Clinico-demographic and Outcome Predictors in Solid Tumor Patients with Unplanned Intensive Care Unit Admissions: An Observational Study

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ABSTRACT

Objectives: Critically ill solid organ malignancy patients admitted to intensive care unit (ICU) as unplanned medical admissions behave differently from other subsets of cancer patients (hematolymphoid malignancies and cancer patients admitted for postoperative care). These patients if appropriately selected may benefit from the ICU care. There is paucity of data on critically ill unplanned admissions of solid organ malignancies from South Asia. We analyzed data of patients with solid tumors with unplanned admissions to the ICU to determine the clinical, epidemiological characteristics, and predictors of hospital mortality in an Indian ICU.

Materials and methods: This prospective, observational study was done in our 14-bedded mixed medical–surgical ICU from July 2014 to November 2015. We included all consecutive adult unplanned admissions with solid organ malignancies having ICU stay of >24 hours. Surgical admissions, hematolymphoid malignancies, advanced malignancy with no treatment options, and those cured of cancer >5 years were excluded.

Results: Two hundred and thirty-five consecutive patients were included in this cohort. ICU and hospital mortalities were 36.6 and 40%, respectively. On multivariate analysis, cancer status [odds ratio (OR): 3.204; 95% confidence interval (CI): 1.271–8.078], invasive mechanical ventilation (OR: 5.940; 95% CI: 2.632–13.408), and sequential organ failure assessment (SOFA) score on the day of ICU admission (OR: 1.199; 95% CI: 1.042–1.379) were independent predictors of hospital mortality.

Conclusion: Acute respiratory failure and septic shock are the common reasons of unplanned ICU admission for patients with solid organ malignancies. With good patient selection, more than half of such patients are likely to be discharged alive from the hospital.

Keywords: Critically ill patients, Hospital mortality, Medical admissions, Solid organ malignancy, Unplanned admissions.

Indian Journal of Critical Care Medicine (2021): 10.5005/jp-journals-10071-24052

INTRODUCTION

The intensive care unit (ICU) outcomes of cancer patients have significantly improved due to advances in the fields of both oncology and critical care.[1,2] The reluctance to admit oncology patients to the ICUs has decreased over the last few years.[3] Increasing number of patients with solid tumors are admitted to the ICUs for postsurgical care, management of infections, treatment-related complications, or noncancer-related medical reasons.

In a retrospective study of elderly patients with solid tumors admitted to the ICU, Auclin et al. found that the ICU outcomes of these patients were similar to those admitted without malignancy, despite needing mechanical ventilation (MV), vasopressor therapy, and dialysis. Nearly 53% of survivors were able to resume cancer therapy.[4] It therefore appears that appropriately selected patients with solid tumors may benefit if admitted to the ICU.

In a large retrospective study of nearly 10,000 patients, largely comprising of patients with solid tumors, the ICU and hospital mortalities were found to be 15.9 and 25.4%, respectively.[5] In contrast, Azoulay et al. reported a much higher hospital mortality (39.1%) in patients with hematolymphoid malignancies admitted to the French and Belgian ICUs.[6] Vincent et al.[7] suggested that a clear distinction must be made while discussing the prognosis of cancer patients admitted with hematological malignancies vs those with solid tumors since the hospital survival of patients with solid tumors is much better. Data from a large study[8] of emergent admissions of oncology patients from the Netherlands showed that survival to hospital discharge for patients with solid tumors admitted for

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surgical reasons (82.6%) was higher than those admitted for medical reasons (55.4%).

We aimed to analyze prospectively collected data of patients with solid tumors with unplanned, nonsurgical admissions to our ICU for the clinical and epidemiological characteristics and predictors of hospital mortality.

METHODS

This prospective observational study was conducted after IEC approval and waiver of written informed consent in our 14-bedded mixed medical–surgical ICU of a tertiary referral cancer center from July 2014 to November 2015. The primary outcome was hospital mortality and its predictors. Secondary outcomes were ICU mortality and ICU and hospital length of stay (LOS). All consecutive adults (>18 years) with solid tumors who needed unplanned ICU admissions, and who stayed for >24 hours, were included. An unplanned medical admission was defined as those for whom ICU bed was not requested in advance 12 hours prior to admission and those being admitted from the floor or the emergency department. The most recent hospital admission was considered; in case of multiple hospital admissions and in those requiring readmission to the ICU during the same hospital stay, only the first ICU admission was considered. We excluded surgical admissions (patients who had undergone elective or emergency surgical procedures and patients who were sent to OT from the floor or emergency department) and those with advanced malignancy with no treatment options available. We also excluded patients who were cancer free for ≥5 years.

Patients were considered as newly diagnosed if the diagnosis of cancer was made within 2 months prior to ICU admission. Recurrence or progression of disease was defined as assessed by the medical or radiation oncologist. Similarly, status of malignancy, i.e., controlled or in-remission, was defined by the primary treating team.

Demographic, clinical, and laboratory variables over the first 24 hours of ICU admission and outcomes at ICU and hospital discharge were recorded. We also collected data related to the type of malignancy, cancer status, cancer-directed treatment(s), presence of locoregional or metastatic disease, ICU-related data like reason of ICU admission, source of ICU admission, pre-ICU hospital LOS, physiological status by Eastern Cooperative Oncology Group (ECOG) scale at hospital admission, presence of neutropenia [absolute neutrophil count (ANC) <500 cells/mm^3], ICU interventions during the first 24 hours of ICU admission [need for noninvasive or invasive mechanical ventilation (NIV or IMV), vasopressors, renal replacement therapy], sequential organ failure assessment (SOFA) score and simplified acute physiology score III (SAPS III) on day 1 of ICU admission, ICU and hospital LOS, and end-of-life decision (wherever applicable).

Statistical Analysis

SPSS software version 21 (SPSS-21, IBM, Chicago, USA) for Windows was used for statistical analysis. Data are presented as mean ± standard deviation (SD) or median with interquartile range (IQR) when indicated. Continuous variables were compared using independent t-test. Categorical data were analyzed by either Pearson's Chi-square or Fisher's exact test. Ordinal data were analyzed using Mann–Whitney U test. Binary logistic regression model was used to analyze the effect of multiple covariates on hospital mortality.

Variables yielding $p <0.20$ in the univariate analyses were entered in a stepwise logistic regression model using enter method. A p-value less than 0.05 was considered statistically significant.

RESULTS

Clinical and Demographic Characteristics

We screened 542 patients and included 235 patients of solid tumors with unplanned admissions in the study (Flowchart 1). The mean age of the patients was 53.57 (±15.67) years and 56.2% were males. Most common (51.9%) source of ICU admission was ward (Table 1). Majority of the patients had locoregional disease (184, 78.3%), while metastatic disease was present in the remaining (51, 21.7%) patients.
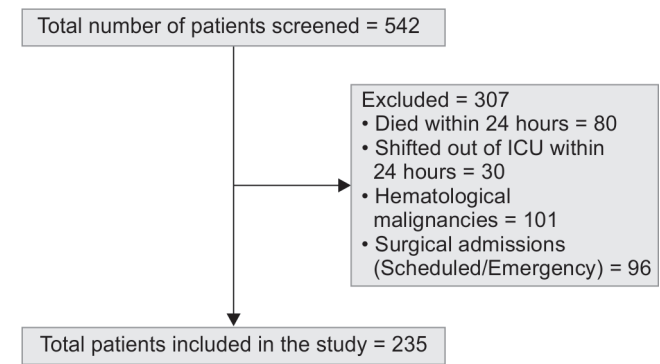
Flowchart 1: CONSORT diagram

Total number of patients screened = 542

Excluded = 307
• Died within 24 hours = 80
• Shifted out of ICU within 24 hours = 30
• Hematological malignancies = 101
• Surgical admissions (Scheduled/Emergency) = 96

Total patients included in the study = 235

Table 1: Demographic and clinical characteristics of patients with solid tumor admitted to the ICU

Variables	Patients (n = 235)
Age (years) mean ± SD	53.57 ± 14.597
Gender Male *n* (%)	132 (56.2)
Neutropenia *n* (%)	20 (8.5)
Cancer-status *n* (%)	
Controlled/Remission	97 (41.3)
Active—newly diagnosed	91 (38.7)
Active—recurrence/progression	47 (20)
Cancer-directed treatment *n* (%)	
No treatment	43 (18.3)
Chemotherapy only	37 (15.7)
Surgery only	53 (22.6)
Radiotherapy only	05 (2.1)
Surgery + chemotherapy	58 (24.7)
Chemotherapy + radiotherapy	12 (5.1)
Surgery + radiotherapy	04 (1.7)
Chemotherapy + surgery + radiotherapy	23 (9.8)
Source of admission *n* (%)	
Ward	122 (51.9)
Emergency room	59 (25.1)
Others (outpatient department, radiology suite, other ICUs)	54 (23)
Cancer diagnosis *n* (%)	
HPB	40 (17)
UGI	33 (14)

Breast		31 (13.2)
GY		29 (12.3)
H&N		25 (10.6)
GU		21 (8.9)
LGI		18 (7.7)
Sarcoma		16 (6.8)
Lung		14 (6)
Others		8 (3.4)
Cancer type		
Locoregional		184 (78.3)
Metastatic		51 (21.7)
SAPS III mean ± SD		59.97 ± 12.807
SOFA score ± SD		3.98 ± 2.27
Performance status (ECOG)	0–2	178 (75.7%)
	3–4	57 (24.3%)
ICU mortality		86 (36.6%)
Hospital mortality		94 (40%)
Median ICU length of stay (IQR) days		5 (3–8)
Median hospital length of stay (IQR) days		15 (8–22)
End-of-life decisions *n* (%)		39 (16.6)

HPB, hepatopancreaticobiliary that includes tumors of the liver, gallbladder, biliary tree, and pancreas; UGI, upper gastrointestinal that includes tumors of esophagus and stomach excluding pharynx; GY, gynecological malignancies; GU, genitourinary malignancies; H&N, head and neck malignancies that include carcinoma of oral cavity, larynx, pharynx, and thyroid; LGI, lower gastrointestinal: malignancies of gastrointestinal tract beyond ligament of Trietz; ECOG, Eastern Cooperative Oncology Group; ICU, intensive care unit; SD, standard deviation; SOFA, sequential organ failure assessment; IQR, interquartile range; SAPS, simplified acute physiology score

The commonest ICU therapies used were IMV (155; 65.96%) and vasopressor infusion (107; 45.5%). Hundred (42.5%) patients needed combination of two or more ICU therapies within 24 hours of ICU admission (Table 2). The hospital mortality observed in the study was 40%. Eighty-six patients died in the ICU (36.6%) while an additional eight deaths occurred in the hospital. The ICU and hospital LOS were 5 (IQR 3–8) days and 15 (IQR 8–22) days, respectively. End-of-life decision was taken in 39 (16.6%) patients and one patient left the hospital against medical advice.

Univariate and Multivariate Analysis

On univariate analysis, source of ICU admission, cancer type, cancer status, need for IMV and vasopressor therapy, pre-ICU hospital LOS, SAPS III and SOFA score on the day of ICU admission yielded *p*-value of <0.2 (Table 3). On multivariate regression analysis, cancer status, need for IMV, and SOFA score on day 1 of ICU admission were found to be independent predictors of hospital mortality (Table 4).

DISCUSSION

In our patient cohort, the hospital and ICU mortalities were 40 and 36.6%, respectively. Cancer status, need for IMV, and SOFA score on the day of ICU admission were independent predictors of hospital mortality.

In several previously published trials on outcome of patients with solid tumors with unplanned ICU admission, the hospital mortality ranged from 25.1 to 39.1%.[5,7,8] A recent multicenter study from South Korea reported hospital mortality similar to our

Table 2: Reasons of ICU admission and ICU interventions required in the first 24 hours

Variables	Patients (n = 235)
Reason for ICU admission *n* (%)	
Acute respiratory failure	66 (28.1)
Septic shock	64 (27.2)
Gastrointestinal	22 (9.4)
Renal/metabolic	18 (7.7)
Postcardiac arrest	18 (7.7)
Neurological	16 (6.8)
Other shock states	14 (6.0)
Cardiovascular	9 (3.8)
Others	8 (3.4)
ICU intervention within 24 hours *n* (%)	
IMV$^\$$	155 (65.96)
NIV[#]	25 (10.6)
Vasopressor (V)	107 (45.5)
Dialysis (D)	13 (5.5)
Combination ICU therapies	
IMV + V	92 (39.1)
IMV + D	4 (1.7)
IMV + V + D	4 (1.7)

IMV, invasive mechanical ventilation; NIV, noninvasive ventilation; V, vasopressors; D, dialysis; $^\$$Patients who required intubation and institution of invasive mechanical ventilation within the first 24 hours of ICU admission; [#]Patients who required noninvasive ventilation only within the first 24 hours of ICU admission

study.[9] Other single-center studies have reported lower hospital mortalities than in our study (22, 29.8, and 31%, respectively).[10–12] The hospital mortality rates vary widely based on inclusion and exclusion criteria, with wide regional differences in epidemiology of cancers and their management. A systematic review published by Puxty et al., which included 31 studies with nearly 75,000 patients, reported an average hospital mortality of 38.2% (33.8–42.7%), with a range of 4.6–76.8%.[13]

Acute respiratory failure is the commonest reason for ICU admission in cancer patients.[9,11,12,14–16] In our study, 180 (76%) patients required ventilatory support within the first 24 hours of ICU admission, out of which majority (86.1%) needed IMV (Table 2). In our cohort, the mortality rate in those needing IMV was 48.5%, which is similar to many other studies.[12,15,17] IMV was an independent predictor of mortality in our patients [odds ratio (OR) 5.94, 95% confidence interval (CI) 2.63–13.41, *p* <0.001], which is similar to that reported by Vincent et al. (OR 2.81, 95% CI 2.00–3.95]).[17] While other studies have also reported MV as an independent predictor of mortality, they did not categorize whether MV was of invasive or noninvasive type.[9,12,15]

The other independent predictor of hospital mortality in our study was SOFA score on the day of ICU admission. SOFA score has been shown to be an independent predictor of hospital mortality in many other studies.[16,18] Worsening SOFA score over consecutive days has also been shown to be an independent predictor of mortality in this subset of patients;[12] however, we recorded SOFA score only on the admission day. A variety of severity of illness scores [acute physiology and chronic health evaluation (APACHE) II, SAPS II, SAPS III] have been used in evaluating outcomes in similar

Table 3: Univariate analysis for hospital mortality

Variables		Patients (n = 235)	Survivors (n = 141)	Nonsurvivors (n = 94)	p value
Age (years) mean ± SD		53.57 ± 14.597	52.84 ± 14.531	54.66 ± 14.705	0.351
Gender male (%)		132 (56.17)	76 (57.58)	56 (42.42)	0.422
Cancer diagnosis					0.518
HPB		40	21	19	
UGI		33	19	14	
Breast		31	19	12	
GY		29	19	10	
H&N		25	15	10	
GU		21	15	6	
LGI		18	12	6	
Lung		14	5	9	
Others		24	16	8	
Source of admission					0.195
Emergency room		59 (25.11)	41 (69.49)	18 (30.51)	
Other locations		54 (22.98)	29 (53.70)	25 (46.30)	
Ward		122 (51.91)	71 (58.20)	51 (41.80)	
Neutropenia (%)		20 (8.51)	13 (65)	7 (35)	0.812
Cancer status n (%)					0.009
Controlled/remission		97 (41.28)	64 (65.98)	33 (34.02)	
Newly diagnosed		91 (38.72)	58 (63.74)	33 (36.26)	
Recurrence/progression		47 (20)	19 (40.43)	28 (59.57)	
Cancer type n (%)					0.016
Locoregional		184 (78.30)	118 (64.13)	66 (35.87)	
Metastatic		51 (21.70)	23 (45.10)	28 (54.90)	
IMV[$] n (%)		155 (65.96)	74 (47.74)	81 (52.26)	<0.001
NIV[#] n (%)		25 (10.64)	18 (72)	7 (28)	0.280
Vasopressors on day 1 of ICU admission (%)		107 (45.53)	51 (47.66)	56 (52.34)	0.001
Dialysis on day 1 of ICU admission (%)		13 (5.53)	6 (46.15)	7 (53.85)	0.384
Pre-ICU hospital LOS in days		4.28 ± 6.054	3.55 ± 5.029	5.38 ± 7.217	0.034
Median SAPS III on day 1 of ICU admission (IQR)		59 (52,68)	56 (50.5,62.5)	65 (57,73.25)	<0.001
Median SOFA score on day 1 of ICU admission (IQR)		4 (2,5)	3 (2,5)	4 (3,6)	0.004
Performance status (ECOG)	0–2	178 (75.74)	111 (62.36)	67 (37.64)	0.215
	3–4	57 (24.26)	30 (52.63)	27 (47.37)	

SD, standard deviation; IQR, interquartile range; IMV, invasive mechanical ventilation; NIV, noninvasive ventilation; SAPS, simplified acute physiology score; SOFA, sequential organ failure assessment; LOS, length of stay; [$]Patients who required intubation and institution of invasive mechanical ventilation within the first 24 hours of ICU admission; [#]Patients who required only noninvasive ventilation within the first 24 hours of ICU admission; ECOG, Eastern Cooperative Oncology Group

Table 4: Multivariate analysis for variables predictive of inhospital mortality (binary logistic regression analysis)

Variables	Odds ratio	95% confidence interval for odds ratio		p value
		Lower	Upper	
Cancer status	3.204	1.271	8.078	0.014
IMV on day 1 of ICU admission	5.940	2.632	13.408	<0.001
SOFA score on day 1 of ICU admission	1.199	1.042	1.379	0.011

IMV, invasive mechanical ventilation; SOFA, sequential organ failure assessment; ICU, intensive care unit

group of patients, and APACHE II and SAPS III have been found to be independent predictors of mortality.[9–12,14] However, we did not find SAPS III to be an independent predictor of hospital mortality.

We also did not find distant metastasis to be an independent predictor of hospital mortality. This may be a reflection of the fact that in a specialized cancer hospital, the physicians from most teams may have better attitude toward advance care planning in malignancy patients as compared to a general multidisciplinary hospital, where physicians may be more circumspect and conservative in transferring the patients to the ICU. This is reflected in our study cohort having a smaller proportion of patients (21.7%) with metastatic disease. This is in contrast to other studies, which had relatively higher proportion (33–76%) of such patients.[10,11,17,18] To the

best of our knowledge, only two studies from Asia[9,12] have reported outcomes in this subset of patients. However, these reports did not record whether the presence of distant metastasis was a predictor of mortality or not. Xia and Wang[12] suggested that patients should not solely be permitted or denied ICU admission based on type or stage of cancer. The Korean study[9] did not describe the presence of distant metastasis in their patients but found performance status as one of the independent predictors of mortality. After a very small study ($n = 28$) in patients with metastatic chemoresistant gastrointestinal cancer, the authors suggested that caution should be exercised in admitting these patients to ICU.[19] The authors suggest that their findings can be of help in establishing realistic expectations and determining the appropriate goals of care in such patients. We feel that just the presence of distant metastasis should not be used to deny ICU care to patients with solid tumors, without considering performance status, quality of life before ICU admission, and availability of further treatment options.

We found cancer status as an independent predictor of mortality and highest mortality was found in the subset of patients who presented to ICU with recurrence/progression of cancer. Soares et al.[16] in their prospective, multicenter study from Brazilian ICUs evaluating mixed cancer patients for predictors of hospital mortality recorded active cancer (recurrence/progression) as an independent predictor of mortality. Contrary to our findings, other studies[15,17] evaluating critically ill solid organ malignancy patients did not find cancer status as an independent predictor of hospital mortality.

Some studies have found the ECOG performance status ≥2 to be an indicator of poor hospital outcomes.[9,15,18] However, we recorded ECOG status at hospital admission and not at the time of ICU admission and this may have been the reason why we did not find ECOG performance status to be a predictor of mortality. However, Xia and Wang[12] recorded Karnofsky performance scale at the time of hospital and ICU admission but found that it did not influence the short-term mortality.

The strength of our study is that it is a prospective study which only included patients admitted to the ICU with solid organ malignancies and unplanned nonsurgical admissions. Also, to the best of our knowledge, this is the first study from South Asian region. The limitations of our study are that first, this study has been carried out in a stand-alone tertiary referral cancer hospital and ICU, which may preclude the extrapolation of our results to general multidisciplinary hospital ICUs. Second, we did not record whether the patients were able to receive further therapy for their malignancy after their discharge.

Conclusion

Acute respiratory failure and septic shock were the commonest reasons for ICU admission for patients with solid tumors in our study cohort. We found that cancer status, need for IMV, and SOFA score on the day of ICU admission were independent predictors of hospital mortality. With good patient selection, more than half of such patients are likely to be discharged alive from the hospital.

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