DOI: 10.1590/1809-2950/e22009623en

ORIGINAL RESEARCH

Changes in functional mobility of patients with solid tumors after discharge from intensive care unit

Mudanças na mobilidade funcional de pacientes com tumores sólidos após a alta da unidade de terapia intensiva

Cambios en la movilidad funcional de pacientes con tumores sólidos tras el alta de la unidad de cuidados intensivos

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ABSTRACT | This study aimed to analyze changes in the level of functional mobility (FM) between patients with solid tumors discharged from intensive care units (ICU) and hospital discharge and the possible factors associated with FM recovery. This is a retrospective cohort study based on the analysis of medical records of patients with solid tumors who were discharged from an oncology ICU from January 1, 2018 to February 28, 2020. The primary outcome was the change in FM after ICU discharge, considering the difference between the final score at ICU discharge and the final score at hospital discharge, estimated by the ICU Mobility Scale (IMS). The association between continuous variables and outcomes was performed by univariate linear regression analysis. In total, 65 patients with a median age of 61.4 years (interquartile range – IQR 54–69) were included. The mean length of hospital stay after discharge from the ICU was 19.0 days (±24.04). The mean IMS score at ICU discharge was 2.62 (±2.56) and the mean IMS score at hospital discharge was 6.08 (±3.26). Patients who underwent surgery to treat the primary tumor had a score 1.89 higher compared to those who did not undergo surgery (p=0.048). Therefore, we observed improvement in FM in patients with solid tumors between ICU discharge and hospital discharge, and patients who underwent surgery showed better FM.

Keywords | Intensive Care Unit; Mobility Limitation; Cancer.

RESUMO | Este estudo teve como objetivo analisar as mudanças na mobilidade funcional (MF) de pacientes com tumores sólidos entre a alta da unidade de terapia intensiva (UTI) e a alta hospitalar e os possíveis fatores associados à recuperação da MF. Trata-se de um estudo de coorte retrospectivo baseado na análise de prontuários de pacientes com tumores sólidos que receberam alta da UTI de uma unidade oncológica entre 1º de janeiro de 2018 e 28 de fevereiro de 2020. O desfecho primário foi a mudança na MF após a alta da UTI considerando a diferença entre a pontuação final na alta da UTI e a pontuação final na alta hospitalar, calculada através da *ICU mobility scale* (IMS). A associação entre as variáveis contínuas e os desfechos foi realizada por meio da análise de regressão linear univariada. No total, foram incluídos 65 pacientes com idade mediana de 61,4 anos (variação interquartil – IQR 54-69). O tempo médio de internação após a alta da UTI foi de 19,0 dias (±24,04). A pontuação média da IMS no momento da alta da UTI foi de 2,62 (±2,56), e a pontuação média da IMS no momento da alta hospitalar foi de 6,08 (±3,26). Os pacientes que realizaram cirurgia para o tratamento do tumor primário tiveram uma pontuação 1,89 vez maior em comparação aos que não foram submetidos a tratamento cirúrgico (p=0,048). Concluindo, foi observada melhora da MF em pacientes com tumores sólidos entre a alta da UTI e a alta

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hospitalar, e os pacientes submetidos à cirurgia apresentaram uma melhor recuperação da MF.
Descritores | Unidade de Terapia Intensiva; Limitação da Mobilidade; Câncer.

RESUMEN | Este estudio tuvo como objetivo analizar los cambios en la movilidad funcional (MF) de pacientes con tumores sólidos entre el alta de la unidad de cuidados intensivos (UCI) y el alta del hospital, y los posibles factores asociados con la recuperación de la MF. Se trata de un estudio de cohorte retrospectivo realizado desde el análisis de historias clínicas de pacientes con tumores sólidos que fueron dados de alta de la UCI oncológica entre el 1 de enero de 2018 y el 28 de febrero de 2020. El resultado primario fue el cambio en la MF después del alta de la UCI considerando la diferencia entre la puntuación final al alta de la UCI y la puntuación final al alta del hospital, que se calculó mediante la *ICU mobility scale* (IMS). La asociación entre las variables continuas y los resultados se realizó mediante análisis de regresión lineal univariante. Se incluyeron un total de 65 pacientes con mediana de edad de 61,4 años (rango intercuartílico –RIC 54-69). La estancia media de hospitalización tras el alta de la UCI fue de 19,0 días (±24,04). La puntuación media de IMS al alta de la UCI fue de 2,62 (±2,56), y la del alta del hospital 6,08 (±3,26). Los pacientes que se sometieron a cirugía para tratar el tumor primario tuvieron una puntuación 1,89 veces mayor en comparación con los que no se sometieron a tratamiento quirúrgico (p=0,048). Se concluye que hubo una mejoría en la MF en pacientes con tumores sólidos entre el alta de la UCI y el alta del hospital, y los pacientes sometidos a cirugía mostraron una mejor recuperación de la MF.
Palabras clave| Unidad de Cuidados Intensivos; Limitación de la Movilidad; Cáncer.

INTRODUCTION

Historically, the management of patients in the intensive care unit (ICU) involves immobilization and sedation, which may be related to increasing expenses, worsening of quality of life, and altering patient survival[1]. However, over the years and by technological advances, the survival of patients admitted to the ICU has increased[2]. Intensive care units care must be managed to promote health, well-being, and motor function in the long term[3].

This change in practice involves less sedation and more physical activity, including stimuli for the recovery of functional mobility (FM) such as sitting, reaching orthostatism, and achieving deambulation[4], which begins in the ICU and continues during hospitalization[5,6]. Some specific instruments can objectively classify patients according to the FM level, such as the ICU mobility scale (IMS). This instrument has a single domain and its score ranges from 0 to 10, in which 0 indicates low mobility and 10 indicates high mobility[7].

Cancer is the second leading cause of death among Brazilians, accounting for 12% to 20% of ICU admissions[8-10]. Recently, cancer treatment have been developing, improving the prospects for cure and control. However, the advanced staging associated with more aggressive treatments increased the risk of complications[11].

Mortality rates in oncology patients remains high in the ICUs. In 2018, the World Health Organization (WHO) estimated cancer-related mortality at about 10 million people[12]. During ICU stay, patients with cancer have a higher risk of death compared to patients without cancer[10-13].

Approximately 40% to 70% of critically oncologic patients are discharged from the ICU to the ward and are considered survivors[14]. Studies show that the FM of patients with cancer improves between ICU admission and hospital discharge. However, factors associated with functional recovery in the oncologic population are not well documented[6].

The discovery of new pieces of information would facilitate the identification of important variables related to functional recovery, aiming to develop an individualized care plan. Thus, this study aimed to analyze the changes in functional mobility of patients with solid tumors between ICU discharge and hospital discharge and the factors associated with FM recovery, based on the review of hospital records. As a secondary objective, this study aimed to investigate the factors associated with the overall survival of ICU survivors after one year.

METHODOLOGY

This is a retrospective cohort study that included clinical histories, based on the review of hospital records of patients with solid tumors who were discharged from the ICU from January 1, 2018 to February 28, 2020.

For this study, informed consent form was waived. The study population was identified by the hospital information system (ABSOLUTE) of a tertiary oncology unit (*Hospital do Câncer I*, National Cancer Institute).

The clinical histories of patients who were discharged from the ICU, aged 18 years or older and who spent at least 72 hours on mechanical ventilation were eligible for the study. Patients with hematological neoplasms, neurological dysfunctions associated with motor changes prior to ICU admission were excluded from the study. Patients who were discharged from the ICU and who evolved to in-hospital death were excluded from this analysis (Figure 1). In cases of readmission, only the first ICU stay was analyzed.

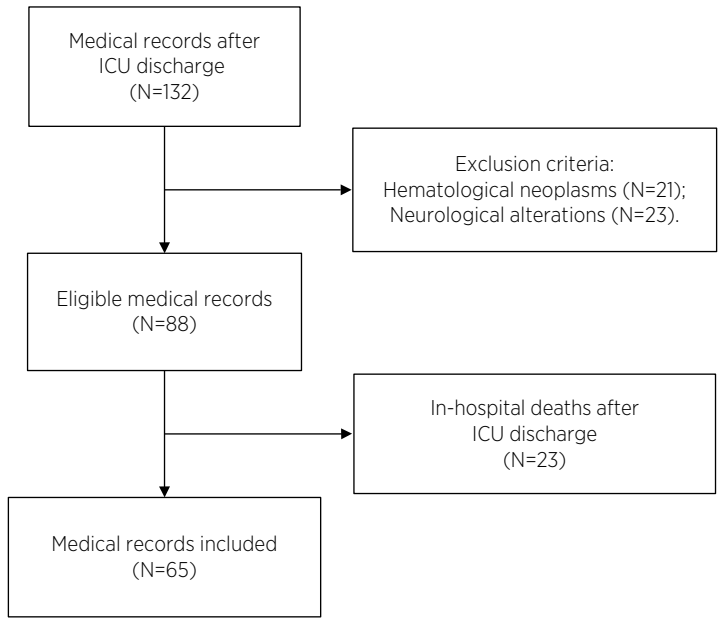

Figure 1. Flowchart of medical records of patients included in the study

Data were extracted from physical and electronic medical records of patients with cancer from cancer diagnosis until death, loss to follow-up, or end of the study (one year after discharge from the ICU). Clinical and sociodemographic variables were collected: sex, age, comorbidities, tumor topography, reason for hospitalization, ICU length of stay, ward length of stay, reason for ICU admission, mechanical ventilation duration, type of treatment, and decision to interrupt treatment after ICU discharge. The topography of primary solid tumors was classified as: digestive system (gastrointestinal, esophagus, liver, and pancreas), head and neck, breast and others (sarcoma, lung, testicle, skin, and prostate).

The primary outcome was the change in FM after ICU discharge considering the difference between the final score at ICU discharge and the final score at hospital discharge estimated by the ICU mobility scale. The Serviço de Fisioterapia of Hospital do Câncer I (Physical Therapy Service of Hospital of Cancer I), since 2017, established in its routine the use of the IMS for the evaluation of FM in its standardized evolution via a checklist. IMS scores were assigned by previously trained physical therapists and the information was obtained from the electronic medical records of patients with cancer. The IMS is a scale with a single domain, ranging from 0 (bedridden/passive exercises in bed) to 10 (high mobility, independent ambulation)[7]. As a secondary outcome, the overall survival of patients was evaluated. Patients were followed from the ICU discharge to the event (death), to the end of follow-up (one year after ICU discharge) or until the last visit to the hospital, prior to the loss to follow-up (censorship), based on the information contained in the physical and electronic medical records.

The collected data were structured in a database using Excel for Windows 10. Moreover, processing and analysis were performed using SPSS (Statistical Package for Social Science for Windows, São Paulo, Brazil) version 21.0. A descriptive study of the sample was carried out, using mean and standard deviation for continuous variables and frequency distribution for

categorical variables. To evaluate the difference in the IMS score between ICU discharge and hospital discharge, the Student's *t* test was applied. The association between continuous variables and outcomes was performed using univariate linear regression analysis. Survival analysis was performed using the Kaplan-Meier method for exploratory evaluation between the independent variables and the time until death.

To estimate the independent factors that were associated with death, the Cox multiple regression model was used. Values of $p<0.05$ were considered statistically significant for all analyses.

RESULTS

We included 65 medical records of patients with a median age of 61.4 years (interquartile range – IQR 54–69). Most patients were males (58.5%), with comorbidities (72.3%), and who underwent surgery for the treatment of primary tumor (80.0%). The main reasons for ICU admission were cardiovascular alteration (33.8%), sepsis (29.2%), and acute respiratory failure (26.2%) (Table 1). The most common primary tumors were colon and rectum (24.6%), oral cavity (12.3%), and breast (12.3%).

Table 1. Characteristics of patients (n=65)

Characteristic	n (%)
Sex	
Female	27 (41.5)
Male	38 (58.5)
Age	
≤60 years old	25 (38.5)
>60 years old	40 (61.5)
Comorbidities	
Yes	47 (72.3)
No	18 (27.7)
Tumor topography	
Digestive system	25 (38.5)
Breast	7 (10.8)
Others	14 (21.5)
Head and neck	19 (29.2)
Metastasis	
Yes	23 (35.4)
No	42 (64.6)
Surgery	
Yes	52 (80.0)
No	13 (20.0)
Chemotherapy	
Yes	20 (30.8)
No	45 (69.2)
Radiotherapy	
Yes	13 (20.0)
No	52 (80.0)
IOT	
Yes	15 (23.1)
No	50 (76.9)
Reason for ICU admission	
Cardiovascular	22 (33.8)
Sepsis	19 (29.2)
ARF	17 (26.2)
Others	7 (10.8)
ICU length of stay	
<16 days	35 (53.8)
≥16 days	30 (46.2)

ICU: intensive care unit; IOT: interruption of oncological treatment; ARF: acute respiratory failure.

The mean length of stay in ICU was 18.5 days (±12.38), the mean duration of invasive mechanical ventilation (IMV) was 10.7 days (±10), and the mean length of stay in the wards was 19.0 days (±24.04). After ICU discharge, 32 (49.2%) patients had undergone tracheostomy.

The mean IMS score at ICU discharge was 2.62 (±2.56) and the mean score at hospital discharge was 6.08 (±3.26). Table 2 shows the changes in FM between ICU discharge and hospital discharge, according to patients' demographic and clinical characteristics. We found an increase in FM between ICU discharge and hospital discharge in all variables. However, only surgery showed statistical significance for FM recovery ($p=0.048$). Patients who underwent surgery for the treatment of primary tumor scored 1.89 times higher compared to those who did not undergo surgical treatment.

Table 2. Factors associated with functional recovery (univariate analysis)

	IMS				
Characteristic	ICU discharge, Mean (SD)	Hospital discharge, Mean (SD)	Difference between groups, Mean (SD)	Difference between mean β (95% CI)	p
Sex				−1.05 (−2.63-0.51)	0.185
Female	2.96±2.65	5.88±3.51	3.86±3.12		
Male	2.37±2.49	6.22±3.11	2.80±3.00		
Age				−1.19 (−2.78-0.39)	0.139
≤60 years old	2.28±2.62	6.54±3.12	4.16±3.00		
>60 years old	2.83±2.53	5.79±3.35	2.97±3.10		
Comorbidities				0.38 (−1.39-2.15)	0.669
Yes	2.55±2.46	5.93±3.25	3.32±3.10		
No	2.78±2.86	6.47±3.35	3.70±3.15		
Tumor topography					
Digestive system	2.96±2.73	6.44±3.12	3.48±3.12	1.24 (0.33-4.56)	0.741
Breast	1.71±1.60	4.50±3.72	2.50±2.25		
Others	3.86±2.77	7.54±3.12	3.61±3.09		
Head and neck	1.58±2.03	5.11±3.12	3.52±3.45		
Metastasis				0.35 (−1.31-2.02)	0.670
Yes	2.70±2.54	6.00±3.08	3.19±3.04		
No	2.57±2.59	6.12±3.38	3.54±3.15		
Surgery				−1.89 (−3.78-0.14)	**0.048**
Yes	2.31±2.32	6.16±3.20	3.82±3.11		
No	3.85±3.15	5.77±3.58	1.92±2.62		
Chemotherapy				0.76 (−0.93-2.46)	0.373
Yes	3.25±3.07	6.32±3.18	2.89±2.80		
No	2.33±2.27	5.98±3.33	3.65±3.22		
Radiotherapy				1.04 (−0.94-3.03)	0.297
Yes	3.00±3.21	5.58±3.75	2.58±3.31		
No	2.52±2.39	6.20±3.16	3.62±3.04		
IOT				0.45 (−1.43-2.34)	0.629
Yes	3.07±3.41	6.36±3.17	3.07±3.12		
No	2.48±2.27	6.00±3.31	3.53±3.11		
Reason for ICU admission				0.14 (−0.51-0.81)	0.658
Cardiovascular	2.36±2.95	6.68±2.98	2.89±3.19		
Sepsis	3.26±2.55	6.16±3.42	2.89±3.19		
ARF	2.47±2.12	5.63±3.68	3.18±3.05		
Others	2.00±2.38	4.83±2.78	2.50±1.37		
ICU length of stay				−0.07 (−2.28-0.86)	0.372
<16 days	3.40±2.84	7.14±3.18	3.74±3.24		
≥16 days	1.70±1.84	4.75±2.90	3.03±2.91		

ICU: intensive care unit; IMS: ICU mobility scale; IOT: interruption of oncological treatment; ARF: acute respiratory failure; CI: confidence interval. Bold figures represent statistically significant values.

At one year, 65.8% of the patients were alive (Figure 2). Table 3 shows factors associated with deaths in the first year, in the univariate analysis. Patients who interrupted oncologic treatment had a 3.19 times higher risk of dying within one year than patients who continued the treatment (HR 3.19; 95% CI 1.48–6.90; p=0.003).

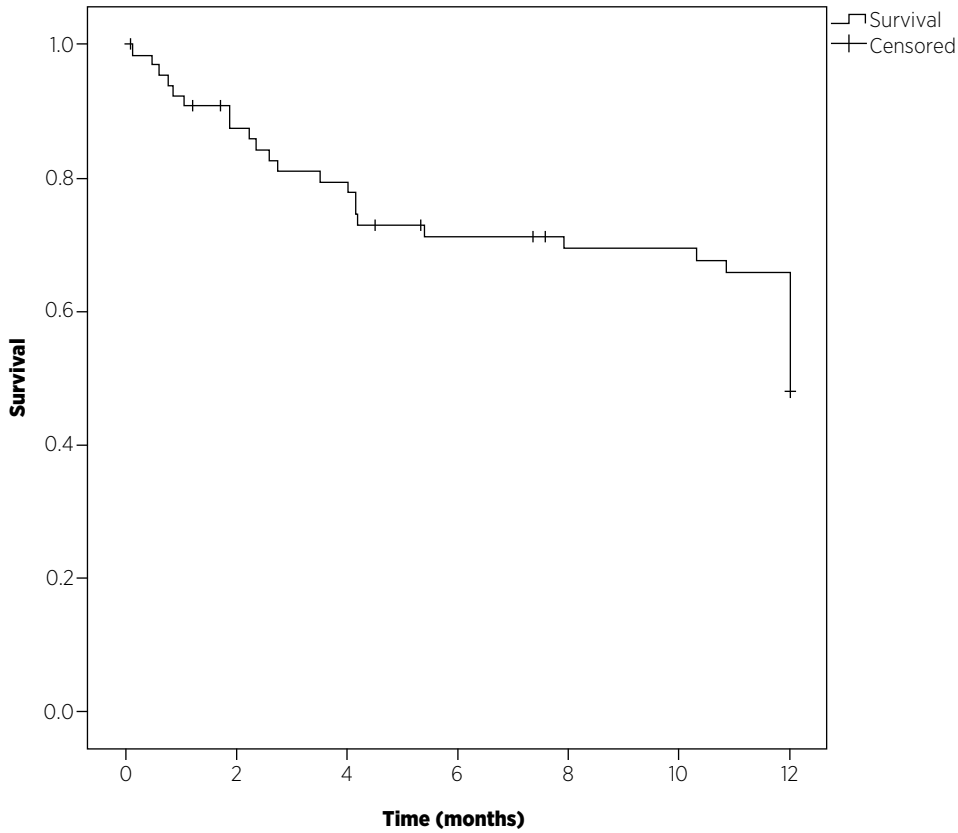

Figure 2. Survival of patients at one year after intensive care units discharge

Table 3. Factors associated with one-year hospital mortality (univariate analysis)

	Mortality			
Characteristics	**Yes (n=28)**	**No (n=37)**	**HR (95% CI)**	**p**
IMS (score, mean±SD)	2.71±2.84	2.54±2.36	1.01 (0.86–1.16)	0.967
Sex				
Female	13 (46.4)	14 (37.8)	1.41 (0.67–2.98)	0.357
Male	15 (53.6)	23 (62.2)		
Age				
≤60 years old	11 (39.3)	14 (37.8)	1.07 (0.50–2.28)	0.357
>60 years old	17 (60.7)	23 (62.2)		
Comorbidities				
Yes	20 (71.4)	27 (73.0)	1.06 (0.44–2.28)	0.989
No	8 (28.6)	10 (27.0)		
Tumor topography				
Digestive system	11 (39.3)	14 (37.8)	1.39 (0.48–4.01)	0.539
Breast	4 (14.3)	3 (8.1)	2.41 (0.64–8.99)	0.190
Head and neck	8 (28.6)	11 (29.7)	1.26 (0.40–3.74)	0.357
Others	5 (17.9)	9 (24.3)		
Metastasis				
Yes	13 (46.4)	10 (27.0)	2.01 (0.95–4.23)	0.06
No	15 (53.6)	27 (73.0)		
Surgery				
Yes	22 (78.6)	30 (81.1)	1.03 (0.42–2.55)	0.938
No	6 (21.4)	7 (18.9)		
Chemotherapy				
Yes	9 (32.1)	11 (29.7)	1.14 (0.51–2.53)	0.733
No	19 (67.9)	26 (70.3)		

(continues)

Table 1. Continuation

Characteristics	Mortality			
	Yes (n=28)	No (n=37)	HR (95% CI)	p
Radiotherapy				
Yes	6 (21.4)	7 (18.9)	1.70 (0.80–3.60)	0.163
No	22 (78.6)	30 (81.1)		
IOT				
Yes	11 (39.4)	4 (10.8)	3.19 (1.48–6.90)	**0.003**
No	17 (60.7)	33 (89.2)		
Reason for ICU admission				
Others	3 (10.7)	4 (10.8)	1.33 (0.35–5.02)	0.672
Sepsis	8 (28.6)	11 (29.7)	1.75 (0.67–4.56)	0.248
ARF	9 (32.1)	8 (21.6)	1.24 (0.33–4.56)	0.741
Cardiovascular	8 (28.6)	14 (37.8)		
ICU length of stay				
<16 days	15 (53.6)	21 (56.8)	1.22 (0.58–2.57)	0.594
≥16 days	13 (46.4)	16 (43.2)		

ICU: intensive care unit; IMS: ICU mobility scale; IOT: interruption of oncological treatment; ARF: acute respiratory failure; CI: confidence interval. Bold figures represent statistically significant values

DISCUSSION

Patients with solid tumors showed improvement in FM between ICU discharge and hospital discharge and surgical patients showed greater improvement in mobility during their stay in the ward. Interruption of cancer treatment was associated with a higher risk of death one year after intensive care unit discharge.

The mean IMS score was 2 points after discharge from the ICU, indicating patients who are passively transferred to the chair, and 6 points at hospital discharge, indicating patients who perform walking in place. According to Santos-Moraes et al.[15], this score difference would be a change from low mobility at ICU discharge to moderate mobility at hospital discharge. Other retrospective studies have shown similar results in improving functionality in patients who were discharged from the ICU[16-19]. A retrospective study evaluated, with the IMS, the mobility of 121 patients who were discharged from the ICU, dividing patients into three groups: 0 to 3 (low mobility), 4 to 6 (moderate mobility), and 7 to 10 (high mobility). At the ICU discharge, 23% of the patients had low mobility, 27.3% moderate, and 49.6% high mobility[15]. The retrospective study by Curzel, Forgiarini, and Rieder[16] evaluated the functionality of 44 patients who were discharged from the ICU and, 30 days later, presented improved mobility, self-care, and locomotion, but did show improved sphincter control. Recently, an American study evaluated 42 patients with cancer subjected to early mobilization during ICU stay. The study reported that most participants showed cognitive and FM improvement between ICU admission and discharge and between ICU discharge and hospital discharge[5]. This finding corroborates a Brazilian study, which showed that, at hospital discharge, 50% of its patients had improved at least one level of FM[20]. Thus, despite the inclusion of patients with cancer, who often have a poor prognosis, it is possible to increase FM during hospitalization in the ward after discharge from the ICU.

Our data showed that patients who underwent surgery for the treatment of primary tumor had a score 1.89 times higher than those who did not undergo surgery (p=0.048). Similarly, another Brazilian study showed that patients with a surgical profile had a higher level of mobility compared to clinical patients. The mean IMS for clinical patients was 4 points and 8 points for surgical patients. Furthermore, surgical patients were 81 times less likely to have low mobility[15]. The aforementioned study did not exclusively evaluate oncologic patients, as in our study.

Mortality at one year after discharge from the ICU ranged from 13.4% to 43%[21,22]. Studies that do not include only patients with cancer usually present lower mortality at one year[13,21]. A Korean retrospective study evaluated 3,679 adult patients who were discharged from the hospital after ICU admission from 2006 to 2011, and found a one-year mortality of 13.4[21]. In retrospective study from the USA, evaluating 296 patients who were discharged after being admitted to a surgical ICU from 2009 to 2014, 29% of patients

died within the first year after ICU discharge[13]. Some studies demonstrate that patients with cancer have a higher risk of death than patients without cancer[21]. According to Nguyen et al.[13], patients with cancer have a 2.99 times higher risk of death at one year. Thus, mortality rate changes when only patients with cancer are evaluated. A French retrospective study that evaluated patients with solid tumors who were discharged from the ICU showed a 41% mortality rate[22]. Moreover, we selected only patients with solid tumors and presented a one-year mortality of 34.2%, confirming that most patients with solid tumors surviving the ICU have a poor prognosis.

Recently, some retrospective studies have evaluated the factors associated with death of patients with solid tumors one year after ICU discharge[22]. Gheerbrant et al.[12] analyzed 253 patients who were discharged from the ICU and the factors associated with mortality at six months, which were: score on a scale of 3–4 from the Eastern Cooperative Oncology Group performance status (ECOG-PS), metastatic disease, ICU admission for cancer progression, simplified acute physiology score II (SAPS II), and decision to limit treatment at ICU admission. For Borcoman et al.[22], who analyzed 622 patients discharged from the ICU, the factors associated with one-year mortality were: locally advanced disease, metastatic disease, ECOG-PS of 3-4, cancer diagnosis shortly before ICU admission, interruption of oncological treatment after ICU discharge, and noninvasive support during ICU admission. In this study, the interruption of cancer treatment after ICU discharge presented a higher risk of death at one year. Comparing the articles cited, our study evaluated fewer individuals, which may have influenced the lack of confirmation of important variables related to tumor progression and patient FM. According to Gross, Borkowski, and Brett[23], the report of functional deterioration by the family member or patient in the year preceding ICU admission is associated with higher mortality one year after ICU discharge.

However, this study presents some limitations that should be considered when interpreting the results. This is a retrospective study based on reviews of hospital records, in which some important information on the clinical course of the disease may be incomplete. To limit this lack of information, data were collected from physical and electronic medical records to obtain quality data for a vigorous analysis. The institution must perform daily physical therapy sessions with all patients who were discharged from the ICU and referred to the wards. However, because it is a real-life study, it was impossible to collect robust data on the time and level of exercise activity. Finally, there is also the institutional bias, since the study was conducted in an institution integrated to the Brazilian Unified Health System, which is a reference in oncology in the state of Rio de Janeiro.

CONCLUSION

We found improvement in the functional mobility of patients with solid tumors in the period between ICU discharge and hospital discharge. Furthermore, patients undergoing surgery for the treatment of primary tumor presented the best functional recovery. Interruption of cancer treatment was associated with a higher risk of death one year after ICU discharge. The results should not be extrapolated to the general population, since the study was conducted with patients hospitalized in the wards of a reference institute in oncology that has a physical therapy routine established for its patients. Therefore, we suggest further studies to identify the factors associated with functional recovery, aiming at individualized treatment and improving the quality of life of the oncologic population surviving the ICU.

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