and clinical information including ESAS.

**Results** The oldest old group had less advanced tumors and worse performance status and was receiving less cancer therapy. Eighty percent or more of these patients reported fatigue, sleep disturbance, appetite, and drowsiness. They experienced lower frequencies of pain ( $p < 0.0001$ ), fatigue ( $p = 0.0338$ ), nausea ( $p = 0.0151$ ), feeling of well-being ( $p = 0.0245$ ), sleep disturbance ( $p = 0.0484$ ), financial distress ( $p = 0.0002$ ), and spiritual distress ( $p = 0.0010$ ) compared to the younger groups. Twenty-six to fifty-one percent of the oldest old patients' symptoms improved on the first follow-up visit.

**Conclusions** Oldest old cancer patients have high frequencies of multiple symptoms on initial referral. However, these symptom frequencies are lower when compared to younger age groups. Additionally, many of their symptoms improved on first follow-up visit in the palliative care clinic. More research is needed to address the needs of this growing cancer population and focus symptoms that can improve with palliative care intervention.

**Keywords** Oldest old · Aged · Symptoms · Palliative care · Geriatric oncology

## Introduction

The oldest old is often described as those aged 85 and older [1]. Between 2000 and 2010, the older adult population increased at a faster rate than the total the US population. The population aged 85–94 years old experienced the fastest growth, increasing by 30% from 3.9 million to 5.1 million [2]. This vulnerable population is also undergoing active cancer treatment. Recent studies have evaluated the oldest old undergoing surgery [3] and chemotherapy [4, 5].

Older adults undergoing treatment for cancer may experience multiple symptoms [6, 7]. Not all studies agree with how older adults experience symptoms compared to the younger population. In one of the earlier studies, Yan et al. noted higher symptom distress scores in older adults as compared to the younger population [8]. With regard to pain, older patients were noted to experience similar pain intensity but require less opioid analgesia [9]. Cataldo et al. evaluated differences in symptom between adults  $< 60$  and  $\geq 60$  years undergoing cancer treatment [10]. Using the Memorial Symptom Assessment Scale, they found that older patients reported lower occurrence rates for almost 50% of the symptoms assessed. There are limited studies specifically evaluating the symptoms of the oldest old population undergoing cancer treatment. In one study comparing pain assessment of hospitalized patients between the young old (aged 65–84 years) and oldest old (aged 85–100 years), no significant differences were found between the two groups with regard to pain characteristics [11].

There is limited data on patient reported symptoms among the oldest old cancer patients. As this population continues to

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increase and also is participating in active cancer treatment, there is a growing need for health care teams to better assess and hopefully improve their symptoms during treatment. The purpose of this study was to evaluate the symptom frequency as assessed by the Edmonton Symptom Assessment System (ESAS) of the oldest old adults (aged  $\geq 85$ ) as compared to the young old (aged  $65 < 85$ ) and general adult age groups (aged  $< 65$ ). We also aimed to evaluate the frequency of symptom changes in the individual ESAS scores between the initial supportive care outpatient consultation visit and the first follow-up supportive care visit within 1 month.

## Methods

This retrospective study of a total of 441 patients was conducted at the University of Texas MD Anderson Cancer Center supportive care clinic between January 2013 and December 2016. The study was approved by the institutional review board, and a waiver of consent was obtained. To be eligible for inclusion, patients had to have prospectively completed an ESAS questionnaire, routinely assessed in our clinic, for at least the initial and follow-up visits  $\geq 7$  days and  $\leq 30$  days from the initial consultation. From the entire pool of eligible patients, the biostatistics department generated a random list for the two groups, general adult and young old, given the large number of patients in these groups. We randomly sampled 200 patients each in the general adult, defined as persons aged 65 and younger, and young old, defined as persons aged older than 65 to less than 85, age group and compared to 41 consecutive patients in the oldest old, defined as persons aged 85 and older, age group. Within the dates of our study, the oldest old patient group was very limited, so we were unable to randomly sample and included all 41 patients in that age group. We obtained demographic, clinical information, and patient reported symptoms such as ESAS from chart review. ESAS is a clinical tool initially developed to document symptom burden in patients with advanced cancer. It has since been validated by multiple research groups and is used to screen for the presence and severity of symptoms in advanced cancer patients [12]. In our current version of ESAS, the tool assesses symptoms of pain, fatigue, nausea, depression, anxiety, drowsiness, shortness of breath, appetite, sensation of well-being, financial distress, and spiritual pain. In this study, symptom occurrence was defined as score  $> 0$  for any symptom. Minimal clinically important difference on ESAS was used to determine symptom change on follow-up visit. This was defined as a change of at least 1 point for both improvement and deterioration of all symptoms assessed by ESAS except for financial distress and spiritual pain, which were not included [13].

## Statistical analysis

Data was summarized using standard descriptive statistics. We used median and range as well as mean and standard deviation for continuous variables and frequency and proportion for categorical variables. Association between categorical variables was examined by chi-squared test or Fisher's exact test when the frequency in any age group was  $< 5$ . Kruskal-Wallis test was used to examine the difference in continuous variables among age groups. All computations were carried out in SAS 9.4 (SAS Institute Inc., Cary, NC, USA).

## Results

Data from 441 supportive care outpatients were evaluated. Table 1 shows the baseline demographics of patients evaluated in the supportive care clinic. The median age of the patients in the general population, young old and oldest old, was 55, 70, and 87 years of age respectively. Fifty percent were female. The oldest old group was receiving less cancer treatment including less chemotherapy (31.7%), surgery (31.7%), and targeted therapy (2.4%). They also had less advanced tumors at time of initial supportive care consultation. The oldest old had worse performances status with 53.7% of patients noted to have ECOG 3 or higher. The most common primary cancers in this group were breast and gastrointestinal (35.4%). They also were assessed to have higher MDAS scores with a mean of 2.73.

Table 2 provides a summary of symptom frequency for the total sample for each of the ESAS symptoms measured at initial consultation. The highest symptom frequencies experienced by the oldest old was fatigue (85.4%), sleep (85.4%), loss of appetite (82.9%), feeling of well-being (82.5%), and drowsiness (80%). The most common symptom frequency for the general population and the young old population were pain (92.5% and 85.4%), fatigue (96% and 92.5%), loss of appetite (83% and 84.7%), feeling of well-being (91.5% and 94.9%), and sleep (94.8% and 88.9%). The oldest old group experienced statistically lower frequencies of pain ( $p < 0.0001$ ), fatigue ( $p = 0.0338$ ), nausea ( $p = 0.0151$ ), feeling of well-being ( $p = 0.0245$ ), sleep ( $p = 0.0484$ ), and spiritual distress ( $p = 0.0010$ ).

Table 3 describes the percentage of patients in each age group that achieved minimal clinical changes in improvement on follow-up visit. In the oldest old age group, the highest improvement was in fatigue (43.6%), anxiety (46.2%), appetite (44.7%), drowsiness (44.7%), and sleep (51.3%). More patients improved than deteriorated in the oldest old age group in all symptoms except for spiritual pain. More than 50% of the oldest old had no change in nausea and spiritual pain. In the two younger age groups, the highest improvement was in pain (51.8% and 49.2%), fatigue (47.7% and 48.4%), anxiety

**Table 1** Summary of demographic and clinical characteristics on initial consult

Category	Levels	Total	Age groups			<i>p</i> value		
			18–64	65–84	≥ 85			
			<i>N</i> (%)					
All patients		441 (100%)	200 (100%)	200 (100%)	41 (100%)			
Age	Median (min, max)	65 (21, 98)	55 (21, 64)	70 (65, 84)	87 (85, 98)			
Gender	Male	222 (50.3%)	96 (48%)	105 (52.5%)	21 (51.2%)	0.6623		
Race	Asian	20 (4.5%)	10 (5%)	8 (4%)	2 (4.9%)	0.1261		
	Black	54 (12.2%)	28 (14%)	22 (11%)	4 (9.8%)			
	Hispanic or Latino	56 (12.7%)	33 (16.5%)	22 (11%)	1 (2.4%)			
	White	300 (68%)	122 (61%)	144 (72%)	34 (82.9%)			
	Other/unknown	11 (2.5%)	7 (3.5%)	4 (2%)	0 (0%)			
Radiation		203 (46%)	87 (43.5%)	96 (48%)	20 (48.8%)	0.6211		
Chemotherapy		322 (73%)	165 (82.5%)	144(72%)	13 (31.7%)	< 0.0001		
Surgery		177 (40.1%)	99 (49.5%)	65 (32.5%)	13 (31.7%)	0.0013		
Medical or hormonal therapy/target therapy		182 (41.3%)	106 (53%)	75 (37.5%)	1 (2.4%)	< 0.0001		
Tumor location	Advanced	316 (74.7%)	159 (86.4%)	134 (67.7%)	23 (56.1%)	< 0.0001		
	Localized	107 (25.3%)	25 (13.6%)	64 (32.3%)	18 (43.9%)			
Diagnosis	Breast	55 (12.5%)	31 (15.5%)	22 (11%)	2 (4.9%)	0.0043		
	Gastrointestinal	101 (22.9%)	51 (25.5%)	41 (20.5%)	9 (22%)			
	Genitourinary	32 (7.3%)	13 (6.5%)	18 (9%)	1 (2.4%)			
	Gynecological	30 (6.8%)	23 (11.5%)	6 (3%)	1 (2.4%)			
	Head and Neck	56 (12.7%)	21 (10.5%)	26 (13%)	9 (22%)			
	Leukemia	2 (0.5%)	2 (1%)	0 (0%)	0 (0%)			
	Lymphoma/myeloma	12 (2.7%)	6 (3%)	5 (2.5%)	1 (2.4%)			
	Sarcoma	17 (3.9%)	8 (4%)	8 (4%)	1 (2.4%)			
	Skin (including melanoma)	18 (4.1%)	6 (3%)	8 (4%)	4 (9.8%)			
	Thoracic	97 (22%)	24 (12%)	61 (30.5%)	12 (29.3%)			
	Other	21 (4.8%)	15 (7.5%)	5 (2.5%)	1 (2.4%)			
	ECOG <sup>1</sup>	0	3 (0.7%)	1 (0.5%)	1 (0.5%)		1 (2.4%)	0.0043
		1	97 (22%)	51 (25.5%)	40 (20%)		6 (14.6%)	
2		194 (44%)	96 (48%)	86 (43%)	12 (29.3%)			
3		143 (32.4%)	51 (25.5%)	72 (36%)	20 (48.8%)			
4		4 (0.9%)	1 (0.5%)	1 (0.5%)	2 (4.9%)			
MDAS <sup>2</sup>	Median (min, max)	1 (0, 20)	1 (0, 6)	1 (0, 20)	2 (0, 16)	0.0057		

<sup>1</sup> Eastern Cooperative Oncology Group<sup>2</sup> Memorial Delirium Assessment Scale

(49.7 and 43.2%), well-being (49.2 and 44.9%), and sleep (51.9% and 44.8%). The minimal clinical changes among these three age groups are not significantly different in most of the symptoms. However, the changes in nausea ( $p = 0.0978$ ), financial distress ( $p = 0.0534$ ), and spirit pain ( $p = 0.0708$ ) are marginally different among the age groups.

## Discussion

This is one of the few studies evaluating symptom expression focusing on the oldest old cancer patients. Despite having less

advanced disease and receiving less cancer modifying therapies, the oldest old group still reported substantial symptom frequencies on initial supportive care consultation as documented by ESAS. However, similar to prior studies noting lower symptom occurrence in older compared to younger cancer patients [10], our study continues to show in 58% of symptoms; the oldest old had significantly lower symptom frequencies when compared to both the younger old and the general population. One reason may be the lower number of oldest old adults in our sample undergoing cancer-related treatments. These treatments have often been cited to cause or exacerbate symptoms, such as chemotherapy induced nausea/vomiting or

**Table 2** ESAS symptom frequency

Symptom	Age groups			<i>p</i> value
	18–64	65–84	≥ 85	
Pain	185 (92.5%)	170 (85.4%)	26 (65%)	< 0.0001
Fatigue	192 (96%)	185 (92.5%)	35 (85.4%)	0.0338
Nausea	119 (59.8%)	102 (51%)	15 (36.6%)	0.0151
Depression	128 (64.6%)	123 (61.8%)	24 (58.5%)	0.7077
Anxiety	145 (73.6%)	144 (72.7%)	30 (73.2%)	0.9809
Appetite	166 (83%)	166 (84.7%)	34 (82.9%)	0.8907
Drowsiness	156 (78.4%)	144 (72.4%)	32 (80%)	0.3018
Well-being	182 (91.5%)	187 (94.9%)	33 (82.5%)	0.0245
Shortness of breath	119 (60.4%)	140 (70.4%)	26 (65%)	0.1149
Sleep	181 (94.8%)	176 (88.9%)	35 (85.4%)	0.0484
Financial distress	135 (69.6%)	94 (49.5%)	21 (52.5%)	0.0002
Spiritual pain	97 (51.9%)	66 (36.1%)	10 (26.3%)	0.0010

neuropathy, or pain with radiation treatments [14–16]. Similarly noted in other studies, we may also be seeing a “response shift” phenomenon where older adults may recalibrate and lower their personal standard of good health over time when facing health decline while not necessarily reconceptualizing or changing their perception of general standards of good and poor health [10, 17]. Due to the survivor effect of those living to the oldest old ages, there may also be possible genetic or lifestyle factors that affect how they perceive symptom frequency and intensity.

Although designed to quantify delirium severity, Breitbart et al. found an MDAS cutoff score of 13 predicted the presence of delirium [18]. In our study, only one adult in the oldest old and older adult group had delirium. Symptom assessment in delirious patients is concerning for the validity of self-reported ESAS especially as it can affect patients’ symptom

**Table 3** Clinical improvement between initial consult and follow-up

Symptom	Age groups			<i>p</i> value
	18–64	65–84	≥ 85	
	<i>N</i> (%)			
Pain	100 (51.8%)	90 (49.2%)	16 (42.1%)	0.2793
Fatigue	92 (47.7%)	89 (48.4%)	17 (43.6%)	0.9777
Nausea	69 (35.9%)	61 (33.2%)	10 (25.6%)	0.0978
Depression	83 (43.9%)	68 (37.2%)	16 (41%)	0.2305
Anxiety	94 (49.7%)	79 (43.2%)	18 (46.2%)	0.1936
Appetite	72 (37.3%)	71 (39.7%)	17 (44.7%)	0.7249
Drowsiness	76 (40%)	67 (37%)	17 (44.7%)	0.8748
Well-being	93 (49.2%)	80 (44.9%)	16 (42.1%)	0.7127
Shortness of breath	80 (42.6%)	71 (39%)	15 (39.5%)	0.4540
Sleep	95 (51.9%)	81 (44.8%)	20 (51.3%)	0.1838

expression. Additionally, MDAS is also not designed to evaluate for early cognitive impairments which can also affect symptom expression. Cognitive impairment affect symptom expression is especially important in the older population as the prevalence of dementia doubles every 5 years of age after age 65, with a prevalence 5–10% in people 65 years and older [19]. For these patients, potential solutions may be the use of a guided assessment with clinic support staff or caregiver assessment to better evaluate symptomatology.

As shown in Table 2, four out of the five most frequent symptoms were the same across all age groups [10]. These symptoms have been shown to consistently be the most common symptoms reported in patients with advanced diseases [6, 10, 20]. There are also a number of differences in the frequency of symptoms among the three age groups with possible explanations related to their differences in cancer diagnoses, severity, and treatment. One difference is the higher frequency of drowsiness in the oldest old population not apparent in the younger population. Drowsiness can be especially important in older adults and may be explained by the aging physiology with potential risk for drug-drug interactions and decreased clearance, putting the older adults at increased risk of delirium [21]. Financial distress was also lowest in the older adult cohort, but increased in the oldest old cohort. Younger cancer patients are at increased risk of financial distress in the setting of higher household expenses such as mortgage payments and also have greater likelihood of dependent children needing financial support [22]. Additionally for older adults, Medicare and social security may help defray costs and potentially lessen the amount of financial distress [23]. Despite this, out of pocket costs for older adults are still significant, especially in prescription medications and home care services [24]. It is also known that frailty is associated with increased health care costs [25]. One hypothesis may be increasing frailty in the oldest old population results in increased utilization of health care services and costs that are superceding their retirement finances.

Despite lower symptom frequencies when compared to the younger age groups, the symptom frequencies in the oldest old is still high, with ≥ 80% reporting fatigue, sleep, appetite, and drowsiness. This is despite their less advanced disease at the time of palliative care referral. It is likely noncancer causes such as multimorbidity and poor functional status, which has been associated with high symptom burden, is attributing to symptom occurrence [26]. In this study, comorbidity was not evaluated, but accrual of comorbidities associated with advancing age likely plays a role in the high symptom expression of cancer patients. For the purposes of delivery of supportive care, the mechanism is not as important as the fact that the symptom is causing the patient suffering and this requires the palliative care team to become involved in alleviation of the suffering in these patients. In caring for our oldest old cancer patients, it is very important for clinicians to

understand these patients continue to experience high symptom frequencies and thus would continue to benefit from timely supportive care referral and intervention.

The American Society of Clinical Oncology has noted the benefit of combining palliative care with standard cancer care to lead to better outcomes including symptoms, quality of life, and patient satisfaction [27]. This approach with palliative care consultation has been shown in prior studies to reduce symptom distress in patients with advanced cancer [28]. In our study, 25–50% of patients reported improvement in symptomatology after a single encounter, with more than 40% improvement in the most troubling symptoms affecting the oldest old adults. The improvement was not statistically different among the age groups. This suggests that outpatient palliative and supportive care can provide meaningful benefits to cancer patients, even in the oldest old adults with lower symptom frequencies. Given the positive improvement seen, early supportive care referral to help manage symptom distress continues to be of utmost importance.

This study has several limitations. First, we reviewed patients at our supportive care clinic in a tertiary care cancer center. The number of oldest old referrals for palliative care was low for the study period. While this may indicate a lower number of oldest old patients seen at our comprehensive cancer center, there may be a referral bias from oncologists regarding the oldest old adults. Pain is often the primary reason for referral in many instances and the lower expression of pain for the oldest old may have been an invisible barrier for referral [29–31]. Further research and upstream assessment of non-pain symptoms may be especially beneficial in serving the oldest old population and help improve referral to palliative care for symptom management. Second, our study only evaluated the changes in symptom severity on the first follow-up visit. Although it was encouraging to note that one contact was able to improve symptom severity for many patients, multiple follow-up encounters may result in greater improvement of symptom severity. Finally, while the sample size was relatively large in the two younger patient cohorts, additional differences may emerge with larger samples of the oldest old adults.

This study continues to expand on the knowledge regarding the symptoms of oldest old cancer patients. In our study, there was a smaller number of oldest old adults referred to the supportive care clinic. However, they were still noted to have high frequency of symptom burden and follow-up in a supportive care clinic improved their symptoms. Our study highlights the need for the oldest old cancer patients to be more frequently referred to supportive care clinic to help with their symptom distress. Given the increasing numbers of cancer in the oldest old population, more research is needed to address the needs of this growing cancer population and focus on the most distressing symptoms that can improve with supportive care intervention.

## Compliance with ethical standards

**Conflict of interest** Dr. Bruera reports grant funding from Helsinn Healthcare. All other authors declare that they have no conflict of interest.

**Ethical approval** The study was approved by the institutional review board (IRB) at the University of Texas MD Anderson. A waiver of informed consent was granted by the IRB in compliance with federal and institutional guidelines.

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