Original Article

Symptoms Burden in Elderly Male Patients Receiving Palliative Care.

Amira Reyad Mohamed¹, Hala Samir Sweed¹, Aya Mostafa Sayed¹, Hesham Mosad Elbehery¹⁹².

¹Department of Geriatrics and Gerontology, Faculty of Medicine, Ain Shams University, Cairo, Egypt.

²Geriatric Palliative Care Unit, Ain Shams University Hospitals, Cairo, Egypt.

ABSTRACT

Background: A high-quality symptom assessment is crucial to providing patient-centered palliative care resulting in positive outcomes for patients and their families.

Objective: To study the symptom burden in elderly male patients receiving palliative care at the geriatric palliative care unit; from the patient's, caregiver's, and physician's perspective.

Subjects and Methods: This cross-sectional study included hundred (100) elderly male patients admitted to palliative care unit (due to cancer and non-cancer conditions) and fulfilling the recruitment criteria. They were subjected to comprehensive geriatric assessment and detailed symptom inquiry utilizing the abbreviated version of Memorial Symptom Assessment Scale (MSAS-SF). The study illustrates the most distressing symptoms affecting quality of life from the caregiver and the attending physician perspective.

Results: The most prevalent symptoms were lack of appetite, lack of energy, cough, difficulty sleeping and pain. The participants had a mean total MSAS score of 0.54, which mean the average the 32 symptom that were investigated. Each symptom is scored out of 4, with possible average ranges from 0 (least) to 4 (highest). Participants reported an average of 8 symptoms. From caregivers' perspective, the most distressing symptoms were shortness of breath, pain and decreased oral intake. From attending physicians' perspective, the most distressing symptoms were shortness of breath, pain, and decrease oral intake. Patients with Mesothelioma had the highest numbers of symptoms.

Conclusion: Elderly male patients admitted to geriatric palliative care unit experience significant symptom burden. Supportive care for patients in palliative care units should be personalized, taking into consideration that specific patient' groups that may require more extensive symptom management.

Keywords: Elderly, palliative care, cancer, memorial symptom assessment scale.

INTRODUCTION

Palliative care is an approach that improves the quality of life of patients with lifethreatening illness and their families by preventing and alleviating suffering through early detection and treatment of pain and other physical, psychosocial, emotional problems, religious, cultural aspects and complex medical legal and ethical issues [1]. Patients requiring such care suffer from various symptoms of varying frequency and intensity, mainly related to neuropsychiatric problems, increased social needs, various spiritual, religious, and cultural considerations, and complex medical legal and ethical issues. Symptom control is an important part of palliative care and important for optimal quality of life [2].

Research has shown that patients with all types of advanced cancer suffer from a variety of and often severe symptoms. Between 11 and 56 different symptoms were identified in two systematic reviews of patients of all ages with advanced cancer [3].

Most cancer patients experience symptoms that vary in frequency and severity depending on the type of cancer, stage, treatment, and other conditions. Patients usually experience more than one symptom at a time [4]. Good symptom management is associated with improved patient and family quality of life, greater treatment compliance, and may even offer survival [5]. Multiple researchers have consistently stressed the necessity of thorough symptom assessment as a fundamental requirement for successful symptom management [6].

There are commonalities in the prevalence of problems across cancer and non-cancer patients, highlighting the need for palliative care to be provided irrespective of diagnosis. The methodological heterogeneity across the studies and the lack of non-cancer studies needs to be addressed in future research [7]. Using standardized questionnaires to collect patient-reported symptoms improves communication between doctors and patients. It is critical that subjective symptom measures be accurate and easy to administer, requiring minimal effort from both clinician and patient [8].

Assessment of symptom burden has also been shown to be useful in non-cancer patients; to identify those patients with high symptom burden who may benefit from consultation with a palliative care team [7].

The Memorial Symptom Assessment Scale has proven its usefulness in detailing the epidemiology of symptoms, understanding symptoms, and role in pain, fatigue, and spirituality, predicts survival, and acts as a pain proxy. This scale has been used in studies of cancer patients and patients with advanced disease [9].

Therefore, the aim of this work was to investigate the burden of symptoms in elderly male patients receiving palliative care (both with cancer and non-cancer diagnoses) in the geriatric palliative care unit, considering the perspective of the patient, the caregiver and attending physician.

METHODS

Selection criteria through which patients admitted to palliative care unit, determined by the following scoring system (A value of 5 of more has the best predictive value for palliative care referral) [10] This is a cross-sectional study of one hundred (100) elderly male patients admitted for palliative care, in the Geriatric Palliative Care unit, Ain Shams University Hospitals. Participants were selected by the convenience sampling method All patients who were admitted to the palliative care unit were screened for their eligibility criteria. All eligible patients who accepted to participate in the study were included; until a total sample size of 100 patients was completed.

• Presence of

metastatic/relapsed/refractory or locally advanced cancer (score=2)

• Eastern Cooperative Oncology Group (ECOG) performance status score (score=0-4)

- Presence of one or more of serious complications of advanced cancer (score=1)
- Presence of other conditions with poor prognosis (e.g., end stage renal failure) (score=1)
- Symptoms uncontrolled by standard approaches for more than 3 days (score=1)
- Patient/

family/social/psychological/nutritional limitations (score=1)

For non-cancer conditions, patients were eligible for palliative care in the presence of a serious illness (e.g., advanced heart failure) and one or more of the following [11]:

- New diagnosis of life-limiting illness for symptom control, patient/family support.
- Progressive weight loss.
- Difficult-to-control physical or emotional symptoms.
- Limited social support in setting of a serious illness (e.g., overwhelmed family caregivers).

The research protocol gained approval from the Ethics Board at Ain Shams University. Every participant provided signed informed consent through a written form. Uncooperative patients due to cognitive impairment, disturbed consciousness or any factors interfering with communication were

excluded. All the study participants were subjected to the following:

- (1) Comprehensive Geriatric Assessment (CGA) including:
- Detailed full history and physical examination
- Assessment of cognitive function, by using The Arabic version [12] of Mini mental status examination [13].

• Screening for depression by the Arabic version [14] of the geriatric depression scale (GDS) [15].

• Functional assessment by using the Activities of Daily Living (ADL)[16] and

Instrumental Activities of Daily Living (IADL) [17].

• Nutritional Assessment by using the Arabic version [18] of Mini Nutritional Assessment (MNA) [19].

(2) Detailed symptom inquiry using the abbreviated version of the Memorial Symptom Assessment Scale, known as MSAS-SF [20]. It is a patient rated scale. Illiterate patient needs assistance in application of the scale.

Patients using the MSAS-SF are prompted to indicate if they have experienced any of the 32 symptoms (26 physical symptoms and 6 psychological symptoms) in the preceding week. Presence (plus frequency if applicable), severity, and distress of all symptoms were checked. Total MSAS score was the average of the symptom scores of all 32 symptoms (higher score = worse health). The MSAS-SF yielded three subscales: a) Global Distress Index (GDI): represents the mean of the frequency of four psychological symptoms and the distress of six physical symptoms, encompassing 10 symptoms (Pain, lack of energy, lack of appetite, feeling drowsy, constipation, dry mouth, feeling sad, feeling irritable, feeling nervous, and worrying), b) Physical Symptom Subscale (PHYS): represents the mean of 12 physical symptom scores, comprising 12 symptoms (Pain, lack of energy, lack of appetite, feeling drowsy, constipation, dry mouth, nausea, vomiting, change in taste, weight loss, feeling bloated, and dizziness), c) Psychological Symptom Subscale (PSYCH): represents the mean of six psychological symptom scores including 6 symptoms (Feeling sad, feeling nervous, worrying, feeling irritable, difficulty

sleeping, and difficulty
concentrating).
Inquiry about the most
distressing symptom affecting
quality of life; considering the
viewpoint of the patient, the
caregiver, and the attending
physician. Level of agreement was
determined.

Statistical analysis

The data analysis was carried out using IBM SPSS software version 28.0 (IBM Corp. Armonk, NY). The sample size was determined using G-power software. Quantitative data were presented using minimum, maximum, mean, and standard deviation, while qualitative data were represented using numbers and percentages (interquartile range, IQR). The normality of the data was assessed using the Shapiro-Wilk test. The one-way ANOVA test was employed to compare more than two continuous variables. Logistic regression analysis was utilized to calculate the crude odds ratio for each variable. Statistical significance was defined as p-values less than 0.05, and highly significant results were considered for values less than 0.01.

RESULTS

The study sample included one hundred (100) elderly male patients. The average age of the participants was70.78 \pm 7.55 with 57% married, with a notable proportion being literate, totaling 56%. Cancer cases were 51%. A significant portion of the patients has been living with cancer for 1-2 years, The most prevalent non-cancer diagnoses were Chronic Obstructive Pulmonary Disease (COPD), followed by chronic liver disease (CLD) (Table 1).

The most prevalent palliative care diagnoses among the study cohort were liver cell failure (15%) and heart failure (14.0%), while the most frequent causes of palliative care admission were pneumonia (45%) and AKI (18% (Table 2). Regarding symptoms frequencies, the most prevalent symptoms were lack of appetite (93%) followed by lack of energy (83%). While, the most severe symptoms were lack of appetite, weight loss, lack of energy, pain, cough, and shortness of breath. Among these symptoms, and the most distressing were shortness of breath followed by pain (Table 3).

The most frequently patient-distressing symptoms as reported by the physicians were shortness of breath, pain and decreased oral intake, with a respective frequency of 29%, 28%. And 21% (Table 4). On the other hand, shortness of breath, pain and decreased oral intake were the most three patient-distressing symptoms, as reported by the caregiver, with a respective frequency of 26%, 25% and 17% (Table 5).

The study participants had a mean total MSAS score of 0.543, which indicates a significant symptom burden in the studied population. The mean global distress index was 0.820. Breaking down MSAS scores into physical and psychological symptom subscales revealed that both contribute to the overall symptom burden. The physical symptom subscale score was 0.782, while the psychological symptom subscale score was 0.57. Participants reported an average of 8.01 symptoms, as shown in table (6). In table (7), a logistic regression analysis was conducted to identify the predictors of the Memorial Symptom Assessment Scale (MSAS) and its respective subscales. The Total MSAS levels were significantly influenced by CKD, depression (positive GDS), malnutrition by MNA, and palliative care diagnosis. Each unit increase in the Total MSAS level was associated with an increase in the risk of depression (GDS) by 19.2 times, malnutrition (MNA) by 10.6 times, and cancer risk as a palliative care diagnosis by 49.2 times. Conversely, each unit increase in the Total MSAS was associated with a decline in the CKD risk (0.05 times). MSAS-GDI was significantly influenced by CVD, CKD, depression (positive GDS), and palliative care diagnosis. Each unit increase in the MSAS-GDI level was associated with an

increase in the chance of depression (GDS) by 6.5 times, and cancer risk in palliative care diagnosis by 9.1 times. In contrast, each unit increase in the Total MSAS was associated with a decrease in the opportunity of CVD (0.29 times), and CKD (0.23 times). The MSAS-PHYS was significantly influenced by CVD, HTN, CKD, malnutrition (MNA), site of tumor, and palliative care diagnosis. Each unit increase in the MSAS- PHYS level was associated with an increase in the risk of malnutrition (MNA) (4.2 times), but with a decrease in the opportunity of CVD (0.19 times), HTN (0.26 times), and CKD (0.14 times).

The MSAS-PSYCH was significantly influenced by depression (positive GDS).

Each unit increase in the MSAS-PSYCH level was associated with an increase in the risk of depression by 5.8 times. Lastly, the number of symptoms in the patients was significantly associated with risk of depression (positive GDS). For each number of symptoms increase, the chance of depression increased by 1.3 times.

Survey scores varied according to palliative care diagnosis. Mesothelioma had the highest Total MSAS (0.747 ± 0.126).) while urinary bladder carcinoma had the highest Physical Symptom Subscale score (1.27 ± 0.298). Regarding the Global Distress Index, multiple myeloma had the highest score. (Table 8).

	Variables	Frequency	Percent
	Married	57	57
Marialater	Widow	40	40
Marital status	Divorced	2	2
	Single	1	1
	Illiterate	44	44
Education.	Primary	11	11
Education	Secondary	19	19
	University	$ \begin{array}{c ccccccccccccccccccccccccccccccccccc$	26
Smoking	Yes	73	73
Malignant status	Malignancy	51	51
	Biliary cystadenocarcinoma	3	5.9
	Cholangiocarcinoma	2	3.9
	Leukemia	1	2
	Liver	8	15.7
	Lung	10	19.6
	Lymphoma	2	3.9
Cite of tumor	Mesothelioma	2	3.9
Site of tumor	Multiple myeloma	3	5.9
	Pancreas	5	9.8
	Prostate	4	7.8
	Rectum	2	3.9
	Skin	1	2
	Urinary bladder	8	15.7
	< <u>1 year</u>	15	29.4
Cancer duration	1-2 years	26	51
	> 2 years	10	19.6
DM	Yes	43	43
COPD	Yes	57	57
CVD	Yes	34	34
Hypertension	Yes	53	53
CLD	Yes	53	53
CKD	Yes	32	32
TIA or stroke	Yes	46	46
Age in years	Mean \pm SD	70.78	± 7.55

Table	(1): D)emograi	phic an	d clin	ical	characte	ristics (of the	study	populatic)n:
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SD: Standard deviation; COPD: chronic obstructive pulmonary disease, CLD: chronic liver disease, CKD: chronic kidney disease, TIA: transient ischemic attack

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Palliative care diagnosis	Frequency	Percent
basal cell carcinoma	1	1
bronchogenic carcinoma	11	11
cancer head of pancreas	5	5
Cholangiocarcinoma	5	5
Respiratory failure	2	2
Liver cell failure	15	15
HCC	7	7
ESRD	9	9
Heart failure	14	14
Leukemia	1	1
Mesothelioma	3	3
Prostatic cancer	4	4
Urinary bladder carcinoma	8	8
Multiple myeloma	3	3
Recurrent cerebrovascular stroke	6	6
Non-Hodgkin lymphoma	3	3
Cause of palliative care admission		
Acute liver injury	2	2
Acute stroke	1	1
AKI	18	18
Anemia	2	2
Cellulitis	2	2
Decrease oral intake	1	1
Difficulty of swallowing	1	1
Pneumonia	45	45
Obstructive jaundice	1	1
Pulmonary embolism	1	1
Sepsis	2	2
Uncontrolled pain	1	1
UTI	12	12
Vomiting	7	7

Table (2): Palliative care diagnosis and cause of admission among patients in the study:

HCC: hepatocellular carcinoma, ESRD: end stage renal disease, AKI: acute kidney injury.

 Table (3): Symptom prevalence among patients in the study (summary of the MSAS for the study participants)

	Frequency				Severity				Distress						
Symptoms	No	Rarely	Occasionally	Frequently	almost constantly	No	Slight	Moderate	Severe	very severe.	not at all	a little bit	some what	quite a bit	very much
difficulty concentrating	92	7	1	0	0	94	6	0	0	0	94	6	0	0	0
pain	37	1	24	31	7	37	3	23	29	8	37	5	20	21	17
lack of energy	17	13	69	1	0	17	22	58	3	0	18	25	50	6	1
cough	35	4	43	16	2	35	5	40	18	2	35	8	37	16	4
feeling nervous	61	18	20	1	0	61	19	20	0	0	61	21	18	0	0
dry mouth	57	22	21	0	0	59	21	20	0	0	63	23	14	0	0
nausea	82	0	13	2	3	81	0	14	2	3	81	0	11	5	3
feeling drowsy	83	13	4	0	0	83	12	5	0	0	83	12	5	0	0
numbness, tingling	100	0	0	0	0	0	100	0	0	0	100	0	0	0	0
difficulty sleeping	36	15	43	4	2	34	19	41	6	0	34	19	32	14	1
feeling bloated	83	8	9	0	0	85	8	7	0	0	87	7	6	0	0
problems with urination	92	4	4	0	0	92	4	3	1	0	92	4	4	0	0
vomiting	81	3	4	7	5	81	6	1	7	5	83	2	2	6	7
shortness of breath	38	1	27	31	3	38	3	23	32	4	38	6	15	17	24
diarrhea	98	0	0	2	0	98	0	0	2	0	98	0	0	1	1
feeling sad	50	2	44	4	0	52	3	40	5	0	51	6	33	10	0
sweats	95	4	1	0	0	95	4	1	0	0	95	4	1	0	0
worrying	76	7	17	0	0	76	7	17	0	0	76	11	13	0	0
sexual problem	100	0	0	0	0	100	0	0	0	0	100	0	0	0	0
itching	97	0	0	3	0	97	0	0	3	0	97	0	0	3	0
lack of appetite	7	8	34	50	1	7	11	41	39	2	9	13	37	39	2
dizziness	97	2	1	0	0	97	3	0	0	0	98	2	0	0	0
difficulty swallowing	99	0	0	3	0	99	0	0	1	0	99	0	0	1	0
feeling irritable	95	2	3	0	0	95	4	1	0	0	96	4	0	0	0
mouth sores	NA	NA	NA	NA	NA	98	2	0	0	0	98	2	0	0	0
change in food tastes	NA	NA	NA	NA	NA	99	1	0	0	0	99	1	0	0	0
weight loss	NA	NA	NA	NA	NA	8	15	46	25	6	7	16	47	23	7
hair loss	NA	NA	NA	NA	NA	99	1	0	0	0	99	1	0	0	0
Constipation	NA	NA	NA	NA	NA	100	0	0	0	0	100	0	0	0	0
swelling of arms or legs	NA	NA	NA	NA	NA	94	1	3	2	0	95	0	4	0	1
I don't look like my self	NA	NA	NA	NA	NA	100	0	0	0	0	100	0	0	0	0

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Table (4): Frequency of distressing symptoms as reported by the physician.

Symptoms	Frequency	Percent
Swelling of arms and legs	3	3
Cough	10	10
decrease oral intake	21	21
Depression	1	1
Diarrhea	1	1
difficulty swallowing	1	1
increase abdominal girth	1	1
Pain	28	28
shortness of breath	29	29
Vomiting	5	5

Table (5): Frequency of symptom distress as reported by the caregivers.

Symptoms	Frequency	Percent
Cough	13	13
decrease oral intake	17	17
Depression	1	1
Diarrhea	1	1
difficulty swallowing	1	1
increase abdominal girth	2	2
loss of energy	1	1
swelling of arms and legs	3	3
Pain	25	25
shortness of breath	26	26
Vomiting	10	9

Table (6): The Memorial Symptom Assessment Scale (MSAS) survey scores among the study population.

Survey scores	Minimum	Maximum	Mean	Std. Deviation
Total MSAS	0.19	1.03	0.543	0.177
Global Distress Index (10 items)	0	1.80	0.820	0.386
Physical Symptom Subscale (12 items)	0	1.83	0.782	0.332
Psychological Symptom Subscale (6 items)	0	1.67	0.570	0.415
Number of symptoms	3.0	16.0	8.010	2.545

MSAS: Memorial Symptom Assessment Scale. STD: standard

	DM	COPD	CVD	HTN	CLD	CKD	TIA or stroke	IADL
Total MSAS	2.1 (0.22-20.3)	1.4 (0.15-	0.18 (0.02-2.1)	0.55	0.40 (0.04-	0.05(0.01-0.72)*	0.47 (0.05- 4 4)	0.40 (0.03-
MSAS- GDI	0.41 (0.14- 1.12	1.2 (0.44- 3.5)	0.29(0.09- 0.92)*	0.40(0.14- 1.16)	0.79 (0.28- 2.2)	0.23(0.07- 0.78)*	0.39 (0.13- 1.1)	0.77 (0.23- 2.6)
MSAS- PHYS	0.60 (0.18- 2.0)	0.95 (0.29- 3.1)	0.19(0.05- 0.77)*	0.26(0.07- 0.92)*	0.57 (0.17- 1.9)	0.14(0.03- 0.63)*	0.64 (0.19- 2.1)	0.75 (0.18- 3.1)
MSAS- PSYCH	0.92 (0.35- 2.4)	1.1 (0.42- 2.8)	0.58 (0.21-1.6)	0.99 (0.38-2.6)	1.0 (0.40- 2.7)	0.56 (0.20-1.6)	1.0 (0.40- 2.7)	0.52 (0.17- 1.6)
Number of symptoms	1.1 (0.94- 1.3)	1.1 (0.96- 1.3)	1.1 (0.91- 1.3)	1.1 (0.95- 1.4)	1.1 (0.89- 1.2)	0.98 (0.82-1.2)	1.0 (0.87- 1.2)	0.95 (0.78- 1.1)

Table (7): Regression model for the predictors of the memorial symptom assessment scale and its subscales.

Table (7) (continue): Regression model for the predictors of the memorial symptom assessment scale and its subscales.

	ADL	GDS	MNA	Age	marital status	Education	site of tumor	cancer duration	palliative care diagnosis
Total MSAS	0.38 (0.02- 7.2)	19.2 (1.7- 219.3)*	10.6 (1.2- 138.0)*	3.8(0.39- 36.7)	0.89(0.09- 8.5)	2.2(0.23- 21.2)	3.58(0.06- 205.5)	0.11(0.001- 26.3)	49.2(3.7- 650.7)**
MSAS- GDI	0.52 (0.14- 1.9)	6.5 (2.0- 21.1)**	2.1 (0.68- 6.6)	0.80(0.29- 2.2)	0.86(0.31- 2.4)	0.60(0.21- 1.7)	2.0(0.32- 12.0)	1.5(0.14- 16.7)	9.1(2.7- 30.9)**
MSAS- PHYS	1.1 (0.23- 5.19)	2.1 (0.61- 6.9)	4.2 (1.0- 17.2)*	1.4(0.42- 4.6)	1.5(0.46- 5.1)	1.1(0.32- 3.5)	18.3(1.2- 267.8)*	1.2(0.07- 21.0)	33.9(6.4- 179.4)**
MSAS- PSYCH	0.37 (0.11- 1.3)	5.8 (2.0- 17.2)**	1.5 (0.54- 4.3)	1.3(0.50- 3.4)	0.46(017- 1.2)	0.48(0.18- 1.3)	1.9(0.27- 13.2)	0.26(0.02- 4.1)	2.7(0.99- 7.2)
Number of symptoms	0.84 (0.68- 1.1)	1.3 (1.1- 1.6)*	1.1 (0.99- 1.3)	1.2(0.99- 1.4)	1.0(0.86- 1.2)	1.0(0.86- 1.2)	0.94(0.68- 1.3)	0.77(0.49- 1.2)	1.1(0.90- 1.23)

Values represent odds ratio (95% confidence interval). *Significant at P-value< 0.05. **Significant at P-value< 0.01. MSAS: Memorial Symptom Assessment Scale; GDI: Global Distress Index; PHYS: Physical Symptom Subscale; PSYCH: Psychological Symptom Subscale; ADL: Activities of Daily Living; IADL: Instrumental Activities of Daily Living; GDS: Geriatric depression scale; CKD: chronic kidney disease.

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Diagnosis	Total MSAS	Global Distress Index	Physical Symptom Subscale	Psychological Symptom Subscale	Number of symptoms
ESRD	0.477 ± 0.035	0.700 ± 0.100	0.778 ± 0.097	0.222 ± 0.192	5.33 ± 0.577
Liver failure	0.403 ± 0.169	0.615 ± 0.273	0.641 ± 0.279	0.410 ± 0.498	6.69 ± 2.63
нсс	0.464 ± 0.139	0.786 ± 0.422	0.738 ± 0.252	0.467 ± 0.378	7.0 ± 2.58
heart failure	0.544 ± 0.192	0.721 ± 0.366	0.589 ± 0.293	0.631 ± 0.444	9.29 ± 3.71
Mesothelioma	0.747 ± 0.126	1.27 ± 0.305	1.08 ± 0.144	1.00 ± 0.333	10.3 ± 0.577
metastatic lung carcinoma	0.590 ± 0.054	0.850 ± 0.164	0.778 ± 0.114	0.528 ± 0.287	8.17 ± 1.17
metastatic prostatic carcinoma	0.640 ± 0.195	0.875 ± 0.411	0.833 ± 0.263	0.792 ± 0.534	9.25 ± 3.86
multiple myeloma	0.693 ± 0.006	1.50 ± 0.000	1.11 ± 0.048	0.889 ± 0.192	9.0 ± 0.000
Neuro palliative	0.638 ± 0.038	0.725 ± 0.395	0.708 ± 0.083	0.625 ± 0.394	9.25 ± 1.50
renal failure	0.475 ± 0.085	0.667 ± 0.308	0.611 ± 0.188	0.639 ± 0.452	8.0 ± 1.67
urinary bladder carcinoma	0.595 ± 0.164	1.27 ± 0.298	1.27 ± 0.275	0.583 ± 0.518	8.0 ± 2.0
P-value	0.005**	0.001**	< 0.001**	0.468	0.109

Table (8): The Scores of the study scales regarding different palliative care diagnoses

Values represent mean \pm SD. The P-value is calculated by the One-way ANOVA test. * Significant at <0.05. ** significant at <0.01.

DISCUSSION

The field of geriatric medicine focuses on the physical, mental, functional, and social aspects of caring for elderly people during acute, chronic, rehabilitative, preventive, and end-of-life care [21]. In palliative care, most patients experience various symptoms, the prevalence and severity of which vary according to diagnosis, stage, treatment(s), and comorbidities. Patients typically experience more than one symptom at any one time [4].

This is across sectional study that was conducted on 100 elderly male patients who were admitted to the palliative care unit in Ahmed Shawki hospital, Ain Shams University Hospitals, Cairo, Egypt, during the duration from February till July 2023. Notably, 73% of the patients in the study were current smokers. This high percentage underscores the prevalence of this risk factor within the study population and favors the development of chronic diseases related to smoking and increases the risk of tumors proved to be more prevalent among smokers than non-smokers. The study sample included a variety of cancer types, showing the heterogeneity of the study population. Different cancers can lead to distinct symptom burdens, necessitating customized palliative care approaches. The presence of lung, liver and urinary bladder cancers in the sample were particularly of highest prevalence. Regarding the duration of cancer among participants in our study, a substantial portion of patients has been living with cancer for 1-2 years, accounting for 51% of the sample, while the least proportion had more than 2 years duration, representing 19.6% of cancer patients in our study. Understanding the duration of cancer is crucial for designing palliative care interventions that cater to both short-term and long-term needs. Moreover, as the duration increases the expected burden of disease increases.

Our study showed valuable insights into the diagnoses and reasons for patient admission in the palliative care unit. First, the results portray a broad spectrum of palliative care diagnoses, with the most prevalent being liver cell failure (15%) and heart failure (14%). On the other hand, the most frequent causes of palliative care admission are pneumonia (45%) and AKI (18%). This came like the results showed by Capelastegui et al, [22] in their prospective study, who found a substantial burden of CAP, estimating an annual incidence of 3.1 cases per 1000 adults per year, with a 42.8% rate of hospital admission.

Palliative care diagnoses and reasons for admission vary widely throughout research due to the vulnerability of these patients. This was the case for the study by Galal et al, [23] who found the main causes of palliative cancer care admissions to be pain (65.7%), vomiting (31.4%), dehydration (22.9%), fever (22.9%) and infection (20%). The same group of symptoms were also reported by Capelastegui et al, [22] where the most prevalent trigger causes of hospital admission were pain, dyspnea, and worsening of the general health. This diversity of results can be attributed to the Our study also focused on the symptoms reported by the patients, exploring its frequency, severity and the distress related to these symptoms. Regarding the frequencies, symptoms like difficulty concentrating, numbness/ tingling, problems with urination, feeling drowsy, feeling bloated, problems with urination, feeling nervous, vomiting, nausea, diarrhea, sweats, worrying, sexual problem, itching, dizziness, difficulty swallowing, and feeling irritable are rarely prevalent in the study population. However, symptoms of highest prevalence were lack of appetite, lack of energy, cough, difficulty sleeping, pain, shortness of breath, feeling sad and dry mouth. Regarding symptoms' severity, the most severe symptoms observed in our cohort were lack of appetite, weight loss, lack of energy, pain, cough, and shortness of breath, while the most distressing symptoms were shortness of breath followed by pain. This came

matched with a number of other studies, for instance, when comparing to the studies of Tai et al, [24] and that of Lis et al, [25], as the former recruited 824 patients with advanced cancer, and found pain (78.4%), anorexia (64.4%) and constipation (63.5%) to be the most common and severe symptom, while the latter recruited 386 patients and the resulting symptoms were tiredness (32.8%), difficulty sleeping (23.8%), and lack of appetite (20.2%), whereas pain (28.9%) and tiredness (24.3%) were most bothersome. These results were also similar to those reported by Huijer et al, [26] who performed a cross-sectional study on 200 adult cancer patients from three oncology units at a major tertiary teaching hospital who found the most prevalent symptom to be lack of energy. Also, the studies by Tsai et al, [27] and Teunissen et al, [28] resembled our results in the symptoms of fatigue, pain, lack of energy, weakness, and appetite loss being the most prevalent among their cohort's diversity of palliative care diagnosis and stages of illness among the cohorts in each of these studies. In our work, we found the three most distressing symptoms, as reported by the physicians and caregivers, were shortness of breath, pain and decrease oral intake. This was partially similar to the study performed by Noorani & Montagnini [29] where the attending palliative care specialists reported pain also to be one of three symptoms that are most frequent, most intensive, most distressing, and most treatment-requiring symptoms. The other two symptoms were lack of energy and tiredness. These reported symptoms (shortness of breath, pain and decreased oral intake) were also reported by caregivers to be most distressing for the patients in our study, and were also reported by caregivers in other studies, as the study done by Okamoto et al, [30] who analyzed 805 questionnaires fulfilled by caregivers, and aimed to explore the most frequent and distressing symptoms reported by caregivers of palliative patients at end of life. Anorexia was the most distressing symptom experienced by family members, followed by weight loss, pain, edema, and dyspnea.

In our work, we investigated the symptom burden among the study population through the MSAS total score and its subscales. We used the total MSAS, Global Distress Index (MSAS-GDI), Physical Symptom Subscale (MSAS-PHYS), Psychological Symptom Subscale (MSAS-PSYCH) and number of symptoms. The mean for total MSAS score was 0.543. Furthermore, the Global Distress Index score was 0.820, providing insight into ten of the physical and psychological distress associated with these symptoms. To further differentiate between the physical and psychological symptom burden in palliative care patients, we used the Physical Symptom Subscale (MSAS-PHYS) and the Psychological Symptom Subscale (MSAS-PSYCH). The dissection of MSAS scores into physical and psychological symptom subscales elucidates that both aspects contribute to the overall symptom burden, and none of them should be overlooked. In our study population, the burden caused by physical symptoms showed a mean of 0.78, which was higher than that caused by psychological symptoms with a mean of 0.57. Lastly, regarding the number of symptoms, the study population reported an average of 8.01 symptoms.

Our results were close to the study done by Yildirim et al, [31] that was conducted in an outpatient chemotherapy unit at a university hospital in Izmir, Turkey. They found an average total MSAS score of (0.8), the Global Distress Index score of (1.1), The Physical Symptom Subscale score of (0.94), the Psychological Symptom Subscale score of (0.92). However, another cross-sectional study by Huijer et al, [26] that was conducted on 200 adult cancer patients from three oncology units and showed a wider range of variation with our results, as they found a significantly higher burden of symptoms in their study. The patients involved in the study exhibited an average total MSAS score of (2.30), the Global Distress Index score of (2.24), The Physical Symptom Subscale score of (2.23), the Psychological Symptom Subscale score of (2.46). We think that their reported higher burden could be attributed to

the difference in selection criteria as their patients were all receiving active treatment for cancer, which is expected to increase the burden of symptoms, and this was not the case among our study cohort. We investigated the relation between the various MSAS subscales with the studied patient characteristics including the chronic diseases, CGA tools, and the main palliative care diagnosis. A logistic regression analysis was conducted to determine the potential risk factors of the Memorial Symptom Assessment Scale (MSAS) and its subscales (MSAS-GDI, MSAS-PHYS, MSAS-PSYCH), in addition to the number of the symptoms for the different comorbidities and Comprehensive Geriatric Assessment in the study.

Regarding the Total MSAS: depression (positive GDS), malnutrition (by MNA), and diagnosis of cancer were predictors of higher total score, leading to higher symptom burden among palliative care patients. The effect of these conditions on the patients' symptom burden has been widely studied, and various agreements with our results have been reported. For instance, the study done by Change et al, [9] who found a significant difference in physical symptom prevalence between cancer and non-cancer patients. The former group reported a significantly higher prevalence of pain, nausea, unpleasant taste, vomiting and constipation, which are symptoms mostly related to their primary cancer or due to treatment effects. Likewise, a study done by Mao et al, [32] found that the rates of ongoing pain, psychological distress, and insomnia among cancer survivors were 34%, 26%, and 30%, respectively, and were significantly higher than controls without a history of cancer (18%, 16%, and 17%). Regarding depression, its severity was found to be significantly correlated with the number of physical symptoms, symptom distress and symptom severity independent of cancer type, functional status, chemotherapy status and survival time, as reported by Fitzgerald et al, [33]. Even when using other assessment scales such as Edmonton Symptom Assessment Scale (ESAS), as done by

Grotmol et al, [34] in their work that included 935 patients and showed that patients with depression disorder reported significantly higher scores on ESAS items and a twofold higher symptom burden compared with those without.

Malnutrition had an impact on the severity of symptoms and health-related outcomes in individuals with this syndrome. Malnutrition is linked to difficulties like a higher chance of a lower quality of life, a longer hospital stays, higher costs, and other complications like postoperative complications, a lower response to therapy, a lower 90-day survival rate, and an increased death rate [17][35]. Some of the chronic disorders among our study sample were also found to have a substantial impact on the MSAS-GDI. These

conditions specifically included cancer as a palliative care diagnosis and depression. An inverse relationship between the likelihood of developing CVD and CKD and the increase in MSAS-GDI was found, and this significant association was still evident even when symptoms were divided into physical and psychological groups.

Regarding MSAS-PHYS, it was significantly affected by malnutrition (MNA) and cancer diagnosis in palliative care. This highlights the significant impact of malnutrition and cancer on increasing physical symptoms in palliative care patients. The high prevalence and symptom burden of malnutrition in the last days of life is due to starvation and inflammatory cachexia, which leads to a significant increase in symptoms in the last days of life. Other symptoms contributing to malnutrition and dehydration at the end of life include anorexia, dysphagia, weakness, and confusion [12].

Further confirmation for the relationship between malnutrition, depression and quality of life was reported in a study [36], where a statistical significance was found between those entities, highlighting that the quality of life of palliative care patients could be improved by providing adequate nutrition and psychological support. However, this association was not observed in other diseases, where each increase in MSAS-PHYS was associated with a decrease in CVD, HTN and CKD, compared to other studies, these diseases were often associated with increased symptoms, which is not consistent with our results. This was true for the study by Almutary et al, [37] who showed that CKD patients experience multiple symptoms due to both the disease and its treatment, a condition which exerts a total symptom burden on people with CKD. This variation in results can be explained by the limited sample size of our study.

A set of psychological symptoms was significantly associated with and predicted depression. This significant effect of depression on number of symptoms not only influenced the MSAS-PSYCH but also predicted a higher number of symptoms in our study population. Depression was also found to be a major cause of suffering to patients with advanced diseases and their families [29], and it was recommended always to be screened, diagnosed, and acted on, and should not be considered a normal event in advanced disease patients [38].

Examining palliative diagnoses that cause the most symptoms, we found that the most burdensome diagnoses are mesothelioma, multiple myeloma, UB cancer, heart failure, and prostate cancer. The effect of diagnosis on number of symptoms was statistically significant for total score, MSAS-GDI and MSAS-PHYS, while it was not significant for MSAS-PSYCH and number of symptoms. Mesothelioma had the highest Total MSAS (0.747 ± 0.126) and the second highest MSAS-GDI (1.27 ± 0.305) . Our results agreed with Marengoni et al, [21]. This significant burden resulted from mesothelioma patients being referred for palliative care late in the disease, suggesting that earlier integration of palliative care should be considered to alleviate suffering at all stages of the disease - not just at the end of life.

Mercadante et al, [39] found that mesothelioma affected the emotional functioning in patients and their family members to a degree that sometimes exceeds its effect on physical functioning in patients and their caregivers. Also, Moore et al, [7] reported high rates of anxiety (67%), depression (52%), fear (51%) and isolation in patients with mesothelioma. Multiple myeloma scored the second highest mean in total MSAS (0.693 ± 0.006) and in Physical Symptom Subscale score (1.11 \pm 0.048). Moreover, it was the highest in mean MSAS-GDI (1.50 ± 0.000). Our results coincided with the results of 0Zaleta et al. [40] who showed that patients with MM experience greater symptom burden and poorer quality of life compared with those with other hematologic cancers. This was mainly caused by fatigue, pain, and limited physical function, and nearly 50% were distressed by sleep difficulties. Also, this was also supported by Dooley-Hash et al, [41] who stated that the four most prevalent symptoms, occurring in at least 50% of study participants, were fatigue (98.8%), constipation (66.5%), pain (58.6%) and tingling in the hands/feet (53.4%). A diagnosis of MM is a shockingly traumatic experience associated with depressive symptoms and feelings of hopelessness, helplessness and despair. Depressive status is a common psychopathological feature of MM, which worsens as the disease progresses.^[37] This agrees with our results when taking into consideration that the Total MSAS includes some of the psychological symptoms affecting the total symptom burden.

UB carcinoma also showed one of the highest symptom burdens, especially on the physical side. Patients with UB carcinoma scored the highest mean Physical Symptom Subscale score (1.27 ± 0.298) and the second highest mean for MSAS-GDI (1.27 ± 0.298) . This devastating effect was also reported by Schneidewind et al, [42] who found that the burden of advanced urothelial cancer is attributable to the disease and treatment characteristics (hematuria, urinary frequency and urgency, and pain are among the most common signs and symptoms). Additionally, symptoms such as dysuria, constipation, fatigue, emotional distress, and urinary obstruction adversely impact health-related

quality of life in advanced bladder cancer. Treatment-related side effects, like fatigue and the impact on daily activities, are also reported as relevant to these patients. Regarding the number of symptoms, heart failure scored the second highest mean for number of symptoms among our study cohort (9.29 ± 3.71) but was statistically nonsignificant. It is well-known in literature that patients with CVD demonstrated significant symptom burden. Patients with CVD referred to PC are more likely to be older and have poorer functional status. While both patients with CVD and cancer had high symptom burden, dyspnea was more distressing and more commonly seen in CVD patients. [43] The significant symptom burden in patients with advanced CVD was reported by Gavazzi et al, [44] who included breathlessness and gastrointestinal symptoms to be the most common presentations prompting emergency department admission. Although the results showed a high number of heart failure symptoms, they were statistically insignificant. This may be due to different sample selection criteria and sample size, which led to different results in the two studies.

CONCLUSION

Elderly male patients admitted to geriatric palliative care unit experience significant symptom burden. There are different levels of agreement between the patients, their caregivers and their attending physicians as regards the most distressing symptoms. Symptom burden may vary according to palliative care diagnosis and comorbid conditions. Symptom burden must be assessed regularly in palliative care patients to determine the best plan of management. Tailoring supportive care for palliative patients is crucial; especially considering certain groups that may require more extensive symptom management. Paying particular attention to caregivers' perspectives and needs is integral within the palliative care strategy.

Limitations of the study

We recognize that this study had certain limitations. Sample size did not aim to address symptom burden separately for each palliative care diagnosis, so it was difficult to find significant relationships as regards these diagnoses.

REFERENCES

- 1. Tinetti ME, Esterson J, Ferris R, Posner P, Blaum CS. Patient priority-directed decision making and care for older adults with multiple chronic conditions. Clinics in geriatric medicine. 2016 May 1;32(2):261-75.
- 2. Ferrell BR, Twaddle ML, Melnick A, Meier DE. National consensus project clinical practice guidelines for quality palliative care guidelines. Journal of palliative medicine. 2018 Dec 1;21(12):1684-9.
- 3. Gilbertson-White S, Aouizerat BE, Jahan T, Miaskowski C. A review of the literature on multiple symptoms, their predictors, and associated outcomes in patients with advanced cancer. Palliative & supportive care. 2011 Mar;9(1):81-102.
- 4. Al Qadire M, Al Khalaileh M. Prevalence of symptoms and quality of life among Jordanian cancer patients. Clinical nursing research. 2016 Apr;25(2):174-91.
- 5. Breuer B, Fleishman SB, Cruciani RA, Portenoy RK. Medical oncologists' attitudes and practice in cancer pain management: a national survey. J Clin Oncol. 2011 Dec 20;29(36):4769-75.
- 6. Fu L, Hu Y, Lu Z, Zhou Y, Zhang X, Chang VT, Yang Y, Wang Y. Validation of the simplified chinese version of the memorial symptom assessment scale—Short form among cancer patients. Journal of Pain and Symptom Management. 2018 Jul 1;56(1):113-21.
- 7. Moore S, Darlison L, Tod AM. Living with mesothelioma. A literature review. European journal of cancer care. 2010 Jul;19(4):458-68.
- 8. Naaktgeboren MW, Magdelijns FJ, Janssen DJ, van den Beuken-van Everdingen MH. Added value of early consultation of an inpatient palliative care team in hospitalized older patients with high symptom burden: a prospective comparative study. American

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Journal of Hospice and Palliative Medicine®. 2021 Oct;38(10):1258-64.

- 9. Chang VT, Hwang SS, Feuerman M, Kasimis BS, Thaler HT. The memorial symptom assessment scale short form (MSAS-SF) validity and reliability. Cancer: Interdisciplinary International Journal of the American Cancer Society. 2000 Sep 1;89(5):1162-71.
- Dans M, Smith T, Back A, Baker JN, Bauman JR, Beck AC, Block S, Campbell T, Case AA, Dalal S, Edwards H. NCCN guidelines insights: palliative care, version 2.2017. Journal of the National Comprehensive Cancer Network. 2017 Aug 1;15(8):989-97.
- 11. Center to Advance Palliatice Care (CAPC) Palliative Care Referral Criteria. Available at:

https://www.capc.org/documents/download/2 86/. Accessed on: 1 September 2022

- 12. El Okl MA, El Banouby MH, El Etrebi A. Prevalence of Alzheimer dementia and other causes of dementia in Egyptian elderly. MD thesis, faculty of medicine, Ain Shams University. 2002.
- 13. Folstein MF, Folstein SE, McHugh PR. "Mini-mental state": a practical method for grading the cognitive state of patients for the clinician. Journal of psychiatric research. 1975 Nov 1;12(3):189-98.
- 14. Chaaya M, Sibai AM, El Roueiheb Z, Chemaitelly H, Chahine LM, Al-Amin H, Mahfoud Z. Validation of the Arabic version of the short Geriatric Depression Scale (GDS-15). International psychogeriatrics. 2008 Jun;20(3):571-81.
- 15. Metwally AS, El-Banouby MH, Mortagy AK, Ghanem M. Prevalence of depression among Egyptian geriatric community. Faculty of Medicine, Ain Shams University. 1998.
- 16. Katz S. Assessing self-maintenance: activities of daily living, mobility, and instrumental

activities of daily living. Journal of the American Geriatrics Society. 1983 Dec 1;31(12):721-7.

- Lawton MP, Brody EM. Assessment of older people: self-maintaining and instrumental activities of daily living. The gerontologist. 1969 Oct 1;9(3_Part_1):179-86.
- 18. Abd-Al-Atty MF, Abou-Hashem RM, Abd Elaziz KM. Prevalence of malnutrition in recently hospitalized elderly in Cairo using a valid and reliable short form of Arabic version of Mini-Nutritional Assessment (MNA-SF-A). Middle East Journal of Age and Ageing. 2012 Jul 1;9(4):8-12.
- 19. Vellas B, Villars H, Abellan G, Soto ME, Rolland Y, Guigoz Y, Morley JE, Chumlea W, Salva A, Rubenstein LZ, Garry P. Overview of the MNA®-Its history and challenges. Journal of Nutrition Health and Aging. 2006 Nov 1;10(6):456.
- 20. Portenoy RK, Thaler HT, Kornblith AB, Lepore JM, Friedlander-Klar H, Kiyasu E, Sobel K, Coyle N, Kemeny N, Norton L, Scher H. The Memorial Symptom Assessment Scale: an instrument for the evaluation of symptom prevalence, characteristics and distress. European Journal of Cancer. 1994 Jan 1;30(9):1326-36.
- 21. Marengoni A, Angleman S, Meinow B, Santoni G, Mangialasche F, Rizzuto D, Fastbom J, Melis R, Parker M, Johnell K, Fratiglioni L. Coexisting chronic conditions in the older population: Variation by health indicators. European journal of internal medicine. 2016 Jun 1;31:29-34.
- 22. Capelastegui A, España PP, Bilbao A, Gamazo J, Medel F, Salgado J, Gorostiaga I, Esteban C, Altube L, Gorordo I, Quintana JM. Study of community-acquired pneumonia: incidence, patterns of care, and outcomes in primary and hospital care. Journal of Infection. 2010 Nov 1;61(5):364-71.
- 23. GALAL KM, EL-MESIDY SA, ALI E, AL-SIRAFY SA. Causes of admission to a palliative care inpatient unit in an Egyptian cancer center. Pain. 2010;46:65-7.
- 24. Tai SY, Lee CY, Wu CY, Hsieh HY, Huang JJ, Huang CT, Chien CY. Symptom severity of patients with advanced cancer in palliative care unit: longitudinal assessments of symptoms improvement. BMC palliative care. 2016 Dec; 15(1):1-7.
- 25. Lis CG, Gupta D, Lammersfeld CA, Markman M, Vashi PG. Role of nutritional status in

predicting quality of life outcomes in cancer– a systematic review of the epidemiological literature. Nutrition journal. 2012 Dec;11:1-8.

- 26. Huijer HA, Sagherian K, Tamim H. Validation of the Arabic version of the memorial symptom assessment scale among Lebanese cancer patients. Journal of pain and symptom management. 2015 Oct 1;50(4):559-65.
- 27. Tsai JS, Wu CH, Chiu TY, Hu WY, Chen CY. Symptom patterns of advanced cancer patients in a palliative care unit. Palliative Medicine. 2006 Sep;20(6):617-22.
- 28. Teunissen SC, Wesker W, Kruitwagen C, de Haes HC, Voest EE, de Graeff A. Symptom prevalence in patients with incurable cancer: a systematic review. Journal of pain and symptom management. 2007 Jul 1;34(1):94-104.
- 29. Noorani NH, Montagnini M. Recognizing depression in palliative care patients. Journal of palliative medicine. 2007 Apr 1;10(2):458-64.
- 30. Okamoto Y, Morita T, Tsuneto S, Aoyama M, Kizawa Y, Shima Y, Miyashita M. Bereaved family members' perceptions of the distressing symptoms of terminal patients with cancer. American Journal of Hospice and Palliative Medicine®. 2018 Jul;35(7):972-7.
- **31.** Yildirim Y, Tokem Y, Bozkurt N, Fadiloglu C, Uyar M, Uslu R. Reliability and validity of the Turkish version of the Memorial Symptom Assessment Scale in cancer patients. Asian Pac J Cancer Prev. 2011 Jan 1;12(12):3389-96.
- **32.** Mao JJ, Armstrong K, Bowman MA, Xie SX, Kadakia R, Farrar JT. Symptom burden among cancer survivors: impact of age and comorbidity. The Journal of the American Board of Family Medicine. 2007 Sep 1;20(5):434-43.
- **33.** Fitzgerald P, Lo C, Li M, Gagliese L, Zimmermann C, Rodin G. The relationship between depression and physical symptom burden in advanced cancer. BMJ supportive & palliative care. 2015 Dec 1;5(4):381-8.
- 34. Grotmol KS, Lie HC, Loge JH, Aass N, Haugen DF, Stone PC, Kaasa S, Hjermstad MJ. Patients with advanced cancer and depression report a significantly higher symptom burden than non-depressed patients. Palliative & supportive care. 2019 Apr; 17(2):143-9.

- **35.** Leandro-Merhi VA, Aquino JL. Relationship between nutritional status and the clinical outcomes of patients with and without neoplasms according to multiple correspondence analysis. Arquivos de gastroenterologia. 2017 Mar 16;54:148-55.
- **36.** Efendioglu EM, Cigiloglu A, Turkbeyler IH. Malnutrition and depressive symptoms in elderly palliative care patients. Journal of Palliative Care. 2022 Oct;37(4):503-9.
- **37.** Almutary H, Bonner A, Douglas C. Symptom burden in chronic kidney disease: a review of recent literature. Journal of Renal care. 2013 Sep;39(3):140-50.
- **38.** Antunes B, Rodrigues PP, Higginson IJ, Ferreira PL. Determining the prevalence of palliative needs and exploring screening accuracy of depression and anxiety items of the integrated palliative care outcome scale–a multi-centre study. BMC Palliative Care. 2020 Dec; 19(1):1-9.
- **39.** Mercadante S, Adile C, Caruselli A, Ferrera P, Costanzi A, Marchetti P, Casuccio A. The palliative-supportive care unit in a comprehensive cancer center as crossroad for patients' oncological pathway. PLoS One. 2016 Jun 22;11(6):e0157300.
- 40. Zaleta AK, Miller MF, Olson JS, Yuen EY, LeBlanc TW, Cole CE, McManus S, Buzaglo JS. Symptom burden, perceived control, and quality of life among patients living with multiple myeloma. Journal of the National Comprehensive Cancer Network. 2020 Aug 1;18(8):1087-95.
- **41.** Dooley-Hash S, Adams M, Walton MA, Blow FC, Cunningham RM. The prevalence and correlates of eating disorders in adult emergency department patients. International Journal of Eating Disorders. 2019 Nov;52(11):1281-90.
- 42. Schneidewind L, Kiss B, Zengerling F, Borkowetz A, Graf S, Kranz J, Dräger DL, Graser A, Bellut L, Uhlig A. Gender-specific outcomes in immune checkpoint inhibitor therapy for advanced or metastatic urothelial cancer: a systematic review and metaanalysis. Journal of Cancer Research and Clinical Oncology. 2023 Apr 20:1-0.
- 43. Voumard R, Rubli Truchard E, Benaroyo L, Borasio GD, Büla C, Jox RJ. Geriatric palliative care: a view of its concept, challenges and strategies. BMC geriatrics. 2018 Dec;18:1-6.

44. Gavazzi A, De Maria R, Manzoli L, Bocconcelli P, Di Leonardo A, Frigerio M, Gasparini S, Humar F, Perna G, Pozzi R, Svanoni F. Palliative needs for heart failure or chronic obstructive pulmonary disease: results of a multicenter observational registry. International Journal of Cardiology. 2015 Apr 1;184:552-8.