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Mortality of Critically Ill Cancer Patients Admitted to the Intensive Care Unit: A 1-Year Cross-Sectional Study in Colombia

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ABSTRACT

Introduction: Admission to intensive care unit (ICU) of critically ill cancer patients is controversial because of their prognosis, although there is evidence showing short- and medium-term survival benefits. However, this depends on a number of factors that may vary over time, which must be constantly studied.

Methods: Retrospective cross-sectional study that evaluated mortality and related factors in critically ill cancer patients admitted to intensive care in a tertiary referral center in Colombia for one year. A descriptive analysis was performed.

Results: Of 410 critically ill cancer patients, 232 met the inclusion criteria. 55% of the population was male and were mainly between 50 - 79 years old (mean 62.91 ± 14.3). The most frequently observed cancers were of gastrointestinal origin (26.7%), followed by hematologic cause (25.4%). At ICU discharge, 191 (82.3%) patients were alive. Among the most common causes of death, septic shock was found (26.8%), followed by multiple organ failure (14.6%). Of those who died, 70.7% had a history of surgery due to cancer, followed by hypertension and diabetes mellitus with 36.5% and 24.3%, respectively, and the most frequent indication for ICU admission was invasive mechanical ventilation in 63.4% of the cases, followed by the use of vasopressors in 60.9%.

Conclusions: This study found that the mortality of critically ill cancer patients admitted to the ICU was less than 20%. The main cause of admission was postoperative monitoring, followed by vasopressor requirement and sepsis. The main causes of death were septic shock and multiple organ failure.

Key words: Mortality, Hospital Mortality, Neoplasms, Critical Care, Colombia.

Introduction

Cancer is one of the main current public health problems worldwide (1), and the rise in the number of cases is becoming increasingly alarming (2,3). An aging population, improved diagnostic tools for cancer, and the use of new therapies to reduce mortality, all contribute to the high prevalence rates of all types of cancer (4). According to data from the Global Cancer Observatory (GLOBOCAN) (5), breast, lung and colorectal cancer are the most frequent cancers in the world, while gastrointestinal, lung and breast cancers are the deadliest, respectively. This is reflected in more than 19 million new cases of cancer and almost 10 million deaths from this cause by 2020 (5). This overview demonstrates an unsustainable global burden of disease that must be managed rigorously, considering that the oncology patient needs multidisciplinary management, which is very costly, for example, during admission to intensive care unit (ICU) due to decompensation or critical illness (6).

The approach to the critically ill cancer patient is a real therapeutic challenge, due to the patient's general condition, comorbidities, cause of admission to critical care, prognosis and priority according to protocols (7,8). It has been observed that this group of patients has lower survival rates when they present comorbidities, mainly due to heart failure, liver cirrhosis, or other serious chronic diseases (8). However, recent evidence has shown that it is possible to obtain a substantial survival rate, depending on the management and characterization of the patients (9,10). This causes intrigue and controversies regarding the benefits and use of mechanical ventilation, vasoactive agents, renal replacement therapy or other life-sustaining treatments for critically ill cancer patients, who also have multiple organ failure and prolonged hospital stay (11-14).

According to the current objectives and goals of global health, there is the production of research that evaluates the behavior of cancer and its

evolution in specific populations, in order to know which factors influence the prognosis, final outcome and quality of life of the patient. The decision of whether or not to admit a decompensated cancer patient is decisive for the final outcome. Therefore, the benefit and risks of admitting critically ill cancer patients to ICU should be known epidemiologically, considering that they are prone to nosocomial infections, invasive procedures and pain. This is imperative in today's decision making. Taking into account the need to have data that allow us to know the dynamics of the critically ill cancer patient's disease, requirements and outcomes, the aim of this study was to evaluate mortality and related factors in critically ill cancer patients admitted to an ICU in Colombia.

Methods

Study design

The study has been reported in line with the STROBE criteria (15).

A retrospective cross-sectional study was conducted in a regional tertiary center in Bucaramanga, Colombia, including critically ill cancer patients admitted to the ICU during 2019.

Patient Selection and Data Collection

Patients were included if they met all of the following criteria: 1) >18 years of age; 2) Patients with a definite diagnosis of cancer; 3) Critical care stay >24 hours; 4) Patients with a complete record. Patients who had incomplete data (sociodemographic or clinical) on verification of the episode were excluded.

As an outcome, mortality was evaluated, defined as verification of survival at discharge from the ICU and identified through the records. As operative variables, severity was evaluated by APACHE IV score (16) and admission priority (defined by the admission criteria of the American College of Critical Care Medicine) (Table 1) (17). In addition, variables related to clinical, oncologic and management characteristics at admission to ICU were collected.

For data collection, first, the study variables and their operability were defined; second, the instrument for data collection and its respective standardization were constructed, in addition to a pilot test with 25 electronic medical records, where the functionality of the instrument, data availability and final adjustment for tabulation were confirmed; third, ICD-10 diagnosis codes compatible with a confirmed diagnosis of cancer that were admitted to the ICU of the institution during the cut-off time of the study were filtered; fourth, a healthcare professional with experience and knowledge of the clinical area and the institution's electronic medical records system was selected to record the data in the instrument specifically designed for the collection of information and the construction of the database. The information recorded in the instrument was entered by a person external to the working group and recorded in a database designed in Excel. The data was purged and validated, as well as the control of those that did not correspond, verifying the information in the electronic medical record and leaving a record of the event. Data collection was designed to preserve patient anonymity.

Table 1. Levels of admission priority, according to the American College of Critical Care Medicine (17).

Priority	Definition
1	Severe, unstable patients who need monitoring and treatment that cannot be given outside of an ICU. There are no limits initially to the duration or type of therapy they require. In this category could be patients with septic shock without previous pathology.
2	Patients who require surveillance and monitoring measures specific to ICUs and may need immediate intervention. This category includes, for example, patients with respiratory failure who may require mechanical ventilation.
3	Patients who, due to their underlying disease or acute disease, have little chance of recovery. Even if treatment is started in the ICU, measures to limit the therapeutic effort can be considered throughout its evolution. Patients with exacerbated chronic respiratory diseases and limited quality of life could be an example of this category
4	Patients whose admission to the ICU is considered inappropriate, both because they have terminal or irreversible diseases (too sick to benefit) and because they do not require any type of ICU measure (too healthy to benefit from management in ICU)

ICU specifications

Mixed intensive care unit (not exclusive to cancer), three nursing assistants per patient, one professional nurse per patient, additionally, patients requiring palliative care and euthanasia are referred to another site for care and management.

Statistical analysis

A descriptive analysis was performed. The normality of quantitative variables was tested using the Kolmogorov–Smirnov test. Data were presented as mean±standard deviation (SD) for continuous variables and median (interquartile, IQR) for skewed variables. Qualitative variables were summarized using frequency and percentages. All data were analyzed using the STATA v14 statistics software.

Ethical Statements

This study was approved by the institution ethics review board (Minutes number 20 of 2018 – Clínica Foscal Internacional). The protocol was implemented in accordance with the Declaration of Helsinki (18) and Good Clinical Practice guidelines (19). The ethics committee exempted the collection of informed consent, due to the retrospective nature of the study and the minimal risk.

Results

During the study year, a total of 410 critically ill cancer patients were admitted to the ICU. However, after the application of inclusion and exclusion criteria, 232 patients were finally included (Figure 1).

Fifty-five percent of the population was male (n=129), the age range was between 20 and 99 years, and 89.6% were from the urban area. The most frequent age group was 50 - 79 years (70.5% of men and 79.6% of women) with an average age of 62.9 ± 14.3. 40.9% had a history of arterial hypertension, followed by heart disease (19.4%) and type II diabetes mellitus (18.5%). In addition, 10.7% reported having received chemotherapy 15 days before admission to the ICU (Table 2).

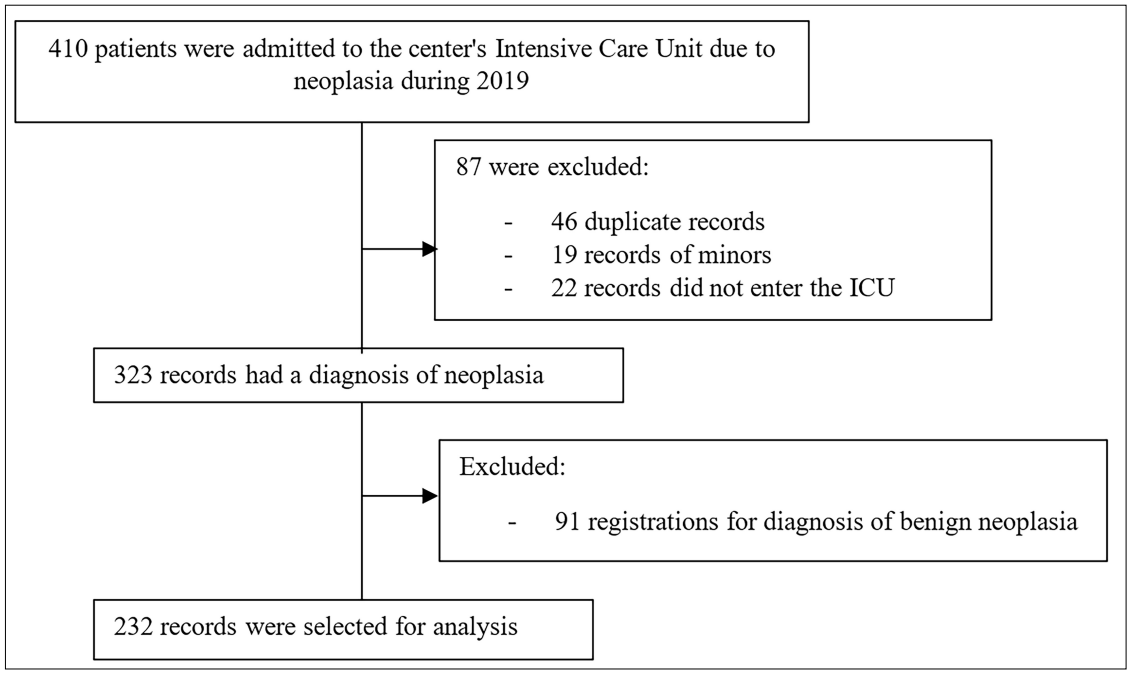

Figure 1. Study participant flow diagram.

Table 2. Baseline characteristics of critically ill cancer patients admitted to the ICU.

	N (%)
Age*	62.91 ± 14.3
Male	129 (55.6)
Female	103 (44.4)
Urban origin	208 (89.6)
Rural origin	24 (10.4)
Personal history	
Arterial hypertension	95 (40.9)
Type II Diabetes Mellitus	43 (18.5)
Chronic Obstructive Pulmonary Disease	25 (10.7)
Chronic Renal Disease	25 (10.7)
Heart Disease	45 (19.4)
Liver Disease	4 (1.72)
HIV/AIDS	3 (1.29)
Other Diseases	157 (67.6)
Pharmacological history	
Steroid use	8 (3.45)
Chemotherapy in the last 15 days prior to admission	25 (10.7)
Surgical history	
Surgery prior to admission	174 (75)
Bone marrow transplant in the last year	7 (3)
Cancer type	
Gastrointestinal	62 (26.7)
Hematological	59 (25.4)
Head and neck	41 (17.6)
Respiratory Tract and Thorax	21 (9.05)
Kidneys and Urinary System	19 (8.19)
Cancer status	
Controlled or remission	7 (3)
Active or newly diagnosed	102 (44)
Recurrent active, relapse or progression	123 (53)
APACHE IV*	11.10 ± 7

*Mean ± SD

Table 3. Indications and diagnoses for admission to ICU of critically ill cancer patients.

	N (%)
Indication	
Invasive mechanical ventilation	63 (27.1)
Non-invasive mechanical ventilation	8 (3.45)
Vasopressors	79 (34)
Renal replacement therapy	12 (5.1)
Post resuscitation	6 (2.5)
Post-operative	130 (56)
Bleeding	29 (12.5)
Sepsis or septic shock	64 (27.5)
Respiratory failure	31 (13.3)
Neurological impairment	9 (3.8)
Other indication	91 (39.2)
Diagnosis	
Sepsis or septic shock	62 (26.7)
Respiratory infection	23 (9.9)
Multiple organ failure	6 (2.5)
Postoperative	133 (57.3)
Acute respiratory distress syndrome	30 (12.9)
Intracerebral hemorrhage	3 (1.2)
Post resuscitation	8 (3.4)
Gastrointestinal bleeding	12 (5.1)
Renal failure with need for replacement therapy	13 (5.6)
Fungemia	11 (4.7)
Acute coronary syndrome	17 (7.3)
Others	143 (61.6)
ICU readmission	
1	32 (13.7)
2	3 (1.2)
3	2 (0.8)
Length of stay ICU	6.12 ± 10.2

*Mean ± SD

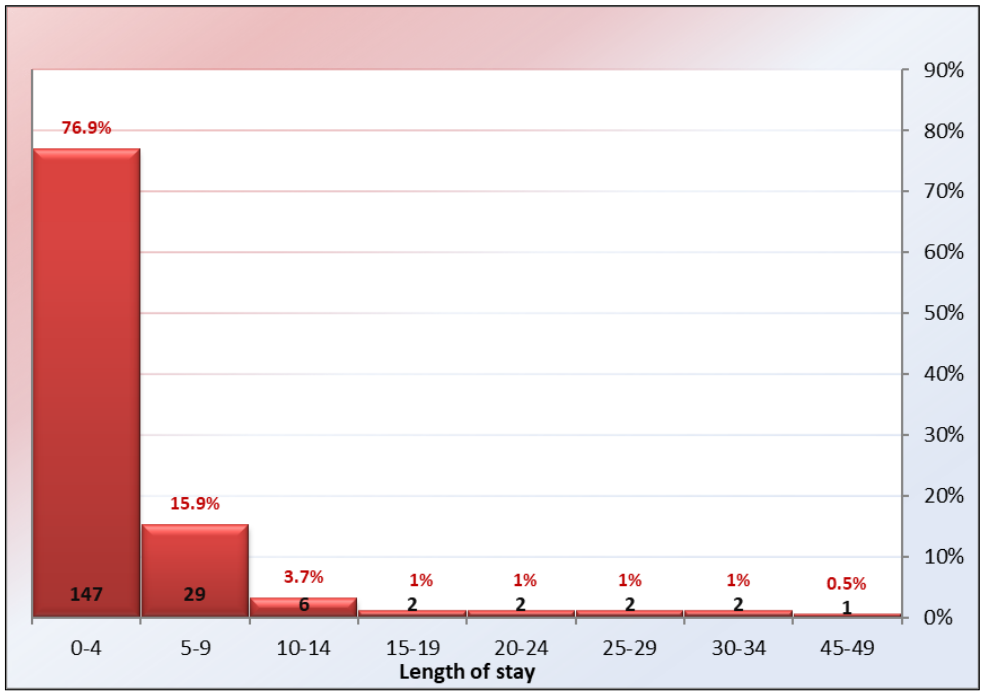

Figure 2. Distribution of length of stay in ICU until discharge of surviving patients.

The predominant type of cancer was solid type (75.4%) and 53% had an active recurrent, relapsed or progressive cancer. The most frequently observed cancers were of digestive and gastrointestinal origin (26.7%), followed by hematologic cause (25.4%), and head and neck cancer (17.6%) (Table 2). On admission to the ICU, 57.3% required continuous monitoring for an immediate postoperative diagnosis and 26.7% for sepsis or septic shock. Less than 5% of patients admitted were post-resuscitation. The main causes of admission to the ICU were postoperative (56%), followed by the use of vasopressors (34%) and sepsis (27.5%). 15.9% required readmission to the ICU (Table 3).

When evaluating the severity of the disease, it was found that 50% of the sample presented scores between 36 and 62 (according to the APACHE IV score), this score being inversely proportional to the number of patients and predicted mortality scores higher than 80. When quantifying the priority of admission to the ICU, 62.9% met the criteria for priority 1. 63.4% of patients with active recurrent cancer, relapse or progression were classified as priority 1; similarly, this group of patients had the highest frequency of presentation in priority 2 with 31.71% (Table 4).

From the ICU stay there was a mean of 6.1 ± 10.2 days, of which, 147 (76.9%) of patients had a stay between 0 - 4 days, 29 (15.1%) between 5 - 9 days, and only 9 (4.7%) had a stay longer than 15 days (Figure 2). At ICU discharge, 191 (82.3%) patients were alive. Among the most common causes of death, septic shock was found (26.8%), followed by multiple organ failure (14.6%); while 41.4% of the causes were categorized as "other" because in the records it was recorded as cardiac arrest without further specifications that could contribute to the analysis of the information (Table 5).

Table 4. Distribution of ICU admission priority according to American College of Critical Care Medicine score and patients' cancer status.

	Controlled or remission	Active or newly diagnosed	Recurrent active, relapse or progression	Total
	N (%)			
Priority 1	5 (71.5)	63 (61.7)	78 (63.4)	146 (62.9)
Priority 2	2 (28.5)	30 (29.5)	39 (31.7)	71 (30.6)
Priority 3	0	9 (8.8)	6 (4.9)	15 (6.5)
Total	7 (100)	102 (100)	123 (100)	232 (100)

Mortality during the ICU stay was 41 patients, of which 70.7% had a history of surgery due to oncological disease, followed by chronic non-communicable pathologies such as arterial hypertension and diabetes mellitus with 36.5% and 24.3%, respectively. From the history that contribute to a deficient immune response and are variables to be considered within the prognosis in the ICU, it was evidenced that 19.51% of the deceased patients had required chemotherapy management in the 15 days prior to admission to the unit. When evaluating the indications for admission to the ICU and mortality, it was observed that of the deceased patients, the most frequent indication was invasive mechanical ventilation in 63.4% of the cases, followed using vasopressors in 60.9% and diagnosis of sepsis or septic shock in 58.5% (Table 5). However, the relationship between mortality and the indication for admission to the ICU as a result of a surgical procedure was only observed in 29.2% of the patients.

Table 5. Relationship between mortality and personal history and indications of critically ill cancer patients admitted to the ICU.

	Alive	Dead	p-value
	N (%)		
Age*	61.9 ± 14.3	69.8 ± 13	
Male	84 (44)	19 (46)	
Female	107 (56)	22 (54)	
Personal History			
Arterial hypertension	80 (41.8)	15 (36.5)	0.93
Type II Diabetes Mellitus	33 (17.2)	10 (24.3)	0.46
Chronic Obstructive Pulmonary Disease	22 (11.5)	3 (7.3)	0.01
Chronic Renal Disease	21 (10.9)	4 (9.7)	1.33
Heart Disease	37 (19.3)	8 (19.5)	1.06
Liver Disease	3 (1.5)	1 (2.3)	1.03
Other Diseases	132 (69.1)	25 (60.9)	-
Surgical history	145 (75.9)	29 (70.7)	0.63
Steroid use	6 (3.1)	2 (4.8)	1.42
Bone marrow transplant in the last year	6 (3.1)	1 (2.4)	-
Chemotherapy in the last 15 days prior to admission	17 (8.9)	8 (19.5)	0.05
Indications			
Invasive mechanical ventilation	37 (19.3)	26 (63.4)	34.52
Non-invasive mechanical ventilation	6 (3.1)	2 (4.8)	0.95
Vasopressors	54 (28.2)	25 (60.9)	23.03
Renal replacement therapy	6 (3.1)	6 (14.6)	15.03
Post resuscitation	1 (0.5)	5 (12.2)	32.47
Post-operative	118 (61.7)	12 (29.2)	21.47
Bleeding	20 (10.5)	9 (21.9)	4.06
Sepsis or septic shock	40 (20.9)	24 (58.5)	27.88
Respiratory failure	16 (8.3)	15 (36.5)	35.91
Neurological impairment	7 (3.6)	2 (4.8)	3.19
Other indication	77 (40.3)	14 (34.1)	-
APACHE IV	9.72 ± 5.66	20.03 ± 8.63	0.01

*Mean ± SD

Discussion

The results of this study are relevant, considering that the overall mortality was <20%, despite the existence of beliefs about the very high mortality that is generated when the critically ill cancer patient is admitted to the ICU. Although this depends on several factors such as the stage of progression of the cancer, comorbidities and timely management, in general it was evident that our population had these characteristics, which makes critical care management difficult, but that a significant survival rate can indeed be achieved.

The distribution of tumors according to gender is variable, finding a predilection in the male sex in studies carried out in Turkey (59%) (20) or Jordan (58.2%) (21), but also in the female sex, for example in Colombia (57%) (22). This is due to the genetic and epigenetic ecology of the population studied, which is influenced by countless risk and protective factors that influence the pathophysiology of the different tumors (23). In the present study, it was found that the vast majority of cases were male and that the main types of cancer reported were gastrointestinal (26.7%) and hematologic (25.4%). This data is relevant, since it is estimated that 1 in 36 men will develop some type of gastrointestinal cancer, compared to 1 in 86 women (24); while it is known that hematologic cancer is predominant in women (23). Thus, a trend similar to that reported in the literature is found (23,25).

Regarding the age of presentation, there was evidence of a progressive increase up to 69 years of age, becoming more representative between 50 and 69 years of age (45% of the cases). Studies conducted in Denmark (26), Korea (27) and Cuba (28) have found this same distribution in 48.8%, 58% and 60.5% of their cases, respectively. In Colombia, in the Caribbean region, a study conducted several years ago found that the mean age at presentation was 55 ± 19 years (29), which is comparable to the findings of this study. These results could be explained by the increase in screening tests after the age of 50, the growth in life expectancy, population demographic changes, exposure to hypercaloric Western diets, unhealthy lifestyles and migratory phenomena, which are risk factors for the appearance of cardiometabolic disorders such as obesity or diabetes, which are potential hormonal and metabolic disruptors that induce cellular damage and subsequent cancerogenesis (30-32). This also explains why arterial hypertension and diabetes mellitus were the most frequent comorbidities found in the study population. However, the presentation at slightly older ages could be explained by

difficulties in timely access to screening tests or delays in definitive diagnoses, delaying the correct management and impairing the prognosis of the patient, who eventually needs to be admitted to critical care due to disease progression and decompensation (33).

According to the stage of the cancer, 53% presented an active recurrent state, relapse or progression, a higher result than other studies in Colombia, where this state has been reported in up to 15% (22); the difference observed could be explained because in those studies one of the exclusion criteria was patients with clinical situations impossible to recover, a variable that is directly related to states in relapse or progression of an oncological disease and that consequently decreases the presentation in the sample. But internationally the scenario is different, for example, in Turkey up to 34% have been found in progressive disease (20) and in Korea up to 55.8% (27), variable data compared to our study, but explaining the high need for continuous monitoring, supportive therapies and palliative care in these types of patients. The stage of the cancer is a risk factor for mortality in approximately 10% (34), with timely therapies and admissions to the ICU can improve the prognosis of life and survival in these cases, which summarizes the high percentage of admissions with active or advanced stages in the context of therapeutic effort (34). The diagnosis and indication for admission reflect the decision for admission to the ICU, contextualizing clinical and individual criteria according to prognosis. In our study, the most frequent diagnoses and causes of admission were postoperative and sepsis, as well as the need for vasopressor therapy. This trend has already been reported in other studies as one of the most frequent complications in this group of patients, taking into account the risk of infection due to immunosuppression and multiorgan failure (22). When evaluating the priority of admission, we observed that the majority of the sample was in category 1 according to the American College of Critical Care score; although mortality in the unit corresponded to 17.67%, data that could confirm that the critically ill patient with oncologic disease benefits from early admission to the ICU, generating a decrease in hospital mortality, as has been reported in other studies (35,36).

Although the overall mortality rate in our study is low, these data should be interpreted with caution because half of our patients were postoperative, with a higher proportion being elective surgeries. In terms of causes of mortality, the first place was occupied by septic shock in 26.8% of cases, a lower figure when compared to another national study conducted in the city of Medellin where 36% died from this cause, finding a statistically significant association (OR 3.19; 95% CI 1.09 - 9.68, p=0.017) (22); confirming that survival in patients who develop this complication is between 20-40%. Thus, sepsis and septic shock are a common cause of critical illness in these patients and are associated with high mortality, and it is known that one in six patients with sepsis admitted to the ICU has cancer, which is the main reason for admission (37,38). These data are consistent with our findings, where more than half of the deaths occurred in patients admitted to the ICU in the context of sepsis (58.5%, n=24), although it does not represent the highest percentage of mortality according to the indication for admission (invasive mechanical ventilation 63.4% and vasopressors 60.9%), it is an important figure and comparable with Latin American reports (39,40). This allows projecting future prospective studies aimed at microbiological surveillance that will allow a better characterization and implementation of preventive measures (for example: elimination of unnecessary invasive devices), since cancer patients have a higher risk of serious infections and multidrug-resistant microorganisms.

The categorized priority of each patient, their clinical stage of oncological disease and the indications for admission to the ICU are variables that have a direct impact on the average length of stay in the ICU. The population evaluated in this study had an average length of stay of 4.3 ± 5.9 days, results compatible with a study carried out in Antioquia with a median of 5 days (interquartile range of 3 - 12.5) and in Mexico with 5.6 ± 6.1 days; data similar to the report made in Turkey, in which an average stay of 5 days was determined (interquartile range 3-12) (20,22,29). Therefore, the average length of stay is influenced by multiple variables that can have a poor prognosis in the short- and medium-term, leading to a shortening of the length of stay in the unit when all therapeutic measures are exhausted, resulting in palliative care or death (41). Likewise, readmissions to the ICU occurred in 13.7% (n=32) of the sample, this calculation was made based on the cross-sectional data recorded in the history at the time of data collection; a higher percentage than a study conducted in Cuba where 4.4% (29) required readmission to the ICU and in Jordan a higher value of readmissions in general of 25.4% (21). The variations in readmission percentages are related to the total number of samples and the follow-up time at discharge from the unit determined for each study, a limitation for our study, which due to its methodological characteristics does not allow follow-up of readmissions and prediction of mortality, which would give a more accurate percentage approximation of survival levels and therapeutic response to the methods used in the ICU, variables that should be included in future studies.

Despite the above, this study provided useful data on the main causes of admission of critically ill cancer patients, the most frequently used management and the outcomes obtained. This information is extremely useful when deciding to admit this group of patients to the ICU, considering that in many cases, due to prognosis, critical care management is omitted and this could have repercussions on final or disease-free survival, in the case of patients under chemotherapeutic treatment. Thus, these data additionally serve as a basis for future studies to perform more complex analyses by subgroups and to determine the association between certain factors, antecedents or interventions, with short- and medium-term outcome.

Study limitations

The findings of this study should be interpreted within the context of its design. It's a single-center descriptive retrospective study. Due to their descriptive nature, the comparisons between groups do not cover the totality of the possible associated variables and are presented without evaluating the differences according to their statistical significance. Therefore, the findings described here are not sufficient to suggest a causal hypothesis. It is necessary to consider a future cohort-type analysis, for which it is possible that the size of the study population will need to be increased, depending on the hypotheses proposed. The usefulness of some

scales for the assessment of organ dysfunction (for example, SOFA - Sequential Organ Failure Assessment), comorbidity or functionality that could not be evaluated due to the absence of data, either because they are not part of the routine evaluation in this institution or for any other reason.

Conclusions

This study found that the mortality of critically ill cancer patients admitted to the intensive care unit was less than 20%, despite the fact that most of the cases were in an active recurrent, relapsed or progressive state. The main cause of admission was postoperative monitoring, followed by vasopressor requirement and sepsis. The main causes of death were septic shock and multiple organ failure. This reflects a trend of possible short-term survival benefit in the critically ill oncology patient requiring multidisciplinary critical care management.

Data availability statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

AUTHOR CONTRIBUTIONS:

Concept: GS, LP, FN; **Design:** GS, IL.GD; **Supervision:** FM, FN, JR; **Materials:** GS, HM, FN; **Data Collection and/or Processing:** GS, LP, FN, HM; **Analysis and/or Interpretation**: GS, IL, GD, JR; **Literature Search:** GS, LP, IL, FN, HM, JR, GD; **Writing Manuscript**: GS, LP, IL, FN, HM, JR, GD; **Critical Review:** GS, LP, IL, FN, HM, JR, GD.

Ethics Committee Approval: This study was approved by the ethics committee of the Universidad Autónoma de Bucaramanga, Colombia. (2018/20)

Informed Consent: Due to the retrospective nature of the study, the ethics committee waived the taking of informed consent.

Peer-review: Externally peer-reviewed.

Conflict of Interest: Authors have no conflicts of interest to declare.

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