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RESEARCH

Characteristics of patients who die in an acute palliative care unit

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Abstract

Aim To evaluate the characteristics of patients with advanced cancer who die in an acute palliative care unit (APCU), and the risk factors for death in APCU.

Methods Adult consecutive patients with advanced cancer admitted to the APCU in a period of 13 months were prospectively assessed. At APCU admission, epidemiologic data, characteristics of admission, cachexia, being on–off anticancer treatment, and Edmonton Symptom Assessment System (ESAS) and MDAS (Memorial Delirium Assessment Scale) were assessed. Patients who died in APCU were extrapolated from the entire sample. A similar random sample of patients who were discharged alive in the same study period, matched for age and gender, was selected for comparison.

Results Fifty-four patients (12%) died in APCU. Statistical differences between died and discharged patients were found in MDAS ($p = < 0.0005$), admission for cognitive/clinical decline ($p = < 0.0005$), referral from specialistic home palliative care ($p < 0.0005$), cachexia ($p = 0.018$), being off cancer treatment ($p = < 0.0005$), and symptom burden (total ESAS) ($p = 0.002$). At the multivariate analysis, independent factors associated with dying in APCU were MDAS ($p = 0.006$), referral from specialistic home palliative care ($p = 0.025$), being off cancer treatment ($p = 0.002$), pain and dyspnea intensity (< 0.05 and $p = 0.038$, respectively), and total ESAS ($p = 0.025$).

Conclusion Mortality risk in APCU is associated with home palliative care referral, high symptom burden, and being off-cancer treatment. More proactive and timely end-of-life care is needed for these patients.

Keywords Advanced cancer · Palliative care · Mortality · Acute palliative care unit

Introduction

Patients with advanced cancer often suffer from severe physical and psychosocial distress that requires intensive interdisciplinary palliative care [1, 2]. Acute palliative care unit (APCU) in a comprehensive cancer center provides aggressive symptom management and assists with the transition to palliative care [2–6]. The APCU has a determining role among the settings of palliative care: it allows rapid pain and symptom control with specialized personnel at any stage of disease even in patients receiving anticancer therapy and provides the possibility of reassessment, using hospital facilities and consultations for the transition of care with experts communicating with family. When anticancer treatments are no longer advised, patients can be referred to other palliative care services, including outpatient clinics, home palliative care, or inpatient hospice [7]. In some cases, patients are admitted to APCU before receiving any anticancer treatment, due to symptom burden or very advanced disease [8]. During this short and intense hospitalization, patients and clinicians are faced with the challenge of making different treatments and discharge planning decisions, which are dependent on the expected patient survival.

Mortality rate in APCU has been reported to be largely variable, possibly reflecting the attitudes to admit patients in an early stage of disease or in a very advanced stage of disease. This often depends on the availability of local resources rather than on a precise choice to select patients to be admitted to APCU [9]. In the APCU at La Maddalena Cancer Center, a limited number of patients have been reported to die during admission [7], possibly because most

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patients were seen during the oncologic treatment for symptom management and specialistic palliative care assessment [10]. The identification of relevant prognostic factors for the unique population of APCU patients is of paramount importance for a timely end-of-life care approach. In some prospective and retrospective studies with different designs and performed in different settings of palliative care, symptom burden was frequently reported to predict death during admission [11–16]. The hypothesis was that a severe symptom burden at admission to an APCU was more likely to be associated with death during admission.

The aim of this study was to evaluate the characteristics of patients with advanced cancer who die in the APCU to evaluate the risk factors for death in a high-volume APCU.

Methods

The APCU at La Maddalena Cancer Center in Palermo is a 12-bed unit in a comprehensive cancer center of 200 hundred beds and is connected with a 10-bed hospice on the same floor, with an available home palliative care service, with a bidirectional referral. In addition to serving the APCU, the supportive/palliative care team also provides services through a consultation-based service and the outpatient clinic. Sources of admission are various and include transfer from the medical oncology ward, outpatient oncology clinic, other department units, specialistic home palliative care, and other hospitals, either as planned admission or as an emergency [7].

Procedures

All consecutive adult patients with advanced cancer admitted to the APCU between April 2023 and April 2024 were prospectively assessed.

At APCU admission (T0), age, gender, primary tumor, Karnofsky status, and the presence of cachexia were recorded, as well as characteristics of admission (re-admission, planned, emergency, and transfer), reason for admission, referral (specialistic home palliative care, home, transfer, other hospitals, being on–off anticancer treatment, MDAS (Memorial Delirium Assessment Scale), and awareness of disease and prognosis (aware, partially aware, unaware). The Edmonton Symptom Assessment System (ESAS) was also recorded. A screening test for the history of alcohol dependence (CAGE: cut down, annoy, guilt, eye-opener), was performed.

Patients were considered off cancer treatment (no longer candidate for anticancer treatments), on therapy (when oncologists considered the patient to be a candidate for further treatments), or uncertain (when oncologists were uncertain on the next step). MDAS is routinely used in APCU and has been used in previous studies to quantify the changes in cognitive function in advanced cancer patients [7]. ESAS is a validated tool widely used to measure the severity of physical and psychological symptoms, including pain, weakness, nausea, depression, anxiety, drowsiness, dyspnea, poor appetite, poor sleep, and poor feeling of well-being on a numeric rating scale ranging from 0 to 10 [17]. CAGE is considered to be positive by "yes" answer to at least two of the questions for men, and at least one for women [18]. According to recognized diagnostic criteria, cachexia was defined as an ongoing loss of skeletal muscle mass (with or without loss of fat mass) that cannot be fully reversed by conventional nutritional support and leads to progressive functional impairment [19].

From this consecutive sample of patients, those who died in APCU were extrapolated. This group was compared with a similar random sample of patients matched for age and gender, who were discharged alive in the same period.

The study was conducted in accordance with the Declaration of Helsinki and was approved by the local ethical committee of Palermo 1, Azienda Ospedaliera Universitaria. Patients provided their informed consent.

Statistical analysis

Differences between groups were assessed using the chi-square test or Fisher's exact test, as appropriate for categorical variables, and the independent Student's *t*-test for continuous parameters. The univariate analysis of variance (ANOVA) was performed for parametric variables with multiple comparisons. Variables significantly related to patient groups were analyzed using a multivariate logistic regression model to examine the correlation between patient characteristics (independent variables) and patient groups (dependent variable). To ensure a more conservative approach, all significant variables in the univariate analysis were included in a multivariate backward stepwise logistic regression model. Crude and adjusted odds ratios (crude ORs and adj-ORs) with corresponding 95% confidence intervals (CIs) for the variables analyzed one by one or evaluating together the significant variables at the univariate analysis were calculated. Effect sizes were used to express the mean score differences between patient subgroups in relation to the standard deviations. Data were analyzed using IBM SPSS Statistics, version 22 (IBM Corp., Armonk, NY, USA). All *p*-values were two-sided, and a *p*-value of less than 0.05 was considered statistically significant.

Results

Of 449 patients who were admitted to APCU in the study period, 54 patients (12%) died in the unit. The mean age of this population was 69.6 ± 9.4 years (range, 30–92 years).

Twenty-nine patients were males (53.7%). The most common primary cancer types were lung and gastrointestinal (35.2% and 29.6%, respectively). A random sample of 54 patients, matched for age and gender, who were discharged alive in the same study period was selected for comparison. The baseline characteristics of 108 patients are summarized in Table 1.

At admission, statistical differences were found in MDAS ($p = < 0.0005$), referral from specialistic home palliative care ($p < 0.0005$), cachexia ($p = 0.018$), being off anticancer treatment ($p = < 0.0005$), and reason of admission for cognitive/clinical decline ($p = < 0.0005$).

Patients who died in the APCU showed higher symptom distress upon APCU admission compared with patients who were discharged alive from the APCU. These patients had higher mean ESAS scores for pain ($p = < 0.0005$), dyspnea ($p = < 0.0005$), depression ($p = < 0.0005$), drowsiness ($p = 0.002$), nausea ($p = < 0.0005$), poor appetite ($p = < 0.0005$), and poor well-being ($p = 0.028$). Total ESAS was also significantly higher in patients who died in the APCU ($P = 0.002$) (see Table 2).

In the univariate analysis, the following factors were associated with dying in APCU: higher MDAS ($p < 0.0005$), referral from specialistic home palliative care ($p < 0.0005$), diagnosis of colon cancer ($p = 0.046$), less disease awareness

Table 1 Characteristics of patients

	Died APCU	Discharged alive	*p*
N°	54	54	
Age	69.6 ± 9.4	68.6 ± 12.6	0.641
Gender (M/F)	29/25	29/25	1.0
Karnofsky	36.9 ± 10.6	37.8 ± 11.2	0.661
MDAS	5.8 ± 2.6	1.9 ± 2.4	< 0.0005
Referral			
Referred from specialistic home palliative care	17	4	
Referred from oncologist (from home or transfers)	29	49	< 0.0005
Referred from other hospitals	2	1	
Referred from surgery Unit	6	0	
CAGE positive	2	0	0.118
Cachexia			
No	26	39	
Yes	27	15	0.018
Not evaluated	1	0	
Cancer treatment: on–off naive			
On	17	54	
Off	18	0	< 0.0005
Naive	19	0	
Primary diagnosis			
Urogenital	6	6	
Lung	19	28	
Gastrointestinal	16	16	0.046
Breast	3	3	
Colon	9	0	
Head and neck	1	1	
Principal reason for admission (multiple choice)			
Pain	11	44	
Clinical/cognitive decline	20	5	< 0.0005
Pulmonary problems	9	2	
Gastrointestinal symptoms	14	3	
Type of admission			
Planned	26	27	
Emergency	25	20	0.310
Transfer	3	7	

MDAS, Memorial Delirium Assessment Scale; CAGE, cut down, annoy, guilt, eye-opener

($p=0.001$), cachexia ($p=0.018$), being off anticancer treatment ($p<0.0005$), admission for clinical/cognitive decline ($p<0.0005$).

In the multivariate analysis, independent factors associated with dying in APCU were MDAS ($p=0.006$), referral from specialistic home palliative care ($p=0.025$), being off cancer treatment ($p=0.002$), pain (<0.05), dyspnea ($p=0.038$), and total ESAS ($p=0.025$) (see Table 3).

Table 2 Symptom intensity (mean ± SD) at admission to the APCU

Symptoms	All patients	Died in the APCU	Discharged	*p*
Pain	3.6 ± 2.5	6.0 ± 2.1	2.8 ± 2.1	< 0.0005
Dyspnea	2.9 ± 3.1	4.7 ± 3.1	1.5 ± 2.1	< 0.0005
Depression	2.7 ± 3.1	4.2 ± 3.2	1.3 ± 2.3	< 0.0005
Anxiety	2.2 ± 2.7	2.6 ± 2.9	1.9 ± 2.6	0.240
Drowsiness	3.5 ± 3.0	4.6 ± 3.4	2.6 ± 2.4	0.002
Poor sleep	3.7 ± 3.2	3.2 ± 3.2	4.1 ± 3.2	0.233
Weakness	5.2 ± 3.1	4.3 ± 3.6	6.0 ± 2.5	0.010
Nausea	2.0 ± 2.6	3.7 ± 2.7	0.6 ± 1.6	< 0.0005
Poor appetite	2.6 ± 3.4	1.1 ± 2.4	3.9 ± 3.7	< 0.0005
Poor well being	5.8 ± 2.6	6.5 ± 2.9	5.3 ± 2.2	0.028
ESAS TOT	33.0 ± 13.6	41.8 ± 16.2	30.1 ± 11.5	0.002

Discussion

The findings of this study provided interesting information. Pain and dyspnea, as well as the symptom burden represented by total ESAS recorded at admission, were found to be independently associated with death. The high symptom burden is likely because patients admitted to APCUs are typically admitted for their level of distress and refractory symptoms [13, 20]. An increased symptom burden in the last days of life is expected when assessing the trajectory of symptom burden in the last 7 days [12].

The findings of this study are consistent with the observation of a Korean study [11], in which patients who died in the APCU while waiting for transfer to hospice were more likely to have higher symptom burdens such as drowsiness and dyspnea. In this Korean study, the mortality rate was 33%, which is largely different from the data of the present study. This is possibly due to less hospice bed availability. In a retrospective Japanese study in APCU, a greater risk of dying was independently correlated with a high level of baseline symptoms such as dyspnea, drowsiness, low level of baseline anxiety, and transfer from the emergency center [14]. In a retrospective study of 500 patients admitted to the APCU in the US, 25% of them died during admission. Factors associated with death in APCU were younger age,

Table 3 Univariate (crude OR with 95% CI) and multivariate logistic regression analysis of factors associated with death of patients in APCU. Adjusted odds ratios (Adj-ORs with 95%CI) were calculated evaluating together the significant variables at the univariate analysis. MDAS, Memorial Delirium Assessment Scale

	Crude OR (95% CI)	*p*	Adj OR (95% CI)	*p*
MDAS	1.646 (1.36–1.99)	< 0.0005	2.095 (1.24–3.54)	0.006
Referral: oncologic ward with respect to specialistic home palliative care	0.142 (0.04–0.46)	0.001	0.096 (0.01–0.74)	0.025
Type of tumor	1.510 (1.05–2.17)	0.027	1.462 (0.65–3.28)	0.356
Awareness	2.663 (1.48–4.78)	0.001	3.160 (0.56–17.67)	0.190
Cachexia	2.820 (1.29–6.17)	0.009	0.750 (0.05–11.76)	0.838
Off anticancer treatment	58.334 (7.56–450.06)	< 0.0005	32.122 (3.70–278.95)	0.002
Causes of admission: clinical/cognitive symptoms with respect to pain	3.467 (2.04–5.89)	< 0.0005	2.516 (0.94–6.73)	0.066
Symptoms				
Pain	2.258 (1.44–3.55)	< 0.0005	2.170 (1.01–4.79)	0.05
Dyspnea	1.523 (1.26–1.84)	< 0.0005	1.850 (1.04–3.30)	0.038
Anxiety	1.096 (0.94–1.28)	0.238	0.764 (0.42–1.40)	0.384
Depression	1.411 (1.19–1.67)	< 0.0005	1.636 (0.94–2.86)	0.085
Poor sleep	0.923 (0.81–1.05)	0.230	0.861 (0.55–1.36)	0.521
Drowsiness	1.257 (1.08–1.46)	0.003	0.922 (0.59–1.44)	0.721
Nausea	1.794 (1.41–2.28)	< 0.0005	1.411 (0.62–3.22)	0.413
Poor appetite	0.733 (0.62–0.87)	< 0.0005	0.624 (0.37–1.07)	0.085
Weakness	0.836 (0.73–0.96)	0.012	0.964 (0.49–1.90)	0.915
Poor well-being	1.213 (1.02–1.45)	0.032	1.010 (0.50–2.02)	0.978
Total ESAS	1.069 (1.02–1.12)	0.006	1.080 (1.01–1.15)	0.025

Reference: Discharged

admission from another oncology floor, some laboratory findings, such as hypo/hypernatremia, high blood urea nitrogen, and some clinical features, including high heart rate, high respiration rate, and supplemental oxygen use [15]. Signs of imminent death (heart rate, respiratory rate, use of oxygen) were likely to appear in the last days of life, suggesting that patients assessed in this study were admitted when they were close to death. In another retrospective study performed in Switzerland, independent factors predicting 72-h mortality after transfer to APCU were no prior palliative care consult, no advance care directive, lower performance status, lower self-care index, and lower blood albumin level [16]. Of interest, in this study, 20% of transferred patients died within 72 h of arrival on the APCU.

In the present prospective study, we did not use blood tests, as our intention was to distinguish patients according to symptom intensity or process (referral), rather than laboratory findings, which are potentially correctable after proper treatments. Referral from specialistic home palliative care was also associated with hospital death in APCU. Local specialistic home palliative care is a well-developed part of the palliative care network and is strictly connected with our center for referring patients with difficult conditions, including those at the end of life, other than for intensive symptom management. The finding can be explained by the rapid deterioration of the clinical condition not manageable at home, including cognitive failure, pain or dyspnea, and consequent request for APCU admission. Beds are more available in APCU, where turnover is faster than in hospice, where instead availability of beds is limited for acute admission and involves a delay due to the bureaucratic approval for admission appropriateness by the local heath care system, which manages the requests only on morning hours.

Of interest, in this study, the mortality rate was quite low, compared to the data of other APCUs from different countries, which reported their data in literature [9], although relatively higher compared to our previous data (7). One possible reason is the change in patients' pattern admitted to APCU, from patients with uncontrolled pain, which was one the principal indications for admission, to patients with worsening general conditions, also generated from a larger bed availability. Moreover, discharge home may be problematic because of a delay in starting home palliative care due to bureaucratic issues of local healthcare, as well as transfer to hospice with full bed occupation. Indeed, mortality risk was independently associated with a referral from specialistic home palliative care for patients, possibly due to general worsening of the clinical condition, as well as being off cancer treatment. In general, however, the mortality rate remains quite low, confirming that in general most patients are admitted early along the course of the disease for many different reasons.

The principal limitations of this study lie in the single-center experience, with specific local peculiarities compared to the larger variability in APCU models. A further limitation is based on the lack of examination of other specific data, for example, heart rate or renal failure, or extrapolating a prediction model. Such clinical signs, however, develop in the last days of life, not necessarily at admission to APCU, which may last several days or weeks. However, the prospective design and the findings provided a typical identikit of patients with a higher probability of dying after admission in APCU in a health system where specialistic home palliative care is particularly developed.

In conclusion, high symptom burden, being off-cancer treatment, and referral from specialistic home palliative care resulted to be associated with mortality risk in APCU. The findings of this study provide new insights, other than laboratory tests and clinical signs, on possible factors evaluable at admission associated with the risk of death during admission in an APCU. On the basis of the present data, more proactive and timely end-of-life care is needed for these patients. Data of this study should be confirmed by further studies in APCUs with different healthcare systems, facilities, and organizations, as well as APCU patterns reported in other countries which have been shown quite differently around the world.

Author contribution SM: preparation, conception design of the work; interpretation of data, drafted the work or substantively revised. ALC: data manager, acquisition, analysis, and creation of new software used in the work. AC: statistics, analysis, drafted the work or substantively revised.

Data availability No datasets were generated or analyzed during the current study.

Declarations All authors have approved the submitted version (and any substantially modified version that involves the author's contribution to the study) and have agreed both to be personally accountable for the author's own contributions and to ensure that questions related to the accuracy or integrity of any part of the work, even ones in which the author was not personally involved, are appropriately investigated, resolved, and the resolution documented in the literature.

Competing interests The authors declare no competing interests .

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