

Determinants of In-hospital Mortality in Cancer Patients after Intensive Care Unit Discharge

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Determinantes para Mortalidade Intra-hospitalar em Pacientes Oncológicos após Alta da Unidade de Terapia Intensiva
Determinantes de la Mortalidad Hospitalaria en Pacientes con Cáncer tras el Alta de la Unidad de Cuidados Intensivos

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ABSTRACT

Introduction: A significant number of cancer patients die after intensive care unit (ICU) discharge, while the factors associated with mortality are scarcely disclosed in the literature. **Objective:** To investigate the determinant factors and identify the frequency of in-hospital mortality of oncologic patients post-ICU discharge to the ward. **Method:** Retrospective cohort study including patients with cancer discharged from the ICU of *Hospital do Câncer I* of the National Cancer Institute between January 1, 2018 and December 28, 2020. The association between the variables exposure (clinical and sociodemographic variables) and the outcomes (death) was performed by crude and adjusted logistic regression. **Results:** 111 ICU survivors were enrolled. In-hospital mortality was 31.5% and the mean length of stay after ICU discharge was 22.1 days (± 24.44). The multiple analysis revealed that patients with lower final ICU Mobility Scale (IMS) scores at discharge (OR 0.7; 95% CI, 0.5-0.9; $p = 0.01$), the presence of metastases at the time of admission (OR 2.8; 1.0-8.2; $p = 0.04$) and admission by clinical reason (OR 5.1; 95% CI, 1.7-15.8; $p < 0.01$) were associated with in-hospital mortality. **Conclusion:** Patient with metastases at ICU admission, admission by clinical reason and worst mobility at discharge are related with in-hospital mortality. **Key words:** Intensive Care Unit; Hospital Mortality; Neoplasms/mortality.

RESUMO

Introdução: Um número significante de pacientes com câncer morre após a alta da unidade de terapia intensiva (UTI). Entretanto, os fatores associados à mortalidade são pouco difundidos na literatura. **Objetivo:** Averiguar os fatores determinantes e identificar a frequência de mortalidade intra-hospitalar em pacientes oncológicos após alta da UTI para a enfermaria. **Método:** Estudo de coorte retrospectivo incluindo pacientes com câncer que receberam alta da UTI do Hospital do Câncer I do Instituto Nacional de Câncer entre 1 de janeiro de 2018 e 28 de dezembro de 2020. A associação entre as variáveis de exposição (clínicas e sócio-demográficas) e os desfechos (óbito) foi realizada pela regressão logística bruta e ajustada. **Resultados:** Foram incluídos no estudo 111 pacientes oncológicos sobreviventes da UTI. A mortalidade intra-hospitalar foi de 31,5% e o tempo médio de internação após a alta da UTI foi de 22,1 dias ($\pm 24,44$). A análise múltipla revelou que os pacientes com escore final da *ICU Mobility Scale* (IMS) mais baixos no momento da alta da UTI (OR 0,7; IC 95%, 0,5-0,9; $p = 0,01$), a presença de metástases no momento da admissão na UTI (OR 2,8; IC 95%, 1,0-8,2; $p = 0,04$) e a internação por motivo clínico (OR 5,1; IC 95%, 1,7-15,8; $p < 0,01$) estavam associados à mortalidade intra-hospitalar. **Conclusão:** A presença de metástases na admissão da UTI, a internação por motivo clínico e a pior mobilidade no momento da alta estão relacionadas à mortalidade intra-hospitalar. **Palavras-chave:** Unidade de Terapia Intensiva; Mortalidade Hospitalar; Neoplasias/mortalidade.

RESUMEN

Introducción: Un número importante de pacientes con cáncer fallece tras el alta de la unidad de cuidados intensivos (UCI). Sin embargo, los factores asociados con la mortalidad son poco conocidos en la literatura. **Objetivo:** Investigar los factores determinantes e identificar la frecuencia de mortalidad intrahospitalaria en pacientes con cáncer después del alta de la UCI a planta. **Método:** Estudio de cohorte retrospectivo que incluyó pacientes con cáncer dados de alta de la UCI del Hospital del Cáncer I del Instituto Nacional del Cáncer entre el 1 de enero de 2018 y el 28 de diciembre de 2020. Se evaluó la asociación entre variables de exposición (clínicas y sociodemográficas) y los resultados (muerte) mediante regresión logística cruda y ajustada. **Resultados:** Se incluyeron 111 pacientes oncológicos sobrevivientes de la UCI. La mortalidad intrahospitalaria fue del 31,5% y la estancia media tras el alta de la UCI fue de 22,1 días ($\pm 24,44$). El análisis múltiple reveló que los pacientes con puntuaciones finales más bajas en la Escala de Movilidad en UCI (IMS) al momento del alta de la UCI (OR 0,7; IC 95%, 0,52-0,93; $p = 0,01$), la presencia de metástasis en el momento del ingreso a la UCI (OR 2,89; IC 95%, 1,01-8,29; $p = 0,04$) y la hospitalización por motivos clínicos (OR 5,1; IC 95%, 1,7-15,8; $p < 0,01$) se asociaron con la mortalidad hospitalaria. **Conclusión:** La presencia de metástasis al ingreso en UCI, la hospitalización por motivos clínicos y la peor movilidad al alta están relacionadas con la mortalidad hospitalaria. **Palabras clave:** Unidades de Cuidados Intensivos; Mortalidad Hospitalaria; Neoplasias/mortalidad.

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INTRODUCTION

Cancer is one of the main public health problems worldwide. Aging, populational growth and life habits are responsible for new cases of the disease¹. For each year of the triennium 2023-2025, 704 thousand new cases of cancer were estimated for Brazil².

The development of new cancer therapeutic modalities and improvement of clinical outcome have increased survival, however, new treatments cause side effects with potential death risk and increased admission of cancer patients in Intensive Care Units (ICU)³⁻⁵. Cancer patients⁶⁻⁸ account for 15% to 20% of these admissions according to some studies.

After ICU admission, nearly 70-78% of the patients with solid tumors are discharged to continue in-hospital treatment^{9,10}. However, after ICU stay, some consequences may occur as increased morbidity, functional restraints and increase of in-hospital deaths after successive ICU discharge to wards^{11,12}.

A study conducted by Lee¹³ et al. concluded that low level of hemoglobin and platelets at ICU discharge, high scores by the Sequential Organ Failure Assessment (SOFA) at ICU admission, hematological neoplasm and solid tumors are associated with in-hospital mortality in patients with multiple diagnoses. The diagnosis of neoplasm indicates increased mortality after ICU discharge. Patients with cancer have 2.9-fold higher risk of death in one year and 2.5-fold higher risk of death in three years after ICU discharge⁷. In addition, functional level as another predictor of hospital mortality, and worst performance status (PS) reflecting low levels of activity (PS 3-4), increases in-hospital mortality of cancer patients¹⁴.

Scarce studies address ICU cancer survivors in Brazil. Teamwork in the hospital developed gradually according to the definition of the professional roles. Currently, the implementation of multidisciplinary work is a reality at the ICUs and wards worldwide focused to death reduction and improvement of the patients' quality of life. The identification of factors associated with in-hospital mortality can guide the efforts to treat cancer patients.

Therefore, the objective of the present study is to investigate the determinant factors of in-hospital mortality in cancer patients post ICU-discharge and identify its frequency.

METHOD

Retrospective cohort study with patients with cancer discharged from the ICU between January 1, 2018 and February 28, 2020. The study population was identified through the hospital information system Absolute of

Hospital do Câncer I of the National Cancer Institute (HCI/INCA).

Patients aged 18 years or older, in mechanic ventilation for at least 72 hours discharged from the ICU were eligible for the study. Those with hematological neoplasms (Figure 1) were excluded. For patients with more than one ICU admission, only the first admission was analyzed.

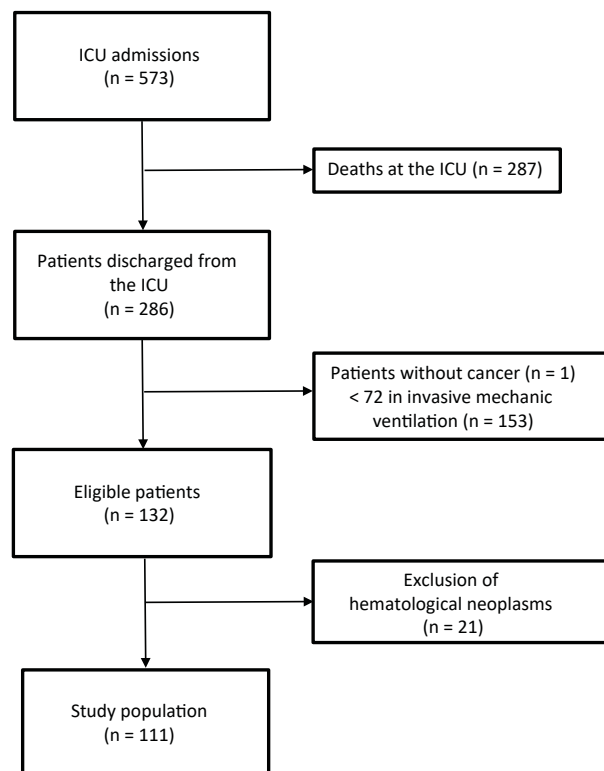


Figure 1. Flowchart of patients enrollment

Physical and electronic charts provided information about sex, age and comorbidities, in addition to type of cancer treatment (surgery, chemotherapy and radiotherapy), tumor topography and decision to interrupt cancer treatment. The topography of primary tumor included digestive system (gastrointestinal, esophageal, liver and pancreas), head and neck, breast and others (soft parts sarcoma, lungs, testicle, skin, central nervous system and prostate).

Other hospitalization information as motive of hospitalization (clinical or surgical), length of hospital stay, motive of ICU indication, time of invasive mechanic ventilation and final score of ICU Mobility Scale (IMS) at ICU discharge were obtained as well. IMS scores were determined by physiotherapists and obtained from charts. It is a single domain scale, ranging from 0 (bed-ridden/passive exercises at the bed) to 10 (high mobility, unassisted ambulation). The primary outcome was in-hospital mortality of the patients and follow-up until discharge or death.

Mean and standard deviation were utilized to describe the data of the study population for continuous variables and absolute and relative frequency for categorical variables. The association between exposure variables and outcome was performed through crude odds ratio (OR). Variables with clinical significance with $p < 0.20$ were selected for multiple regression by the step forward method¹⁵. Variables with $p < 0.05$ were kept in the final model. Data were processed and analyzed with the software Statistical Package for Social Science (SPSS)¹⁶ for Windows, São Paulo, Brazil, version 21.0.

The Institutional Review Board approved the study, report number 2,714,857 (CAAE (submission for ethical review): 89670418.0.00000.5274) on July 15, 2018, in compliance with Directive 466/12¹⁷ of the National Health Council.

RESULTS

111 ICU survivors were identified and included in the analysis, mostly males (55.9%), older (63.1%), with comorbidities (64.9%) submitted to surgery to treat the primary tumor (77.5%) and with tracheostomy (54.1%). The predominant motives for ICU admission were cardiovascular changes (28.8%), acute respiratory failure (27.0%) and sepsis (25.2%). The most common topographies were digestive system (29.7%) and head and neck (27.9%) (Table 1).

In total, 35 patients died at the wards after ICU discharge (31.5%). In-hospital mortality occurred more frequently in males (54.3%), older (65.7%), with tracheostomy (71.4%) and those submitted to surgery (71.4%) (Table 1). The mean time of hospitalization after ICU discharge was 22.1 days (± 24.4).

According to the multivariate analysis, IMS at ICU discharge, comorbidities, tumor topography, interruption of cancer treatment, motive of hospitalization, type of airway and motive for ICU admission influenced in-hospital mortality (Table 2).

Upon adjustment of potential confounding factors, the multiple analysis revealed that patients with low IMS final scores (worst mobility) at ICU discharge (OR 0.7; CI 95%, 0.5-0.9; $p = 0.01$), presence of metastases at ICU admission (OR 2.8; CI 95%, 1.0-8.2; $p = 0.04$) and clinical hospitalization (OR 5.1; CI 95%, 1.7-14.8; $p < 0.01$) were associated with in-hospital mortality (Table 3).

DISCUSSION

Patients with metastasis at ICU admission, clinical hospitalizations and IMS final scores at ICU discharge impacted the patients' risk of death.

For the Brazilian population, the IMS was validated and adapted by Kawaguchi, Yurika Maria Fogaça et al.¹⁸ The objective was to measure the changes of functionality to standardize easily and objectively the evolution of the patients¹⁸.

Some Brazilian studies evaluated the impact of IMS on the mortality of ICU patients^{19,20}. The final IMS score was associated with risk of deaths and the increase of one point of the score was associated with reduction of 30% of risk of in-hospital death post ICU-discharge (OR 0.7; CI 95%, 0.5-0.9; $p = 0.01$).

These results are aligned with another Brazilian study that evaluated 121 patients admitted to the ICU and concluded that the patients with low mobility (IMS score 0-3) had higher risk of in-hospital mortality and poor likelihood of ICU discharge²⁰. These findings can be related to the prolonged period of hospitalization resulting in functional decline and reduced mobility of critical cancer patients. The consequences of clinical evolution and damaging effects of reduced mobility can cause complications as pressure ulcers, venous thromboembolism and infections that, together, may potentialize early death post ICU-discharge.

Other studies^{21,22} that quantified the overall conditions and functionality of the patients through the Eastern Cooperative Oncology Group Performance Status (ECOG-PS) presented similar results. The studies of Normilio-silva et al.²¹ and Puxty et al.²² demonstrated that patients with PS 3-4 (worst functionality and selfcare) had higher risk of death either at the ICU or 90 days post ICU-discharge. A French study with 361 patients with solid tumors concluded that as high PS score is at ICU-discharge, higher is the risk of death 90-days post ICU-discharge⁹.

Admission to ICU for clinical reasons according to the present study impacted in-hospital mortality post-ICU discharge compared with patients submitted to surgery and admitted to the ICU. A systematic review of the literature presented results corroborating this study. Patients admitted to ICU for clinical reasons compared to surgical patients had two-to-four-fold higher risk of death at the ICU and six-to-eight-fold risk of in-hospital mortality post ICU-discharge¹⁹.

The presence of metastases at ICU admission indicates that neoplasms are progressing. Some retrospective studies^{9-14,18-23} demonstrated the impact of metastatic disease post ICU-discharge. The present study concluded that patients with metastases at ICU admission had 2.8-fold (CI 95%, 1.0-8.2) higher risk of in-hospital death. The study of Mendoza et al.²³ evaluated 147 patients with several types of solid tumors and concluded that metastatic disease is associated with in-hospital mortality.



Table 1. Characteristics of the patients (n = 111)

Characteristics	Total (%)	In-hospital mortality	
		Yes (n = 35)	No (n = 76)
Sex			
Male	62 (55.9)	19 (54.3)	43 (56.6)
Female	49 (44.1)	16 (45.7)	33 (43.4)
Age			
≤ 60 years	41 (36.9)	12 (34.3)	29 (38.2)
> 60 years	70 (63.1)	23 (65.7)	47 (61.8)
Comorbidities			
Yes	72 (64.9)	18 (51.4)	54 (71.1)
No	39 (35.1)	17 (48.6)	22 (28.9)
Topography of the primary tumor			
Digestive system	33 (29.7)	6 (17.1)	27 (35.5)
Breast	12 (10.8)	6 (17.1)	6 (7.9)
Head and neck	31 (27.9)	8 (22.9)	23 (30.3)
Others	35 (31.5)	15 (42.9)	20 (26.3)
Presence of metastasis			
Yes	38 (39.2)	14 (53.8)	24 (33.8)
No	59 (60.8)	12 (46.2)	47 (66.2)
Surgery			
Yes	86 (77.5)	25 (71.4)	61 (80.3)
No	25 (22.5)	10 (28.6)	15 (19.7)
Chemotherapy			
Yes	37 (33.3)	15 (42.9)	22 (28.9)
No	74 (66.7)	20 (57.1)	54 (71.1)
Radiotherapy			
Yes	26 (23.4)	11 (31.4)	15 (19.7)
No	85 (76.6)	24 (68.6)	61 (80.3)
DICT			
Yes	32 (28.8)	17 (48.6)	15 (19.7)
No	79 (71.2)	18 (51.4)	61 (80.3)
Motive of hospitalization			
Clinical	48 (43.2)	23 (65.7)	25 (32.9)
Surgery	63 (56.8)	12 (34.3)	51 (67.1)
Airway			
Normal	51 (45.9)	10 (28.6)	41 (53.9)
Tracheostomy	60 (54.1)	25 (71.4)	35 (46.1)
Motive of ICU admission			
Sepsis	28 (25.2)	6 (17.1)	22 (28.9)
Acute respiratory failure	30 (27.0)	10 (28.6)	20 (26.3)
Cardiovascular changes	32 (28.8)	7 (20.0)	25 (32.9)
Other	21 (18.9)	12 (34.3)	9 (11.8)
IMS (score, mean ± SD)		1.0±1.4	2.7±2.5
Time of IMV (days, mean ± SD)		10.6±7.7	10.1±9.4

ICU = intensive care unit; DICT = deciding when interrupt cancer treatment; IMS = ICU Mobility Scale; IMV = invasive mechanic ventilation; SD = standard-deviation.

Table 2. Factors associated with in-hospital mortality (univariate analysis)

Characteristics	OR	CI 95%	p
Sex			
Male		Reference	
Female	1.0	0.4-2.4	0.82
Age			
≤ 60 years		Reference	
> 60 years	1.1	0.5-2.7	0.69
Comorbidities			
No		Reference	
Yes	2.3	1.0-5.3	0.04
Topography of the primary tumor			
Digestive system		Reference	
Breast	4.5	1.0-18.9	0.04
Head and neck	1.5	0.4-5.1	0.46
Others	3.3	1.1-10.2	0.03
Presence of metastasis			
No		Reference	
Yes	2.2	0.9-5.7	0.07
Surgery			
Yes		Reference	
No	1.6	0.6-4.1	0.30
Chemotherapy			
No		Reference	
Yes	1.8	0.8-4.2	0.15
Radiotherapy			
No		Reference	
Yes	1.8	0.7-4.6	0.18
DICT			
No		Reference	
Yes	3.8	1.6-9.1	<0.01
Motive of hospitalization			
Surgery		Reference	
Clinical	3.9	1.6-9.1	<0.01
Airway			
Normal		Reference	
Tracheostomy	2.9	1.2-6.9	0.01
Motive of ICU admission			
Sepsis		Reference	
Acute respiratory failure	1.8	0.5-5.9	0.31
Cardiovascular changes	1.0	0.3-3.5	0.96
Others	4.8	1.4-17.0	0.01
IMS	0.6	0.4-0.8	<0.01
Time of IMV	1.0	0.9-1.0	0.79

Statistically significant values are in bold. OR = odds ratio; ICU = intensive care unit; DICT = deciding when interrupt cancer treatment; IMS = ICU Mobility Scale; IMV = invasive mechanic ventilation.



Table 3. Independent factors associated with in-hospital mortality (multiple analysis)

	OR	CI 95%	p
IMS	0.7	0.5-0.9	0.01
Motive of hospitalization			
Clinical vs. surgical	5.1	1.7-14.8	<0.01
Presence of metastasis			
Yes vs. no	2.8	1.0-8.2	0.04

Statistically significant values are in bold. OR = odds ratio; CI = confidence interval; IMS = ICU Mobility Scale.

A Korean study with 691 patients ICU-discharged found that mechanic ventilation while in ICU, decline of mental status, tachycardia and thrombocytopenia had more risks of readmission and unexpected death at the ward²⁴. Only patients submitted to invasive mechanic ventilation have been enrolled in the present study and time of mechanic ventilation during length of stay did not interfere in in-hospital mortality.

A retrospective German study with patients without cancer concluded that 17.7% of them discharged from ICU died during hospitalization²⁵. Recently, a multicenter cross-sectional study showed that in-hospital mortality reached 15.2% in patients with lung cancer²⁶. A study by Jeang et al.²⁴, exclusively with patients with cancer revealed that 34% died at the ward or were readmitted at the ICU. At HCI/INCA post ICU-discharge, the patients were referred to the ward and during the study period, 31% died during hospitalization.

According to Deana et al.²⁷, while analyzing in-hospital mortality post ICU-discharge, attention should be given to the level of intensity of ward care where the patients were referred to; quite often, ICUs provide intensive care with technology, organization, monitoring and workforce based in best health professionals-patients ratio. For Capuzzo et al.²⁸ one of the motives to lessen in-hospital mortality post ICU-discharge would be the referral of severely ill patients to semi-intensive care units.

The study limitations are the small number of patients which may have induced the occurrence of type II error and the retrospective design based in review of medical charts with potential bias of patient selection. In addition, detailed information about scores of organic dysfunctions and prognosis scores of the disease severity failed to be obtained. Physical and electronic charts were reviewed to minimize the risks of lack of information.

CONCLUSION

The presence of metastases at ICU admission, clinical hospitalization and worst mobility at ICU discharge are

associated with in-hospital mortality. New studies are required to reinforce these findings.

CONTRIBUTIONS

Gustavo Telles da Silva, Camila Martins de Bessa and Carolina da Silva Tavares Costa contributed to the study design, acquisition, analysis and interpretation of the data, wording and critical review. Maria Luiza Valério da Silva, Lavínia Gomes Cavalcante and Diego Medeiros dos Santos contributed to the acquisition, analysis and interpretation of the data, wording and critical review. Tiago Eduardo dos Santos and Ana Cristina Machado Leão Gutierrez contributed to the wording and critical review. All the authors approved the final version to be published.

DECLARATION OF CONFLICT OF INTERESTS

There is no conflict of interests to declare.

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