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Intensive care outcome of patients with a solid tumor in a tertiary care hospital in Saudi Arabia: Results of a prospective ICU Registry

Asiah Salem Rugaan[1], Naved Yousuf Hasan[1]*, Masood Iqbal[1], Elaf Damanhouri[2], Rwan Emad Radi[3], Enshrah Radwan[4], Maher Alhazmi[5]

1 Dept of Intensive Care, King Abdullah Medical City, Muzdalifah Road, Al Mashaer, Makkah, Saudi Arabia
2 Dept of Anatomical Pathology, King Abdulaziz Specialist Hospital, Taif, Saudi Arabia.
3 Dept of Family Medicine, General Directorate of Health Affairs, Makkah, Saudi Arabia
4 Dept of Pediatrics, King Fahad Armed Forces Hospital, Jeddah, Saudi Arabia
5 Administration of Research and Innovation, King Abdullah Medical City, Muzdalifah Road, Al Mashaer, Makkah, Saudi Arabia

*** Corresponding Author:** Naved Yousuf Hasan **E-mail:** naved911@hotmail.com

ABSTRACT

Objective: There is a paucity of research on the factors predicting mortality and a length of stay in the Intensive Care Unit (ICU) with solid tumor patients. This study will assess the characteristics and predictors of outcomes of patients with solid tumors in medical ICU.

Material and Methods: This research has been designed as a retrospective observational study using an ICU database. Patients who have a solid tumor were included in the study (May 2015 to July 2018). Post-surgical and those with a length of stay of more than one day are excluded from the study. We identified the predictors for ICU mortality and ICU long stay (⩾21 days).

Results: Out of 2883 patients, 364 patients with solid tumors were enrolled. The commonest sites for solid tumors were breast (15.9%), colorectal (11.5%), and lung (9.9%). 158 (43.4%) had metastatic disease, and 264 (72.5%) with progressive disease. The major reasons for ICU admission were a respiratory failure (52.7%) and severe sepsis (52.2%). The ICU and hospital mortality rates were 32.4% and 47%, respectively. Fifty patients (13.7%) had long stayed (⩾ 21 days) in ICU. The independent predictors for mortality were Sequential Organ Failure Assessment (SOFA) score (OR, 1.2; 95% CI, 1.1–1.3; P=.000), invasive ventilation (OR, 3.5; 95% CI, 1.5–8.3; P=.004) and vasopressor (OR, 2.6; 95% CI, 1.1–5.9; P=.018), while the independent predictors of long-stay were ICU infections (odds ratio [OR], 18.9; 95% CI, 5.3 – 66.7; P=.0001), SOFA score (OR, 1.5; 95% CI, 1.2–1.8; P=.0001), invasive ventilation (OR, 8.2; 95% CI, 1.6–40.4; P=.009), bilirubin (OR, .5; 95% CI .2–.9; P=.049).

Conclusion: Irrespective of the cancer stage, patients had a reasonable survival, and most do not require a long stay in the ICU. Flexibility in admission should be considered as disease progression and metastatic disease were not independent predictors of ICU mortality or long stay in this study.

Keywords: solid tumors, critically ill, mortality, length of stay

INTRODUCTION

Significant medical advances have been made in cancer management that resulted in dramatic improvement of patients' outcomes and survival, which are associated with increasing demand for intensive care unit admissions and treatment (1-3). Recent studies (1-8) have reported that there has been a significant improvement in the ICU survival rate in cancer patients. This improvement in ICU survival of cancer patients led many investigators to look for factors influencing the ICU mortality to guide case selection for critically ill cancer patients for ICU admission, who could benefit from critical care management strategies (4-8). While many published studies focused on either the predictors of ICU mortality of cancer patients in general or in patients with haematological malignancies, very little research has been conducted on patients with solid tumors, although the critical care outcome-predictors are still controversial in this patients' category.

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Although many critically ill patients are admitted to the ICU for a short period, it is not uncommon that some patients have a complicated clinical course and require long ICU stay (⩾21 days). Extended ICU stay has effects on patient morbidity and mortality and cost (**9-11**). In addition, the long ICU stay has effects on ICU bed availability and subsequent delayed ICU admission. Delayed admission to ICU is a known factor associated with worse patient outcomes (**30-32**). Thus, knowledge about factors that impact the prolonged ICU stay is important for future enhancement of quality of care, and guide better resources utilization. However, there is limited data on the ICU outcomes and predictors of prolonged stay for patients with solid tumors, worldwide and further rare in Saudi Arabia.

In this study, we aimed to describe the characteristics and outcomes of critical care patients with solid tumors admitted to ICU, and to determine the predictors of mortality and prolonged stay in ICU.

MATERIAL and METHODS

This is a retrospective observational study, conducted in the medical ICU of King Abdullah Medical City, a 500-bed tertiary hospital, in Makkah, Saudi Arabia. King Abdullah Medical City is the main referral site that receives patients from the whole western region of Saudi Arabia. The data were extracted for patients admitted from May 2015 to July 2018 from a prospective ICU database, a comprehensive ICU registry (**11**) that includes data on ICU patients' characteristics, procedures, treatments, and outcomes. The study was approved by the institutional review board (IRB) at King Abdullah Medical City. The data collected include patients demographics, cancer type, cancer characteristics (e.g., course of malignancy, staging, and treatment), comorbidities, reasons for ICU admission, source of ICU admission, Length Of Stay (LOS) at the hospital before ICU admission, laboratory results, infection acquired at the ICU admission and during ICU stay, Sequential Organ Failure Assessment (SOFA) score, Acute Physiology and Chronic Health Evaluation (APACHE) II score, therapeutic interventions during ICU stay, LOS in ICU and ICU mortality.

All patients admitted to ICU with age above 14 years, who are diagnosed with solid tumors, were included in the study. To ensure that the study is investigating patients who are sick enough to be certainly in need of active ICU management, the following patients with solid tumors were excluded from the study. All patients discharged from ICU within 24 hours, patients admitted after planned elective surgeries, and patients have signed Do Not Resuscitate (DNR) order within 48 hours of ICU admission. We also excluded cancer patients with hematological malignancy (**Figure 1**). The first critical care admission is considered in the study.

The primary outcomes of the study are the ICU mortality and the ICU length of stay, the secondary outcomes are the predictors of mortality, and a long stay in ICU. This study defined the long ICU stay as an ICU stay for 21 days or more (**10**).

We imported the data from the registry system into SPSS version 23 and saved in an SPSS system file. We reported discrete variables using counts and percentages, while continuous variables using the mean and standard deviation. Comparative analysis was done between different ICU outcomes (survivors vs non-survivors and long stay vs non-long stay) using the t-test or Mann-Whitney U test for continuous variables, and the $\chi 2$ test or Fisher exact test for categorical variables. In the non-prolonged ICU stay, 91 patients were excluded, who died before 21 days. Multivariate logistic regression analyses were used to determine the predictors of ICU mortality and ICU length of stay. The statistical significance is shown by $P < 0.05$.

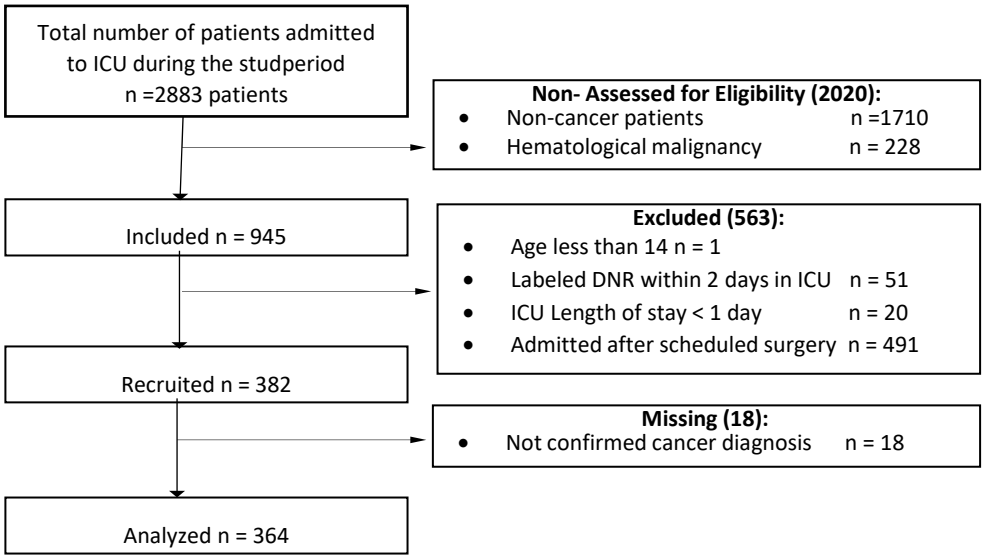

Figure 1: Flow of the patients through the study

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RESULTS

1. Patient Characteristic

During the research period, 2883 patients were admitted to the ICU. Among the total admissions, we identified 1173 (40.7%) cancer patients after screening for inclusion and exclusion criteria, a total of 364 (14.2%) patients with solid tumors enrolled in the study (**Figure-1**). **Table-1** summarizes the baseline characteristics of the study population. The mean age is 57.6 years, male versus female gender represents 51.1% versus 48.9%.

157 (43%) patients were admitted directly to ICU through the emergency room (ER) while 206 (57%) were admitted from inpatient departments. The average length of stay at the inpatients department before admission to ICU is 4.9 days. The most common comorbidities among the study population other than cancer are hypertension (41.5%) and diabetes (35.7%) cardiovascular disease (23%). The most typical reasons for ICU admission were respiratory failure (52.7%) and sepsis (52.2%).

We found that 264 (72.5%) of the study population had progressive disease and 158 (43.4%) with confirmed metastatic cancer. The most common solid tumors were breast (16%), colorectal (11.5%), and lung (9.9%) cancers, while the most common sites of metastasis were liver (18.7%), lung (17.9%), and bone (17%). On the other hand, 295(81%) patients were on active cancer treatment, while 69 patients (19%) were not on active therapy for cancer. In reviewing the active antitumor therapy, it is found those 126 (34.6%) patients on chemotherapy, and 75 (20.6%) patients on radiation therapy, 60 patients (16.5%) on biological treatment, and 34 patients (9.3%) on hormonal therapy.

2. Results of critical care data

Upon admission to ICU, 148 patients (40.7%) were identified with two or more organs dysfunctions. The mean SOFA score is 6.9 ± 4.7, whereas the mean APACHE II score is 19.8 ± 8.4. A total of 211 patients (58%) required mechanical ventilator (MV) support, while 185 patients (50.8%) required invasive MV. The mean duration on the mechanical ventilator is 11.8 ± 15.3days, while the median of 6 days. 53 (14.3%) patients required tracheostomy. Moreover, 182 (50%) patients required vasopressor, and 46 (12.6%) patients received renal replacement therapy.

Among those admitted because of sepsis, 130 (35.7%) patients had positive microbiology culture, the majority bacterial 125 (34%), minority fungal 14 (3.8%). The commonest identified sites of infection are blood stream75 (20.6%) and the lung 35 (9.6%).

The laboratory data upon ICU admission revealed that the mean WBC was 11.3. Haemoglobin mean 9.7 and Platelet mean 237. Leukopenia (WBC <4) identified in 54 (14.8) patients, and thrombocytopenia (Platelet <50) in 11 (3%) patients, 53 (14.6%) patients required blood product transfusion. The calculated mean for AST, ALT, bilirubin, and calcium is high however; the median is within the normal range.

3. Results of Outcome data

Forty nine patients (13.5%) had ICU acquired infections, commonly of lung infection (7.5%) and bloodstream infection (5.5%).

The mean ICU Length of Stay (LOS) was 11.4 ± 13.6 days and the median of 6.4 days. One hundred seventy-two died during hospital stay (47%), 118 patients died in the ICU (32%), among which 74 patients (20.5%) had DNR orders signed after 48 hours from ICU admission.

Table 1: Study population Baseline characteristics

Variable	Patients with Solid Tumor (n=364)
Age at ICU admission	
Mean ± SD	57.6 ± 15.8
Median (IQR)	59 (47 – 70.7)
Gender	
Male	186 (51.1%)
Female	178 (48.9%)
Course of malignancy	
Progressive	264 (72.5%)
Not progressive	100 (27.5%)
Staging	
Metastatic	158 (43.4%)
Non Metastatic	206 (56.6%)
Site of metastasis	
Liver	68 (18.7%)
Lung	65 (17.9%)
Bone	62 (17%)
Peritoneal	18 (4.9%)
Others	40 (10.9%)
Types of cancer	
Breast	58 (15.9%)
Colorectal	42 (11.5%)
Lung	36 (9.9%)
Oral	24 (6.5%)
Upper GIT	23 (6.3%)
gynecological	22 (6%)
Pancreas	19 (5.2%)
Brain	18 (4.9%)
Thyroid	15 (4.1%)
Prostate	15 (4.1%)
Renal cell carcinoma	12 (3.2%)
Hepatobiliary	11 (3%)
Gall bladder	10 (2.7%)

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Table 1. Baseline characteristics and outcomes

Variable	Patients with Solid Tumor (n=364)
Ovary Bladder	9 (2.4%)
Others	11 (3%)
Active cancer treatment	
Chemotherapy	126 (34.6%)
Biologic	60 (16.5%)
Hormonal	34 (9.3%)
Radiation	75 (20.6%)
Source of admission	
ER	157 (43.1 %)
Non-ER	207 (56.9%)
LOS at the hospital before ICU admission	
Mean ± SD	4.9 ± 16.7
Median (IQR)	1 (0 – 5)
Comorbidities	
Diabetes mellitus	130 (35.7%)
Hypertension	151 (41.5%)
Cardiovascular diseases	84 (23.1%)
Reason for ICU admission	
Respiratory failure	192 (52.7%)
Sepsis/septic shock	190 (52.2%)
Neurological disorder	77 (21.2%)
Renal dysfunction	47 (12.9%)
Hepatic dysfunction	20 (5.5%)
Coagulopathy	15 (4.1%)
≥ 2 organ dysfunctions	148 (40.7%)
ICU admission microbiology	
Positive microbiology results	130 (35.7%)
Bacterial infection	125 (34.3%)
Fungal infection	14 (3.8%)
Bloodstream infection	75 (20.6%)
Lung infection	35 (9.6%)
Urine infection	35 (9.6%)
On ICU admission	
APACHE II	
Mean ± SD	19.8 ± 8.4
Median (IQR)	18 (14 – 26)
SOFA	
Mean ± SD	6.9 ± 4.7
Median (IQR)	6 (3 - 10)
Laboratory results	
WBC	
Mean ± SD	11.3 ± 8.1
Median (IQR)	9.9 (5.9 – 14.6)
Platelet	
Mean ± SD	237.2 ± 151.9
Median (IQR)	215 (130 – 323.5)
Hemoglobin	
Mean ± SD	9.7 ± 2.4
Median (IQR)	9.5 (7.9 – 11.3)
ALT	
Mean ± SD	69.4 ± 207.9
Median (IQR)	27 (16 – 51)
AST	
Mean ± SD	147.6 ± 551.4
Median (IQR)	33 (21 – 89.1)
Bilirubin	
Mean ± SD	2.9 ± 22.8
Median (IQR)	0.7 (0.4 – 1.3)
Creatinine	
Mean ± SD	1.7 ± 2.1
Median (IQR)	1 (0.7 – 1.9)
Calcium	
Mean ± SD	10.6 ± 39.9
Median (IQR)	8.4 (7.6 – 9.2)
Serum Albumin	
Mean ± SD	2.8 ±1
Median (IQR)	2.7 (2 – 3.3)
Leukopenia	54 (14.8%)
Thrombocytopenia	11 (3%)
During ICU stay	
Vasopressor use	182 (50%)
Renal replacement therapy	46 (12.6%)
Invasive ventilation	185 (50.8%)
Non-invasive ventilation	26 (7.1%)
Duration of MV	
Mean ± SD	11.8 ± 15.3
Median (IQR)	6 (2 – 14)
Blood product transfusion	53 (14.6%)
Tracheostomy	53 (14.6%)
ICU acquired infections	49 (13.5%)
Bacterial infection	31 (8.5%)
Fungal infection	31 (8.5%)
Bloodstream infection	20 (5.5%)
Lung infection	27 (7.4%)
Urine infection	6 (1.6%)
Outcome	
DNR order 48 hours afteradmission	74 (20.5%)
ICU length of stay	11.4 ± 13.6
Mean ± SD Median (IQR)	6.4 (3.6 – 13.2)
ICU Mortality	118 (32.4%)
Hospital Mortality	172 (47.3%)

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4 Results of univariate analysis

Univariate comparison of the survivors versus non-survivors

The univariate analyses compared ICU survivors versus non-survivors (**Table 2**). We found that non-survivors had significantly more progressive cancer, and were more likely to be admitted to the ICU because of sepsis/septic shock and respiratory failure P=.002 and P=.000, respectively. The APACHE II and SOFA scores were significantly higher in non-survivors compared to survivors (P=.000) for both. According to laboratory results, the aspartate aminotransferase (AST) level, bilirubin, and creatinine were significantly higher in non-survivors P=.000, P=.013, P=.002, respectively.

Non-survivors especially required advanced ICU support vasopressor, renal replacement therapy, and invasive mechanical ventilation, while non-invasive ventilators were used significantly more in survivors (P=.018). We found ICU-acquired infections to be more common among non-survivors (P=.000). Admissions from ER had significantly better survival compared to inpatients admissions (P=.025), non-survivors tend to be hospitalized significantly for a longer duration before ICU admission 8.4 ± 27.8 days, versus survivors 3.2 ± 6.3 days (P=.000). We found the progressive disease to be more significant among non-survivors (P=.002). There is no significant difference between survivors and non-survivors related to age, gender, comorbidities, metastatic cancer, metastatic site, cancer treatment, hemoglobin level, WBC count, and platelet count.

Table 2: univariate analysis comparing the survivor and non-survivor

Variable	Survivor (n=246)	Non-survivor (n=118)	P-value
Age at ICU admission			
Mean ± SD	56.6 ± 15.9	59.6 ± 15.5	.097
Median (IQR)	58 (46 – 70)	61.5 (50.7 – 72)	
Gender			
Male	118 (48%)	68 (57.6%)	.084
Female	128 (52 %)	50 (42.4%)	
Course of malignancy			
Progressive	165 (67.1%)	99 (83.9%)	**.002**
Not progressive	81 (32.9%)	19 (16.1%)	
Staging			
Metastatic	103 (41.9%)	55 (46.6%)	.393
Non Metastatic	143 (58.1%)	63 (53.4%)	
Site of metastasis			
Liver	44 (17.9%)	24 (20.3%)	.574
Lung	42 (17.1%)	23 (19.5%)	.573
Bone	39 (15.9%)	23 (19.5%)	.387
Peritoneal	12 (4.9%)	6 (5.1%)	.932
Active Treatment			
Chemotherapy	81 (32.9%)	45 (38.1%)	.455
Biologic	44 (17.9%)	16 (13.6%)	.298
Hormonal	24 (9.8%)	10 (8.5%)	.694
Radiation	53 (21.5%)	22 (18.6%)	.522
Source of admission			
ER	116 (47.2%)	41 (34.7%)	**.025**
Non-ER	130 (52.8%)	77 (65.3%)	
LOS at the hospital before ICU admission			
Mean ± SD	3.2 ± 6.3	8.4 ± 27.8	**.000**
Median (IQR)	1 (0 – 3)	2 (0 – 9)	
Comorbidities			
Diabetes mellitus	87 (35.4%)	43 (36.4%)	.841
Hypertension	107 (43.5%)	44 (37.3%)	.261
Cardiovascular diseases	50 (20.3%)	34 (28.8%)	.099
Reason for ICU admission			
Respiratory failure	111 (45.1%)	81 (68.6%)	**.000**
Sepsis/septic shock	106 (43.1%)	84 (71.2%)	**.000**
Neurological disorder	54 (22%)	23 (19.5%)	.591
Renal dysfunction	29 (11.8%)	18 (15.3%)	.356
Hepatic dysfunction	10 (4.1%)	10 (8.5%)	.084
Coagulopathy	11 (4.5%)	4 (3.4%)	.431
≥ 2 organ dysfunctions	79 (32.1%)	69 (58.5%)	**.000**

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ICU admissionmicrobiology			
Admission culture	79 (32.1%)	51 (43.2%)	**.038**
Bacterial infection	77 (31.3%)	48 (40.7%)	.078
Fungal infection	6 (2.4%)	8 (6.8%)	**.046**
Bloodstream infection	44 (17.9%)	31 (26.3%)	.064
Lung infection	22 (8.9%)	13 (11%)	.530
Urine infection	26 (10.6%)	9 (7.6%)	.373
On ICU admission			
APACHE II	15.9 ± 6.1	27.9 ± 6.7	**.000**
Mean ± SD Median (IQR)	16 (12 – 19.2)	28 (24 – 32)	
SOFA			
Mean ± SD	4.2 ± 2.4	12.4 ± 3.5	**.000**
Median (IQR)	4 (2 – 6)	12 (10 – 14)	
Laboratory Results			
WBC			
Mean ± SD	11.2 ± 7.8	11.7 ± 8.8	.690
Median (IQR)	9.9 (6.3 – 14)	10.5 (5.2 – 16.2)	
Platelet			
Mean ± SD	235.9 ± 140.7	240.1 ± 173.5	.823
Median (IQR)	215 (134.7 – 315)	217.5 (108 – 340.7)	
Hemoglobin			
Mean ± SD	9.9 ± 2.5	9.4 ± 2	.061
Median (IQR)	9.7 (8.1 – 11.8)	9 (7.7 – 10.6)	
ALT			
Mean ± SD	54.4 ± 105.5	100.6 ± 330.7	.115
Median (IQR)	26.5 (15.2 – 50.7)	29 (18.5 – 58.5)	
AST			
Mean ± SD	108.7 ± 316.4	228.5 ± 850.8	**.000**
Median (IQR)	30 (20 – 67.7)	51.7 (24.5 – 134.5)	
Bilirubin			
Mean ± SD	3.1 ± 27.5	2.6 ± 5.1	**.013**
Median (IQR)	0.6 (0.4 – 1.2)	0.7 (0.5 – 2.3)	
Creatinine			
Mean ± SD	1.7 ± 2.3	1.9 ± 1.6	**.002**
Median (IQR)	0.9 (0.6 – 1.8)	1.1 (0.8 – 2.5)	
Calcium			
Mean ± SD	11.7 ± 48.6	8.2 ± 1.2	**.042**
Median (IQR)	8.4 (7.8 – 9.3)	8.1 (7.5 – 9.1)	
Serum Albumin			
Mean ± SD	2.9 ± 1	2.6 ± 1.1	**.004**
Median (IQR)	2.8 (2.1 – 3.3)	2.4 (1.7 – 3.2)	
Leukopenia	33 (13.4%)	21 (17.8%)	.271
Thrombocytopenia	8 (3.3%)	3 (2.5%)	.498
During ICU stay			
Vasopressor use	84 (34.1%)	98 (83.1%)	**.000**
Renal replacement therapy	22 (8.9%)	24 (20.3%)	**.002**
Invasive ventilation	82 (33.3%)	103 (87.3%)	**.000**
Non-invasive ventilation	23 (9.3%)	3 (2.5%)	**.018**
Blood product transfusion	33 (13.4%)	20 (16.9%)	.371
Tracheostomy	26 (10.6%)	27 (22.9%)	**.002**
ICU acquired infection	22 (8.9%)	27 (22.9%)	**.000**
Bacterial infection	14 (5.7%)	17 (14.4%)	**.005**
Fungal infection	14 (5.7%)	17 (14.4%)	**.005**
Bloodstream infection	6 (2.4%)	14 (11.9%)	**.000**
Lung infection	15 (6.3%)	12 (10.7%)	.143
Urine infection	2 (0.8%)	4 (3.4%)	.090

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Univariate analysis comparing patients with prolonged ICU stay compared to non- prolonged ICU stay

The univariate analyses compared those who stayed in ICU less than 21 days versus those who stayed 21 days or more. In this study, we found that 50 (13.7%) patients with solid tumors required a prolonged stay (**Table-3**). Patients admitted to ICU because of respiratory failure and ⩾ 2 organ dysfunctions were more likely to require a prolonged ICU stay P=.001, P=.004, respectively. Also, APACHE II and SOFA scores were significantly more among patients who needed a prolonged ICU stay P=.000 for both. Patients who had a prolonged ICU stay were required more advanced ICU care, including vasopressors, renal replacement therapy, and mechanical ventilation with significant P=.000. The ICU- acquired infections were significantly more common in patients with a prolonged ICU stay P=.000

Table 3: univariate analysis comparing patients with prolonged stay and non-prolonged stay

Variable	Non-prolonged ICU stay (< 21days) (n=223)	Prolonged ICU stay (≥ 21days) (n=50)	P-value
Age at ICU admission			
Mean ± SD	56.8 ± 15.7	58 ± 17.1	.467
Median (IQR)	58 (46 – 70)	61.5 (47.7 – 68.7)	
Gender			
Male	107 (48%)	27 (54%)	.442
Female	116 (52%)	23 (46%)	
Course of malignancy			
Progressive	149 (73.2%)	34 (68%)	.872
Not progressive	74 (33.1%)	16 (32%)	
Staging			
Metastatic	92 (41.3%)	19 (38%)	.672
Non Metastatic	131 (85.7%)	31 (62%)	
Site of metastasis			
Liver	43 (19.3%)	5 (10%)	.119
Lung	37 (16.6%)	8 (16%)	.919
Bone	33 (14.8%)	8 (16%)	.830
Peritoneal	10 (4.5%)	3 (6%)	.712
Active treatment			
Chemotherapy	75 (33.6%)	14 (28%)	.443
Biologic	43 (19.3%)	4 (8%)	.056
Hormonal	21 (94%)	3 (6%)	.586
Radiation	49 (22%)	7 (14%)	.207
Source of admission			
ER	106 (47.5%)	20 (40%)	.334
Non ER	117 (52.5%)	30 (60%)	
LOS at the hospital before ICU admission			
Mean ± SD	3.1 ± 6.2	11.4 ± 41.7	.274
Median (IQR)	1 (0 – 3)	1 (0 – 7)	
Comorbidities			
Diabetes mellitus	81 (36.3%)	19 (38%)	.824
Hypertension	98 (43.9%)	23 (46%)	.792
Cardiovascular diseases	44 (19.7%)	15 (30%)	.070
Reason for ICU admission			
Respiratory failure	96 (43%)	34 (68%)	**.001**
Sepsis/septic shock	97 (43.5%)	22 (44%)	.948
Neurological disorder	46 (20.6%)	15 (30%)	.150
Renal dysfunction	27 (12.1%)	6 (12%)	.983
Hepatic dysfunction	9 (4%)	2 (4%)	.991
Coagulopathy	9 (4%)	3 (6%)	.465
≥ 2 organ dysfunctions	68 (30.5%)	26 (52%)	**.004**
Microbiology uponarrival to ICU			
Admission culture positive	73 (32.7%)	17 (34%)	.864
Bacterial infection	72 (32.3%)	16 (32%)	.969
Fungal infection	5 (2.2%)	1 (2%)	.916
Bloodstream infection	41 (18.4%)	11 (22%)	.556
Lung infection	18 (8.1%)	6 (12%)	.407
Urine infection	26 (11.7%)	1 (2%)	**.037**
Data collected at ICUadmission			
APACHE II	15.6 ± 6	23.3 ±7.4	**.000**
Mean ± SD Median (IQR)	16 (11 – 18)	24 (18 – 28)	
SOFA			
Mean ± SD Median (IQR)	4.1 ± 2.3	9.4 ± 4.4	**.000**
	4 (2 – 6)	9 (6 – 12)	

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Laboratory results			
WBC			
Mean ± SD	11.3 ± 8	12 ± 7.1	.216
Median (IQR)	10 (6.5 – 14.1)	12 (7.2 – 16.1)	
Platelet			
Mean ± SD	2378 ± 143.8	247.7 ± 140	.466
Median (IQR)	215 (135 – 318)	239 (155.5 – 332.5)	
Hemoglobin			
Mean ± SD	9.9 ± 2.5	9.7 ± 2.4	.624
Median (IQR)	9.7 (8.1 – 11.8)	9.6 (7.6 – 11.5)	
ALT			
Mean ± SD	56.4 ± 110.4	48.2 ± 104.9	.869
Median (IQR)	26 (15.5 – 51)	29 (14.5 – 44.5)	
AST			
Mean ± SD	115.2 ± *331.7*	64.8 ± *117.3*	.789
Median (IQR)	*29 (20 – 68)*	*31 (20 – 62.1)*	
Bilirubin			
Mean ± SD	3.3 ± *28.9*	0.9 ± *1.6*	**.045**
Median (IQR)	*0.6 (0.4 – 1.3)*	*0.5 (0.3 – 0.9)*	
Creatinine			
Mean ± SD	1.7 ± *2.4*	1.4 ± *1.5*	.322
Median (IQR)	*1 (0.7 – 1.8)*	*0.9 (0.6 – 1.6)*	
Calcium			
Mean ± SD	12 ± *51*	8.8 ± *1.1*	**.031**
Median (IQR)	*8.4 (7.7 – 9.2)*	*8.9 (8.1 – 9.6)*	
Serum Albumin			
Mean ± SD	2.9 ± *1*	2.6 ± *0.8*	.122
Median (IQR)	*2.8 (2.1 – 3.4)*	*2.7 (1.9 – 3.1)*	
Leukopenia	29 (13%)	7 (14%)	.851
Thrombocytopenia	7 (3.1%)	3 (6%)	.330
Data During ICU stay			
Vasopressor use	68 (30.5%)	38 (76%)	**.000**
Renal replacement therapy	15 (6.7%)	15 (30%)	**.000**
Invasive ventilation	60 (26.9%)	47 (94%)	**.000**
Non-invasive ventilation	22 (9.9%)	2 (4%)	.270
Blood product transfusion	27 (12.1%)	11 (22%)	.068
Tracheostomy	10 (4.5%)	35 (70%)	**.000**
ICU acquired infection	8 (3.6%)	33 (66%)	**.000**
Bacterial infection	5 (2.2%)	20 (40%)	**.000**
Fungal infection	5(2.2%)	20 (40%)	**.000**
Bloodstream infection	0 (0%)	17 (34%)	**.000**
Urine infection	1 (0.4%)	5 (10%)	**.001**

5. Results of the multivariate analysis

In the univariate analysis, we found that progressive cancer, LOS at the hospital before ICU admission, respiratory failure, and sepsis as reasons for ICU admissions, having two or more organs dysfunction, SOFA score, APACHE II score, some laboratory abnormalities (AST, bilirubin, and creatinine levels) and some therapeutic interventions (vasopressors, renal replacement therapy, and mechanical ventilation) were significantly related to ICU mortality. However, in multivariate analysis, we found only three factors independently predict the ICU mortality: SOFA (OR, 1.2; 95% CI, 1.1–1.3; P=.000), Invasive ventilation (OR, 3.5; 95% CI, 1.5–8.3; P=.004) and Vasopressor (OR, 2.6; 95% CI, 1.1–5.9; P=.018).

Similarly, many factors that found associated with prolonged ICU in univariate analysis, including respiratory failure as a reason for ICU admission, having two or more organs dysfunction, ICU acquired infection, SOFA score, APACHE II score, and some therapeutic interventions (vasopressors, renal replacement therapy, and mechanical ventilation) significantly related to the prolonged stay in ICU.

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Table 4: Independent predictors for ICU mortality

Variable	OR (95% CI)	P-value
SOFA	1.2 (1.1 – 1.3)	**.000**
Invasive ventilation	3.5 (1.5 – 8.3)	**.004**
Vasopressor	2.6 (1.1 – 5.9)	**.018**

Table 5: Independent predictors for prolonged LOS in ICU

Variable	OR (95% CI)	P-value
ICU acquired infection	18.9 (5.3 – 66.7)	**.0001**
SOFA	1.5 (1.2 – 1.8)	**.0001**
Invasive ventilation	8.2 (1.6 – 40.4)	**.009**
Bilirubin	.5 (.2 –.9)	**.049**

DISCUSSION

There is little research about the factors predicting mortality and prolonged stay in ICU in critically ill patients with solid tumors. And further fewer studies in Saudi Arabia identified the factors influencing the outcomes of patients with solid tumors. Knowledge of such factors is important in making appropriate patient selection for improving the quality of ICU care in patients with solid tumors. Thus, the primary objectives of this study were to determine the characteristics and the outcomes of patients with solid tumors admitted to ICU in a tertiary hospital in Saudi Arabia, and to explore factors affecting mortality and prolonged stay in ICU.

Previous studies reported large variation (15% -59%) in the ICU mortality rates of patients with solid tumors (**8, 12-14**), which reported an average rate of 31.2%. This variation in the reported mortality is explained by the variations in the characteristics of patients selection in those studies, the underlying cancer type, cancer staging, and therapeutic intervention decisions, and timing of end-of-life care plan before admission to ICU (**4-8, 12-15**). The early decision about end-of-life care would prevent futile care, including ICU admissions of cases which will not benefit from ICU management (**19**). In this study, we found the ICU mortality in patients with solid malignancies to be 32.4%. Our ICU mortality rate is slightly higher than the average rate reported in the previous studies in patients with solid malignancy. This slight overestimation in mortality can be explained by the composition of cases selected in this study, as all cases with expected to have good outcome were excluded, including cases stayed in ICU for one day and all planned admissions after elective surgery. Most patients enrolled in this study were sick patients who had progressive disease (72.5%), and many of them had metastatic cancer (43.4%). This could have caused a slight overestimation of the ICU mortality rate in this study.

In recent systematic research of patients with a solid malignancy (**15**), it was reported that to predict ICU mortality we need adequate details to be of prognostic value to physicians and for proper selection of cases for ICU care. We found many factors were associated with ICU mortality (**Table 2**).

However, only three independent risk factors were found to predict the ICU mortality rate in multivariate analysis. These factors were SOFA score at ICU admission, use of invasive mechanical ventilation, and vasopressor. The predictors in our study are similar to those reported in previous cancer critical care studies (**16-18**). Although APACHE II is reported to be the main predicting factor for ICU mortality in non-cancer patients (**8**), and SOFA and APACHE II scores are predicting ICU mortality in cancer patient's studies and hemato-oncology studies (**16-18, 20, 21**). However, under the results of the study done by Gulbin (**8**) and another study by Xia (**12**), in our study, we found that only the **Sequential Organ Failure Assessment Score (SOFA) is an independent risk factor for ICU mortality in patients with solid tumors.**

The impact of the characteristics related to cancer, such as the stage of malignancy, the response to chemotherapy, and other characteristics of cancer on short-term outcomes remains controversial (**7, 13, 16, 17**). In this study, although we found that progressive disease is associated with lower survival in univariate analysis however it was not in multivariate analysis. Also, the presence of metastasis did not reveal any impact on the outcome.

To our knowledge, this is the first research investigating prolonged ICU stay in patients with solid malignancies. We found that 13.7% of patients with solid tumors had an ICU stay of 21 days or more. Prolonged ICU stay is known to be associated with an increased risk of severe complications, such as healthcare-associated infections. In this study, 66% of the patients with prolonged ICU stay developed ICU acquired infections. Multivariate analysis revealed four independent predictors of prolonged ICU stay are, ICU acquired infections, SOFA score within 24 hours of ICU admission, use of invasive mechanical ventilation, and bilirubin level. These results confirm what has been reported by Soares M in a published review about the under-estimation of outcome in cancer patients using the critical care scoring systems alone and highlighted the importance of specific clinical prognostic factors such as mechanical ventilator and bilirubin for more accurate predication in cancer cases (**24**) with prolonged stay in ICU. Although APACHE II has shown to be related to prolonged ICU stay.

However, the score was not a significant predictor for prolonged ICU stay in multivariate analysis. We found prolonged stay in ICU was significantly related to higher ICU mortality. However, it was not a significant predictor for ICU mortality. The influence of the prolonged stay in ICU that has on short and long-term outcomes remains controversial. Several studies (**29, 30**) have reported higher ICU mortality in patients with a prolonged stay in ICU, while others (**30, 31**) did not.

Many studies have consistently reported invasive mechanical ventilator as a predictor of poor outcomes in cancer patients (**4, 28, 29**).

This study identified several predictors of mortality and prolonged stay in solid tumor ICU patients. Knowledge of such predictors could offer valuable information for intensive care physicians to avoid futile care and better management of critical care resources by considering end-of-life care planning. ICU survival rate can be significantly increased in patients with solid tumors with careful patient selection during ICU admission (**8**). Patients who are at the initial phase of their malignant disease should be routinely admitted to the ICU. Some selection criteria, including the characteristics of the underlying malignancy, are not currently reliable for making triage decisions (**4-8, 12-15**). We found the SOFA score a key determinant and useful in predicting ICU mortality.

Understanding the factors affecting the prolonged ICU stay may help in improving the quality of care in ICU, such as infection prevention and mechanical ventilator management (**30-33**). Prolonged stay in ICU will affect the critical care bed availability to avoid delayed ICU admission, which had been well documented as a significant factor that related to worse patient outcomes. Factors such as organ failure can be managed easier through earlier admission and evaluation by the ICU team, and this might lead to a shorter stay in the ICU (**34-38**).

This study is a prospective registry study with a relatively large number of patients. However, there are a few limitations, including being single-center research. A large multi-center study involving several ICUs with a larger sample size may bear out the findings. Finally, this study collected data only on short-term outcomes. Collecting data on long-term outcomes after discharge from ICU could have increased the impact of the current research.

CONCLUSION

Although most of the study population had advanced solid tumors, a reasonable mortality outcome was reported in this study. Prolonged stay in ICU was reported to be in only 13% of total ICU admissions and the long stay in this study was not correlated with mortality, the predictors of mortality and a long stay in ICU associated with criteria related to the severity of illness rather than to characteristics related to the solid tumors, based on these study findings, flexibility in admitting patients with solid tumor shall be irrespective of disease characteristics, as the ICU predictors of outcome in patients with solid tumor is like those reported in non-cancer critically ill patients.

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