Original Article

Aggressive Care at the End of Life; Where Are We?

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Abstract

Background: Although, efforts to encourage palliative care only for terminal patients, aggressive end-of-life care (EOL) care still common for those probably to die shortly. **Aim:** Multicenter experiences to investigate where did we stand in this era? **Patients and Methods:** A retrospective study included patients with advanced solid tumors. The presence of one or more of the following indicators in the last month of life (LM) referred to aggressive EOL care: emergency department (ED) visits ≥ twice, admission to the hospital through ED, death in critical care units (CCUs), and palliative chemotherapy (PC) at the past 2 weeks before death. **Results:** A total of 435 patients, 51.5% were men with a median age of 62 years (range: 17–108), were included in the study. Most of the patients (89.2%) belonged to Group II; they had attended ED at least twice (60%), approximately 53% admitted to the hospital through ED, 31% received PC-LM with 41% of them had at the past 2 weeks before death, 13% died in the CCUs, and more than half of them (53%) survived <2 weeks. Kaplan–Meier estimator revealed that median survival was 30 days in Group I versus 13 days in Group II (odds ratio: 1.63; 95% confidence interval: 1.20–2.21; $P = 0.002$). The median survival was statistically significantly associated with PC-LM ≥14 days and the admission mode. There was no statistically significant association with age, sex, and primary cancer sites. **Conclusion:** The majority of our patients continue with anticancer treatments they possibly do not need and associated with poor survival.

Keywords: End-of-life care, palliative chemotherapy, the good death

Introduction

Patients with advanced cancer at the end of life (EOL) want to be comfortable and should be offered privacy and dignity. Many studies had addressed some indicators of aggressive care at the EOL such as multiple emergency department (ED) visits, hospital admission through ED, and critical care units (CCUs), for example, intensive care unit, CCU admission, prolonged stay in the hospital, receiving palliative chemotherapy at the last month of life (PC-LM), and inhospital death.[1-4]

Since then, many studies demonstrated the link between aggressive EOL care and a good death. Referring to coping with cancer study, 243 patients with advanced cancer and their main caregivers were interviewed. After adjustment for different patients' variable, the number of aggressive therapies taken in the past 7 days of life was associated with increased physical distress ($P < 0.0001$), increased psychological distress ($P = 0.003$), bad quality of death ($P = 0.03$), and a lower likelihood of dying in the preferred place ($P < 0.0001$). Whereas, those with long duration of hospice care were linked to less physical distress ($P < 0.0001$), a better quality of death ($P = 0.01$), and a greater likelihood of dying in the preferred place ($P < 0.0001$).[5]

Although this, still the aggressive treatment for terminal advanced cancer patients at the EOL is a common practice.

In the current study, we tried to highlight our practice in dealing with terminal cancer patients near death.

Patients and Methods

This multicentric retrospective cohort study conducted on 479 patients with advanced cancer who died in the Medical Oncology Department, Faculty of Medicine, Zagazig University, Egypt, and Oncology Center, King Salman Armed

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Access this article online

Quick Response Code:

Website: www.jpalliativecare.com

DOI: 10.4103/IJPC.IJPC_59_19

How to cite this article: Mohammed AA, Al-Zahrani O, Salem RA, Elsayed FM. Aggressive care at the end of life; Where are we? Indian J Palliat Care 2019;25:539-43.

Forces Hospital, Tabuk City, Saudi Arabia, through the period from February 2013 to December 2018.

Aggressive EOL care was defined as the presence of at least one of the following indicators during the LM of life: ED visits ≥ twice, admission to the hospital through ED, death in CCUs, and PC at the past 2 weeks of life

Eligibility criteria were age ≥18 years old at the time of death, pathologically documented diagnosis of cancer, evidence of advanced disease, and death during the last hospitalization. Patients receiving anticancer treatment for curative intent and/or have hematological malignancy were excluded from the study. The demographic and clinical data were collected from medical patients' files and the electronic medical records of the Wipro HIS Oncology Management System.

The included patients were divided into two groups: those who had no indicators of aggressive EOL care (Group I) and those who had one or more indicators (Group II).

Statistical analysis

Continuous variables were expressed as the mean ± standard deviation and median (range), and the categorical variables were expressed as a number (percentage).

Continuous variables were checked for normality using the Shapiro–Wilk test. Percentage of categorical variables were compared using Pearson's Chi-square test or Fisher's exact test when was appropriate. Mann–Whitney U-test was used to compare between two groups of nonnormally distributed variables. Overall survival (OS) was calculated as the time from diagnosis to death or the most recent follow-up contact (censored).

Stratification of OS was done according to the study group. The time-to-event distributions were estimated using the method of Kaplan–Meier plot and compared using two-sided exact log-rank test. Cox regression analysis was performed to study the relationship between different study variables as independent predictors and mortality as an outcome or dependent variable.

$P < 0.05$ was considered statistically significant. All statistics were performed using SPSS 20.0 for Windows (SPSS Inc., Chicago, IL, USA) and MedCalc Windows (MedCalc Software bvba 13, Ostend, Belgium).

Results

Four hundred and thirty-five patients were eligible, of whom 51.5% were men with a median age of 62 years (range: 17–108). Patients had colorectal, hepatobiliary, breast, and lung cancers represented the main bulk of the study. Table 1 illustrates the main patients' characteristics.

In the study, overall, 89.2% received aggressive EOL care at the LM of life (Group II) in the form of ED visits at least two or more (60%), hospital admission through ED (53%), PC-LM (31%), with 41% of them at the past 2 weeks before death, 13% died in the CCUs, and more than half of them (53%) survived <2 weeks. Patients who had no indicators of aggressive EOL care, the Group I experienced a better survival. Table 2 shows a comparison between the two groups.

Kaplan–Meier estimator revealed that median survival was 30 days in Group I versus 13 days in Group II (odds ratio [OR]: 1.63; 95% confidence interval [CI]: 1.20-2.21; P =0.002). Figure 1 shows Kaplan–Meier plot of OS for both groups.

On multivariate and univariate Cox regression analysis, the median survived was statistically significant associated with PC-LM ≤14 days and the admission mode, ED versus outpatient department (OR: 1.39; 95% CI: 0.97–1.97; P = 0.04), (OR: 1.49; 95% CI: 1.11–1.42; P = 0.008) and (OR: 1.46, 95% CI: 1.17–1.81; P = 0.001), (OR: 1.42, 95% CI: 1.18–1.72; P = 0.000), respectively. There was no statistically significant association with age, sex, primary cancer sites, and

Table 1: Patients' characteristics

Parameters	All (n=435), n (%)
Age (years)	
Mean±SD	60.78±15.44
Median (range)	62 (17-108)
Sex	
Male	211 (48.5)
Female	224 (51.5)
Primary cancer sites	
Colorectal	76 (17.5)
Hepatobiliary	65 (14.9)
Breast	59 (13.6)
Lung	58 (13.3)
Pancreas	25 (5.7)
Genitourinary	40 (9.2)
Stomach	22 (5.1)
Head and neck	23 (5.3)
Prostate	12 (2.8)
Others	55 (12.6)
Number of ED visits	
0-1	173 (39.8)
≥2	262 (60.2)
Mode of admission	
ED[a]	205 (47.1)
OPD[b]	230 (52.9)
PC-LM[c] (n=134), days	
≤14	55 (12.6)
>14	79 (18.2)
Place of death	
CCUs	67 (15.4)
Regular word	368 (84.6)
Group I[d]	47 (10.8)
Group II[e]	388 (89.2)
Survival (weeks)	
≤2	221 (50.8)
>2	214 (49.2)

[a]ED, [b]Outpatients' clinic, [c]PC at the past month, [d]No indicators of aggressive EOL care, [e]One or more indicators. EOL: End of life, PC: Palliative chemotherapy, LM: Last month of life, ED: Emergency department, OPD: Outpatient department, SD: Standard deviation, CCUs: Critical care units

Table 2: Patients' characteristics in the two groups

Characteristics	Group I; (*n*=47), *n* (%)	Group II; (*n*=388), *n* (%)	*P*[a]
Age (years)			
Mean±SD	62±14.72	60±15.54	0.5
Median (range)	62 (31-88)	62 (17-108)	
Sex			
Male	22 (46.8)	189 (48.7)	0.8
Female	25 (53.2)	199 (51.3)	
Primary cancer sites			
Colorectal	10 (21.3)	66 (17.0)	0.9
Hepatobiliary	5 (10.6)	60 (15.5)	
Breast	5 (10.6)	54 (13.9)	
Lung	7 (14.9)	51 (13.1)	
Pancreas	4 (8.5)	21 (5.4)	
Genitourinary	5 (10.6)	35 (9.0)	
Stomach	3 (6.4)	19 (4.9)	
Head and neck	3 (6.4)	20 (5.2)	
Prostate	1 (2.1)	11 (2.8)	
Others	4 (8.5)	51 (13.1)	
Number of ED visits			
0-1	45 (95.7)	128 (33.0)	0.00
0-2≥2	2 (4.3)	260 (67.0)	
Mode of admission			
ED	0 (0.0)	205 (52.8)	0.00
OPD	47 (100)	183 (47.2)	
PC-LM			
Yes	7 (14.9)	127 (52.8)	0.01
No	40 (85.1)	261 (67.3)	
PC-LM (*n*=134), days			
≤14	0 (0.0)	55 (14.2)	0.01
>14	7 (14.9)	72 (18.6)	
Place of death			
CCU	0 (0.0)	67 (17.3)	0.002
Regular word	47 (100)	321 (82.7)	
Survival (weeks)			
≤2	13 (27.7)	208 (53.6)	0.001
>2	34 (72.3)	180 (46.4)	

PC: Palliative chemotherapy, LM: Last month of life, ED: Emergency department, OPD: Outpatient department, SD: Standard deviation, CCUs: Critical care units

the aggressive EOL care. Table 3 illustrates the multivariate and univariate Cox regression model for cancer-specific survival.

Discussion

Although the American Society of Clinical Oncology released what is called the top five list of oncology, the physician–patient interaction to minimize unnecessary care or those with costly resources despite little benefit, there was no significant achievement in aggressive EOL care.[6]

Our results revealed that colorectal, lung, breast, and hepatobiliary cancers represented the main bulk of our patients (59.3%), which is corresponding to the global cancer incidence.[7] Gallbladder cancer, hepatocellular carcinoma, and cholangiocarcinoma were included in one item named hepatobiliary cancers.

There is no agreement on the number of ED visits to be accepted; however, some authors suggested that more than one ED visit to the LM of life is not accepted.[8]

During the LM of life, 60.2% of our patients had at least two ED visits with 47% hospitalized. There are many studies which had evaluated ED visits near the EOL. In a retrospective and descriptive

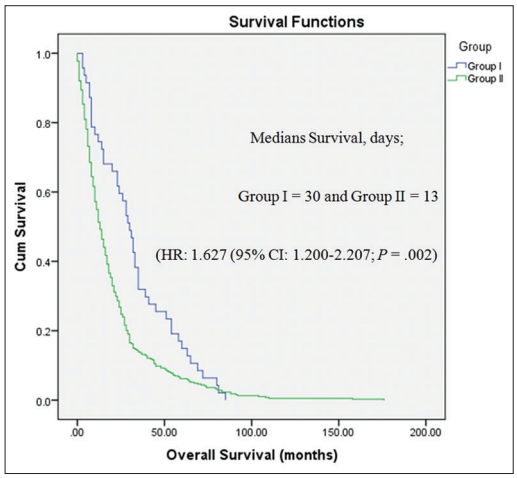

Figure 1: Kaplan–Meier plot of overall survival for both groups

Table 3: Multivariate and univariate Cox regression model for cancer-specific survival

	Multivariate Cox regression			*P*	Univariate Cox regression			*P*
	OR	95.0% CI			OR	95.0% CI		
		Lower	Upper			Lower	Upper	
Age	1.001	0.995	1.008	0.7	1.003	0.996	1.009	0.4
Sex	1.025	0.824	1.276	0.8	1.059	0.877	1.279	0.5
PC-LM: Yes versus no	0.856	0.647	1.134	0.3	1.168	0.951	1.434	0.1
PC-LM ≤14 days	1.381	0.968	1.971	0.04	1.485	1.110	1.421	0.008
Admission mode: ED versus OPD	1.457	1.171	1.814	0.001	1.421	1.175	1.718	0.000
ED visits: 0-1 versus ≥2	1.058	0.854	1.311	0.6	1.022	0.841	1.242	0.8
Death place	1.070	0.813	1.408	0.6	1.098	0.843	1.429	0.5

PC: Palliative chemotherapy, LM: Last month of life, ED: Emergency department, OPD: Outpatient department, CI: Confidence interval, OR: Odds ratio

study done in Ontario between 2002 and 2005, 91,561 patients died of cancer. Patients who visited ED during the past 2 weeks of life, 85.3% of them made one visit and 12.4% made two.[9]

Another study done by Alsirafy *et al*. reported that 77% of patients with terminal cancer had at least one ED visit to the past 3 months of life with 54% admitted to inpatients' services.[10]

The increased percentage of ED visits in our study may be related to the limited palliative care services for all patients, so symptoms' management is usually inadequate. Moreover, the lack of hospice care and home health care in our regions forces the patients to attend the ED if there are any symptoms.[11]

The use of futile chemotherapy is still a common practice worldwide. In the current study, about 31% of our patients received PC-LM. Several studies had demonstrated the same range of results.[12-15]

There are many justifications for this phenomenon. It seems very difficult to tell the patient he is terminal and no further anticancer treatment, the widespread of using target therapy and the maintenance strategies are other attributing factors. Moreover, a considerable number of oncologists' worldwide sought for the prolongation of survival without looking to the quality of life, even in cases that are near to death.

Some trials evaluated the patient–physician discussion about the disease prognosis reported that the prognosis was discussed by only 35%–39% medical oncologists.[16-18]

Actually, when the patients or their families requesting an aggressive treatment for the EOL, they may believe that the aggressive management will help in relieving the suffering, but mostly, it does not for me, it is considered as a warning sign. The transitioning from curative treatment to palliative care is usually difficult for patients, families, and even physicians.

Death at the hospital is considered one of the aggressive EOL cares, in contrast to death at home (also called good death) due to autonomy and better care. Early palliative care referral may help patients with terminal cancer to select the preferable site of death.

Of the 435 patients in our study, 15.4% died in CCUs. Similar results were found in many previous studies, which are consistent with different studies.[11,19,20]

About 90% of patients with advanced terminal cancer who did not receive aggressive management at the EOL died in their preferred place. Meanwhile, those were valid of only one-third of patients receiving ≥2 lines of treatment.[21]

Patients with advanced cancer who received PC were more subjected to die in CCUs (11% vs. 2%) and less probably to die at home (47% vs. 66%).[22,23]

Through our results, 89.2% of our patients had aggressive EOL care with 53.6% lived <2 weeks. Several studies confirmed our results.[24-30]

Until recently, little awareness has been offered to quality of life for patients who are near to death. In our countries, the physician did not have the courage to inform the patients that they are near the death and may not find it handy to consent their status, and the emotional and religious factors may also have a role in this situation. We need to improve the physician–patients' communication, and more education for both to realize actual changes aims to change the statement of patient–physician preferences to be an agreement for EOL care.

In my point of view, the story of EOL care can be summarized in two factors – the first one is physician attitude to the management and the second one is patient related which includes both geographical and religious factors.

Furthermore, we must not forget the financial issue; it is calling spending on EOL. It is significant to believe the cost-effectiveness of delivered health-care services. Especially, there is a substantial increase in health-care spending shortly before death.[31-33]

Conclusion and Recommendation

The aggressive EOL during the LM of life appeared to be extremely high and linked to poor quality of death. The majority of our patients with terminal advanced cancer had multiple ED visits, death in CCUs, and received PC near their death. We recommend starting the discussion about the aims of the therapy, treatment preferences, and disease outcome at an earlier stage of the disease. Hence, both the patient and the physician can decide the possibility of the treatment for the EOL prospectively and determine if it may effect on the bereavement adjustment of the family.

We are in need to improve our practice to minimize the over care for terminal cancer patients at the EOL and should consider the anticancer treatment at a suitable time for suitable patients.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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