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Original Article

Retrospective evaluation of cancer patients in Intensive Care Unit

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ABSTRACT

Objective: We aimed to investigate factors affecting the prognosis of cancer patients in an intensive care unit and provide guidelines for the admission and follow-up processes.

Design: This is a retrospective study.

Setting: The study was conducted at the Health Sciences University, Kartal Dr Lütfi Kırdar Training and Research Hospital, Istanbul, Turkey.

Subjects: In total, 965 patients admitted to the general intensive care unit during a 1-year period from July 2017 to July 2018 were studied.

Intervention: Cancer patients

Main outcome measure: Age, sex, malignancy type, comorbidities, presence of metastasis and surgeries, reason for intensive care unit admission, length of stay, hospital unit referring the patient to the intensive care unit, mechanical ventilator, inotropic drug administered, hemofiltration requirements, resuscitation history, and survival rates were recorded.

Results: We observed significantly lower survival rates among patients who were diagnosed with breast or hematological cancer; who had comorbid conditions or metastases; who underwent surgeries; who were admitted to the intensive care unit due to septic shock, cerebral infarction, cardiopulmonary resuscitation, or multiple organ failure; who were on mechanical ventilation; who had been treated with hemofiltration; or who had received inotropic support; however, multivariate analysis showed that presence of comorbid diseases, presence of metastases, admission to the intensive care unit, and inotropic support were the only independent factors that negatively affected patient survival.

Conclusions: Patients with cancer having high risk of mortality may be provided hospice or palliative intensive care instead of admission to the limited number of general intensive care units.

KEY WORDS: intensive care unit, mortality, oncological patients, prognosis, survival

INTRODUCTION

Cancer has become an important health problem worldwide in recent years in terms of its associated morbidity and mortality rates. Among deaths with a known cause, it is the second leading cause of death after cardiovascular diseases^[1]. However, cancer-related deaths have been reduced by improvements in diagnostic tools, introduction of new and successful therapies into the field of oncology, and advanced supportive care, whereas there has been a rise in the number of people living with cancer with the growing elderly population^[2].

Cancer patients require monitoring in the intensive care unit (ICU) due to reasons related to the disease and treatment throughout their lifespan, which is prolonged by the therapies being administered^[3]. Indications for admission to an ICU may be cancer-related causes such as organ involvement and pulmonary embolism, but may also be treatment-related factors, such as sepsis and drug toxicity, or comorbid diseases, such as renal failure, heart failure, and chronic obstructive pulmonary disease (COPD)^[4,5].

Although the advances in healthcare services have improved survival compared with previous years, persistently high mortality rates indicate that the management of these patients is still important. The aim of the present study was to investigate the factors affecting outcomes in cancer patients admitted to the ICU of our hospital, which is a major oncology center, by retrospectively reviewing the data in patient charts and archived records, and to provide an insight into the admission and follow-up processes and the use of ICU facilities, which are limited in Turkey and around the world.

SUBJECTS AND METHODS

In our study, following approval by the ethics committee, the records of patients who were diagnosed with cancer and followed up in the general ICU of our hospital's Anesthesiology and Reanimation Clinic during a 1-year period from July 2017 to July 2018 were retrospectively reviewed. Pediatric patients with cancer were excluded from the study. In cases with multiple admissions, only the first admission was considered. Age, sex, malignancy type, comorbidities (hypertension, diabetes mellitus, coronary artery diseases, heart or renal failure, COPD, hyper or hypothyroidism, cerebrovascular disease, connective tissue diseases, liver diseases, *etc.*), metastasis and surgical history, reason for admission to the ICU, length of stay, unit prior to ICU admission, mechanical ventilator (MV) use, inotropic drug use, hemofiltration requirement, cardiopulmonary resuscitation (CPR) history, and survival were recorded.

The data obtained in the study were statistically analyzed using SPSS version 18.0. The variables were expressed using mean and maximum and minimum values, and percentages were used for expressing qualitative variables. Student's t-test was used for comparisons between the groups, Pearson's chi-square test in the analysis of qualitative variables, and Fisher's exact test in case of small sample size. Posthoc analysis was also performed with Bonferroni correction. A p value of <0.05 was considered to be statistically significant. For multivariate analysis, statistically significant parameters in the single variable analysis were used, and the hazard ratios were calculated.

RESULTS

Of the 965 patients who were hospitalized in the general ICU of our hospital's Anesthesiology and Reanimation Clinic during a 1-year period and whose data were accessible, 244 (25.28%) had been diagnosed with cancer. The mean age of the patients with cancer was 64.7 ± 13.3 years, and the majority of the patients were male. The mean length of stay in the ICU was 8.0 ± 27.4 days. The demographic data of the patients are shown in Table 1. In total, 24.6% (n=60) of the patients were diagnosed with rectal cancer, 16.4% (n=40) with lung cancer, 11.5% (n=28) with colon cancer, 10.2% (n=25) with gastric cancer, 10.2% (n=25) with brain cancer, 6.1% (n=15) with laryngeal, pharyngeal or tongue cancer, 4.5% (n=11) with pancreatic cancer, 4.1% (n=10) with hematological cancer, 3.3% (n=8) with bladder cancer, 3.3% (n=8) with breast cancer, 2.5% (n=6) with liver cancer, 1.2% (n=3) with prostate cancer, 1.2% (n=3) with unknown primary cancer, and 0.8% (n=2) with adrenal carcinoma. When these cancers were grouped under seven main headings, gastrointestinal tract (GIT) cancers were the most common type of cancer (n=132, 54.8%; Table 1).

In the comparison among cancer types, there was no significant difference between the groups in terms of mean age ($p=0.217$), age group ($p=0.424$), and presence of comorbidity ($p=0.323$), whereas there was a significant difference in terms of sex and metastasis ($p<0.001$ and $p=0.001$, respectively). In patients with GIT and brain cancers, sex distribution was approximately equal, and there was a difference in sex distribution patterns among patients with respiratory, urological, hematological, and breast cancers. A higher number of metastasis was found in patients with breast and hematological cancers ($p<0.001$; Table 2).

It was observed that 62.3% of patients ($n=152$) were admitted to the ICU postoperatively, whereas 20.9% ($n=51$) were transferred from the regular ward and 16.8% ($n=419$) were transferred from the emergency room. Of the patients, 67.6% ($n=163$) were admitted to the ICU due to conditions that occurred after surgeries. There was a statistically significant difference in both the referring ward and surgical history among the cancer groups ($p<0.001$ and $p<0.001$, respectively). Patients with GIT, respiratory, urological, and brain cancers were most commonly admitted to the ICU due to a postoperative event, and those with breast and hematological cancers were most commonly transferred to the ICU from the regular ward or emergency room (Table 2).

When posthoc analysis was performed with Bonferroni correction, there was a difference between patients with GIT cancers and those with lung cancer ($p<0.0001$) and between patients with lung cancer and those with breast and between those with lung cancer and those with hematological cancers in terms of sex ($p<0.0001$, $p=0.001$, respectively). When metastasis was compared using the same method, there was a significant difference between patients with GIT cancers and those with breast cancer ($p=0.007$) and between patients with brain cancer and those with breast cancer ($p=0.005$). There was a difference between patients with GIT cancers and those with hematological cancers ($p<0.0001$) and between patients with lung cancer and those with hematological cancers ($p=0.006$) in terms of operation rate. When a posthoc analysis was performed in terms of the unit of admission to the ICU, there was a difference only between patients with lung cancer and those with brain cancer ($p=0.005$).

The most common reason for admission to the ICU was respiratory failure ($n=132$, 54.1%; Table 1). Among the cancer types, there was no statistical difference in terms of reason for admission to the ICU ($p=0.601$). There was no difference among the cancer groups in terms of admission to the ICU due to respiratory failure ($p=0.544$), septic shock ($p=0.563$), sepsis ($p=0.870$), multiple organ failure (MOF; $p=0.735$), hemorrhagic shock or disseminated intravascular coagulation (DIC; $p=0.261$), postoperative CPR ($p=0.686$), and renal failure ($p=0.592$). While age, age group, and sex had no effect on admission to the ICU ($p>0.05$), the incidence of respiratory failure was higher in patients who underwent surgeries (67.7% vs. 26.3%, $p<0.001$) and the incidence of MOF was higher in patients who did not undergo surgery (21.3% vs. 1.8%, $p<0.001$); patients who were admitted after undergoing CPR were mostly those who did not undergo surgery (16.3% vs. 2.4%, $p<0.001$).

It was found that 69.7% ($n=170$) of patients received MV support, and 12.7% ($n=31$) required hemofiltration. Inotropic support was required by 50% ($n=122$) of patients, and 25% ($n=61$) underwent CPR at least once.

Of cancer patients followed up in the ICU, 43.9% (n=107) died and 56.1% (n=137) survived. The mean age of survivors was 64.0±12.9 years and the mean age of non-survivors was 65.7±13.8 years. The mortality rate of patients was 40.2% for GIT cancers, 45.5% for respiratory tract cancers, 36.0% for brain cancers, 36.4% for urological cancers, whereas it was 87.5% for breast cancer and 70% for hematological cancers. The mortality rate was 20.5% for respiratory failure, 43.5% for sepsis, 50% for hemorrhagic shock or DIC, 50% for renal failure, 84.6% for septic shock, 90% for MOF, 94.1% for ICU admission after CPR, and 100% for cerebral infarction.

Age (p=0.337), sex (p=0.272), and age being above 65 years (p=0.625) had no effect on survival, whereas a significantly higher number of deaths were observed in patients with breast or hematological cancers (p=0.002); in patients with a comorbid condition (p=0.001) and metastasis (p<0.001); in those who underwent surgeries (p<0.001), in those admitted to the ICU due to septic shock, cerebral infarction, MOF, or after undergoing CPR (p<0.001); in those who received MV support (p<0.001) or underwent hemofiltration (p<0.001); and in those who required inotropic support (p<0.001). In multivariate analysis, comorbidity (p=0.01); metastasis (p=0.02); admission to the ICU without undergoing surgery (p=0.001); admission to the ICU due to septic shock, cerebral infarction, MOF, or CPR (p=0.05); and inotropic support (p<0.0001) were factors that had an independent adverse effect on survival (Table 3).

DISCUSSION

Admission of patients with cancer to ICUs, which have a limited number of beds and equipment in Turkey, is a very controversial and sensitive issue. Improvements in cancer therapies, supportive management of organ dysfunctions and infections, and advances in ICU interventions have improved the survival rates of critically ill cancer patients^[6]. As patients with malignancies constitute 15%–20% of all ICU patients and still have higher mortality rates than other patient groups (39%–77%)^[7], there are problems considering ICU bed numbers and the financial budget of hospitals. Therefore, it may be possible to improve and enhance intensive care services by determining the mortality risk factors and deficiencies and taking precautions. The aim of this retrospective study was to evaluate the demographic characteristics, comorbidities, mean length of stay and its causes, and factors affecting mortality in patients with cancer who were treated in the ICU of our hospital, which also serves as a major oncology center, and whose patient records were retrieved.

In a retrospective review of 2,240 patients who were admitted to the ICU between 2011 and 2012, Aksoy *et al* reported that 23.9% of the patients were diagnosed with malignancy, the mean age was 59.9 years, the male-to-female ratio was 1.55, and colorectal (19.71%), lung (15.77%), and GIT cancers (11.62%) were the first, second, and third most common cancers, respectively, and the mean length of stay in the ICU was 3.94 days in patients aged <70 years and 6.52 days in patients aged ≥70 years, with a mean of 4.69 days^[8].

A study by Silva *et al* involving 177 patients with cancer who were admitted to medical and surgical oncology ICUs reported that the mean age was 52.4±17.25 years, the male-to-female ratio was 1.49,

gynecologic (29.4%) and GIT (22.6%) cancers were the first and second most common cancers, respectively, and the mean length of stay in the ICU was 3 (1–6) days^[9].

In a multicenter study by Taccone *et al* involving a total of 3,147 patients in 198 ICUs in 24 European countries, 473 (15%) patients with malignancies were investigated; they reported that the male-to-female ratio was 1.27, the mean age was 66.4±12.1 years in patients with solid tumors and 62.1±15.9 years in those with hematological cancers, and the mean length of stay in the ICU was 3 (1.8±6.4) days in patients with solid tumors and 3.8 (1.7±8.6) days in those with hematological cancers^[10].

In a retrospective study by Tow *et al*, in which patients with solid tumors were analyzed by the Mayo Clinic Institutional Review Board between 2008 and 2009, 120 patients were investigated, and it was found that GIT (34.1%) and lung cancers (28.3%) were the first and second most common cancers, respectively^[11].

In our study, 25.28% of patients admitted to the ICU were diagnosed with cancer. The mean age was 64.7±13.3 years, the male-to-female ratio was 1.21, the mean length of stay in the ICU was 8±27.4 days, and gastrointestinal and respiratory tract cancers were the first and second most common cancers, respectively. The higher proportion of patients with malignancy in our ICU compared with that in other studies may be because our hospital is an oncology center. According to the data of the Ministry of Health and the World Health Organization^[12], cancer is more common in males, and our findings are consistent with these data and those of other researchers. The longer stay in the ICU in our study may be due to higher mean age and higher comorbidity rate. In addition, consistent with many other studies, we found that the first and second most common cancers in our oncology patients admitted to the ICU were GIT and respiratory tract cancers^[8,11].

According to recent data of the Turkish Ministry of Health, the most common cancer type in Turkey is lung cancer, followed by prostate and bladder cancers in males, and breast cancer followed by thyroid and gynecological cancers in females^[13]. In our study, consistent with these data, we found that the most common cancer type in ICU patients was respiratory cancer followed by urological cancers in males, and breast cancer followed by hematological cancers in females.

Furthermore, 57% of 717 patients reported by Soares *et al*^[5], 66% of 177 patients reported by Silva *et al*^[9], and 59.1% of 482 patients reported by Aksoy *et al*^[8] were admitted to the ICU in the postoperative period. Consistent with the results of the previous studies, of 244 patients with cancer in the present study, 62.3% were admitted to the ICU postoperatively, 20.9% were transferred from the relevant wards, and 16.8% were transferred from the emergency room.

The reasons for admission to the ICU in patients with cancer are variable among studies; however, the most common reason is respiratory failure^[14,15]. In many studies, the most common reasons for admission to ICU were respiratory failure, shock, sepsis, and renal failure^[15,16,17]. Similarly, in our study, we found that the most common reason for admission to the ICU in patients with cancer was acute respiratory failure (54.1%), followed by septic shock (10.7%), sepsis (9.4%), and MOF (8.2%), and the reason for admission had an effect on the mortality rate.

In studies involving patients with various types of cancer, variable mortality rates (30%–90%) have been reported in patients with malignancies followed up in ICUs. In the study by Aksoy *et al*, malignancies with the highest mortality rate were hematological cancer (81%), breast cancer (72%), and lung (68%) cancer, respectively^[8]. Consistent with the rates reported in previous studies, the rates in our study were 70%, 87.5%, and 45.5%, respectively. Considering the fact that patients with hematological and breast cancers are terminally ill cancer patients with widespread metastases who are referred from clinics, such as internal medicine or oncology clinics, or from the emergency room, these results are significant.

In a study of 717 patients with cancer who were admitted to the ICUs of 28 hospitals in Brazil, Soares *et al* reported that the reasons for admission to the ICU was postoperative care in 57%, sepsis in 15%, and respiratory failure in 10%, and among these patients, the mortality rate was 11% among patients who were admitted after a planned surgery, 37% among patients who were transferred from the emergency room, and as high as 58% among patients who were admitted after medical complications^[5]. The results of our study supported their results. We determined that the mortality rate in patients with cancer who were admitted to the ICU postoperatively was lower than in those who were admitted to the ICU due to medical reasons, such as MOF, CPR, and cerebral infarction. In their study, Silva *et al* reported a 21.4% mortality rate in the ICU and found that this rate is as high as 81.6% among patients with failure in three or more organs^[9]. Mokart *et al*^[14] reported an ICU mortality rate of 32%, whereas Hawari *et al*^[18] reported a rate of 36.5% in a 5-year study. In our study, the ICU mortality rate in patients with cancer was 43.9%. We consider that these different results can be attributed to patient selection criteria, differences in cancer types and stages, presence of comorbid conditions, patients being terminally ill or not, and ICU admission criteria.

Different studies have indicated various independent risk factors for ICU mortality in patients with cancer. Silva *et al* determined that the length of stay in the ICU, a Charlson comorbidity index of >2, and vasopressor requirement are independent prognostic factors for mortality after discharge from the ICU, and vasopressor requirement and APACHE II score are independent prognostic factors for ICU mortality^[9]. Mokart *et al* reported that malignancy characteristics, age, and neutropenia had no effect on mortality, whereas high logistic organ dysfunction score on day 7 and viral infection and/or reactivation were associated with mortality^[14]. Soares *et al* found that MOF, performance status, and MV requirement had more effect on mortality in patients with cancer than cancer-related factors, such as malignancy type^[5]. Many researchers have also found that neutropenia, use of chemotherapy in the terminal phase, and autologous stem cell transplantation had no effect; positive blood culture, antibiotic combinations in neutropenic sepsis, and removal of central venous line had little effect; and age, tumor stage, number and severity of organ failures, acute respiratory failure, need for invasive MV, ICU admission in the late period or after cardiac arrest, comorbidities, prehospital performance status, development of acute graft versus host syndrome following allogeneic stem cell transplantation, and invasive pulmonary aspergillosis had considerable effect on the short-term mortality of patients with cancer who were admitted to ICUs^[4,19,20,21]. The same authors have also concluded that the characteristics and prognostic features of malignancy affected mortality in the long term in these patients. Consistent with the results of

studies conducted by various researchers, the present study found a significantly higher number of deaths among patients with breast or hematological cancers; patients with comorbid conditions and metastasis; patients who did not undergo surgeries; patients who were admitted to the ICU due to septic shock, cerebral infarction, MOF, or after undergoing CPR; patients who received MV support or underwent hemofiltration; and patients who required inotropic support; however, in multivariate analysis, the presence of comorbidity or metastasis; admission to the ICU without undergoing surgery; admission to the ICU due to septic shock, cerebral infarction, MOF, or after undergoing CPR; and inotropic support were factors that independently affected survival.

CONCLUSION

In conclusion, the presence of comorbid conditions and metastasis, admission to the ICU without undergoing surgery and due to septic shock, cerebral infarction, MOF, or after undergoing CPR, and the need for inotropic support should be regarded as strong predictors of increased mortality of patients in the ICU. For this reason, we consider that cancer patients with these risk factors should be evaluated more carefully while deciding on the admission to and follow-up in the ICU. It can be concluded that the establishment of new regulatory protocols and the creation of new ICU concepts, including hospice and palliative intensive care, may be more useful in the management of these patients. In our country, there has been progress in this regard, and in future, such patients will be admitted to hospice and palliative ICUs, to ensure that their admission to general ICUs reduces.

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Conception: Çevik E. B

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Supervision: Çevik E. B, Arslan G

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Materials: Arslan G, Çevik E. B

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Critical review: Çevik E. B, Arslan G

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Table 1: Demographic data of patients

Demographic parameters (n=244)	Data
Age, year average	64.7±13.3
Age group, n (%)	
<65 years	112(45.9%)
>65 years	132(54.1%)
Sex	
Male	134(54.9%)
Female	110(45.1%)
Cancer type, n (%)	
GIT ^a	132(54.8%)
Respiratory ^b	55(22.8%)
Brain	25(10.4%)
Urological ^c	11(4.6%)
Hematological	10(4.1%)
Breast	8(3.3%)
Unknown primary	3(1.2%)
Comorbidity rate, n (%)	196(80.3%)
Metastasis, n (%)	86(35.2%)
Reason for admission to ICU, n (%)	
Respiratory failure	132(54.1%)
Septic shock	26(10.7%)
Sepsis	23(9.4%)
MOF	20(8.2%)
Hemorrhagic shock, DIC	18(7.4%)
Post-CPR	17(7.0%)
Renal failure	6(2.5%)
Cerebral infarction	2(0.8%)
Length of Stay in ICU (days)	8.0±27.4

^aGIT; gastric, colon, rectal, pancreatic, and adrenal cancers

^bRespiratory; lung, larynx, pharynx, and tongue cancers

^cUrological; bladder and prostate cancers.

Table 2: Comparison of cancer groups*

Characteristics of cancer groups (n=244)	GIT (n=132)	Respiratory (n=55)	Brain (n=25)	Urological (n=11)	Hematological (n=10)	Breast (n=8)	p value
Age (years)	66.0±12.7	62.8±10.9	61.4±16.9	72.4±11.1	58.7±19.6	64.0±17.8	0.217
Age range							0.424
<65 years	59(44.7%)	27(49.1%)	13(52.0%)	5(45.4%)	6(60.0%)	4(50.0%)	
>65 years	73(55.3%)	28(50.9%)	12(48.0%)	6(54.6%)	4(40.0%)	4(50.0%)	
Sex							<0.001
Male	62(47.0%)	46(83.6%)	14(56.0%)	7(63.6%)	2(20.0%)	-	
Female	70(53.0%)	6.4%)	11(44.0%)	4(36.4%)	8(80.0%)	8(100%)	
Presence of Comorbidity n (%)	109(82.6%)	44(80.0%)	16(64.0%)	8(72.7%)	9(90.0%)	7(87.5%)	0.323
Presence of Metastasis n (%)	37(28.0%)	2(40.0%)	5(20.0%)	5(45.5%)	7(70.0%)	7(87.5%)	0.001
Operation rate n (%)	100(75.8%)	36(65.5%)	16(64.0%)	7(63.6%)	1(10.0%)	3(37.5%)	<0.001
Department prior to ICU admission n (%)							<0.001
Emergency room	12(9.1%)	30.9%)	-	1(9.1%)	5(50.0%)	4(50.0%)	
Other units	25(18.9%)	8(14.5%)	9(36.0%)	3(27.3%)	4(40.0%)	2(25.0%)	
Postoperative	95(72.0%)	54.5%)	16(64.0%)	7(63.6%)	1(10.0%)	2(25.0%)	
Length of stay in the ICU (days)	6.9±30.5	7.5±12.8	15.2±45.1	5.6±6.3	9.1±11.7	9.5±11.3	0.703

*Because the number of patients with unknown primary cancer was very low (n=3), it was excluded.

Table 3: Factors affecting survival

Factors affecting survival	Ratios*	Univariate	Multivariate	Hazard Ratio
Male vs. Female	47.0% vs. 40.0%	0.272		
Age <65 vs. ≥65 years	45.5% vs. 42.4%	0.625		
With vs. without breast or hematological cancer	78.8% vs. 40.2%	0.002	0.103	1.125
With vs. without comorbidity	49.0% vs 22.9%	0.001	0.01	2.444
With vs. without metastasis	<72.1% vs. 28.5%	<0.001	0.02	2.288
With vs. without surgery	<81.3% vs. ≥18.8%	<0.001	0.001	3.249
Septic shock, cerebral infarction, or MOF vs. others	89.3% vs. 27.4%	<0.001	0.05	1.914
Received vs. did not receive MV support	61.2% vs. 4.1%	<0.001	0.08	1.723
With vs. without hemofiltration	80.6% vs 38.5%	<0.001	0.340	0.954
With vs. without inotropic support	78.7% vs 9%	<0.001	<0.0001	6.296

*Rates are mortality rates in the mentioned variables