

## Research Article

# Assistance to Patients with Terminal Cancer in the Last 30 Days Prior to Death: Differences in the Care of the Usual Health Care Units and a Palliative Care Unit

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Received: May 01, 2022; Accepted: May 16, 2022; Published: May 30, 2022

## Abstract

**Objectives:** To compare aspects related to the care of patients with terminal cancer during the 30 days prior to death between usual care units (UCUs) and a palliative care unit (PCU).

**Methods:** A retrospective cohort, for the last 30 days preceding the death of patients with terminal cancer, followed in UCUs and PCU. Demographic, clinical and nutritional (baseline) data were collected; also, performance of medical examinations and procedures, prescription of nutritional therapy (referring to 30, 7 and 3 days before death); and prescription of drugs and administration routes (relating to the last 3 days of life).

**Results:** We evaluated 239 patients, of which 131 (54.8%) have been assisted in UCUs and 108 (45.2%) in the PCU. Prescription of nutritional therapy, number of laboratory tests, imaging and procedures performed in the UCUs was higher than in the PCU. Regarding the four drugs considered essential for end-of-life care, we found that all were prescribed to patients in the PCU, while in the UCUs there was no prescription of haloperidol and scopolamine in any of the cases.

**Conclusion:** In the PCU, there was a better use of health resources, as clinical guidelines recommend limiting the use of disproportionate resources to the advancement of the disease in patients with limited life expectancy.

**Keywords:** Advanced cancer, Terminal cancer, Health care, Oncology, Usual care units, Palliative care unit

## Introduction

The elaboration of the care plan for patients with terminal cancer must be based on a careful evaluation of clinical, bioethical and prognostic elements. The prognostic assessment can lead to the improvement of treatment strategies and support the planning of care and the efficient use of available resources, helping to minimize the risks of under treatment or excessive and futile treatments, especially in the phase close to death [1]. In the hospital setting, it is common for patients with terminal cancer to receive inadequate and ineffective care, with no provision for palliative care and pain relief. Even in a reality of scarce resources, there is an unnecessary use of invasive and high-tech methods, focused on trying to cure, which are unable to treat the most prevalent symptoms of the disease, prolonging suffering and pain [2].

Furthermore, the *World Health Organization* (WHO) [3] points out that palliative care with quality requires access to essential medicines (basic basket of medications) able to treat the most prevalent symptoms in terminal disease, rather than the use of measures and futile drugs. In 2013, a study published in the *Journal*

*of Palliative Medicine* carried out through an international consensus of specialist physicians and practitioners in large Palliative Care centers described the relevance of four essential drugs (Morphine, Midazolam, Haloperidol and Scopolamine) for the relief of the most prevalent symptoms in patients with terminal cancer in the days before death. Therefore, physicians caring for patients with terminal cancer must be familiar with these medications to prescribe them and achieve their benefits [4].

In Brazil, the possibility of a patient with chronic illness in a terminal stage of disease, including oncological disease, not having access to basic medications to control symptoms and also remaining without access to the team and palliative care, is very large [5]. It is necessary to improve care for this group so that their real demands are met. In the end-of-life care (EOLC) phase, the patient may present different signs, symptoms and suffering that demand a reorganization of the therapeutic plan. Thus, this study proposes the comparison of aspects related to the care of patients with terminal cancer during the last 30 days prior to death between usual care units (UCUs) and a palliative care unit (PCU) of an oncological center of national reference.

## Methods

This is a clinical, observational, retrospective cohort study, referring to the last 30 days of life of patients with terminal cancer, followed up in the different care units of an oncological center of national reference, located in Brazil. The study was approved by the Research Ethics Committee. The oncological center of national reference is composed UCU where treatments are carried out aimed at cytoreduction, whether by chemotherapy, surgery or radiotherapy. It also has the exclusive PCU, where patients from UCUs are referred to control symptoms and promote quality of life and death, at the end of the possibilities of treatment lines and failure to cure, disease progression during treatment or worsening of their clinical condition.

All patients who died of any reason in the period of interest defined in the research proposal (06/01/2019 to 07/31/2019) were identified through an electronic system and selected according to the criteria of inclusion, namely:  $\geq 20$  years of age; confirmed diagnosis of advanced-stage malignant tumor (locally advanced and/or with distant metastasis); having died between June and July 2019; having been enrolled at least 30 days before the date of death for follow-up at INCA; and having been admitted to INCA in at least one of the last three days of life. Patients with missing or inconsistent data on the date of death were considered losses.

### Data Collection

The thirtieth day before death was considered the baseline and the day of death was the study deadline. The data were extracted from medical records and recorded in a specific form, as shown in Figure 1.

#### Data Sociodemographic, Clinical, Nutritional and Performance Status (for the Baseline Study)

Age (<60 vs.  $\geq 60$  years old); gender (male vs. female); diagnosis [cancer of the gastrointestinal tract (GIT) vs. breast vs. head and neck vs. gynecological vs. lung vs. connective bone tissue vs. others]; disease progression (local vs. local + distance); Previous cancer treatment (yes vs. no)].

Information was collected on the Patient-Generated Subjective Global Assessment short form (PG-SGA SF) (©FD Ottery, 2005, 2006, 2015), available at pt-global.org. The tool is answered by the patient and allows for the assessment of: (1) change in body weight: the score can range from 0 to 5; (2) food intake: with a score from 0 to 4; (3) presence of symptoms of nutritional impact: scoring up to 24; and (4) functional capacity assessment: scoring from 0 to 3. At the end of the assessment, a numerical score is generated based on the sum of each of the items in the questionnaire. The higher the score, the worse the

nutritional status. Patients with scores  $\geq 9$  were classified as being at nutritional risk [6,7].

The cachexia is defined by the modified Glasgow prognosis score (mGPS) at four different stages: not cachexia, malnutrition, pre-cachectic and refractory cachectic [8] (Table 1).

The performance status data obtained in the UCU refer to the Performance Status Eastern Cooperative Oncology Group (ECOG-PS) that ranges from 0 (normal activity) to 5 (death) [9]; while in the PCU was used the Karnofsky Performance Status (KPS) that ranging from 100 (normally active) to 0 (dead) [10]. These scales were converted and categorized as PS < 3 or KPS  $\geq 40\%$  (yes or no), as proposed by Ma et al. [11]

### Laboratory Tests and Procedures (Referring to the Period of 30, 7 and 3 Days before Death)

Total number of laboratory tests performed; total number of full images of examinations and the most frequent types [e.g.: computed radiography (CR), computed tomography (CT), endoscopy, ultrasound and magnetic resonance image (MRI)]; and the total number of procedures performed and the most frequent types [e.g., chemotherapy (QT), radiotherapy, blood and platelet transfusion, biopsy, and gastrostomy].

### Nutritional Therapy Prescription (Referring to the Period of 30, 7 and 3 Days before Death)

Prescription of oral (ONT), enteral (ENT) and parenteral (PNT) nutritional therapy.

### Prescription and Administration Routes (Referring to the Period of 3 Days before Death)

Prescription of medications and routes of administration.

### Statistical Analysis

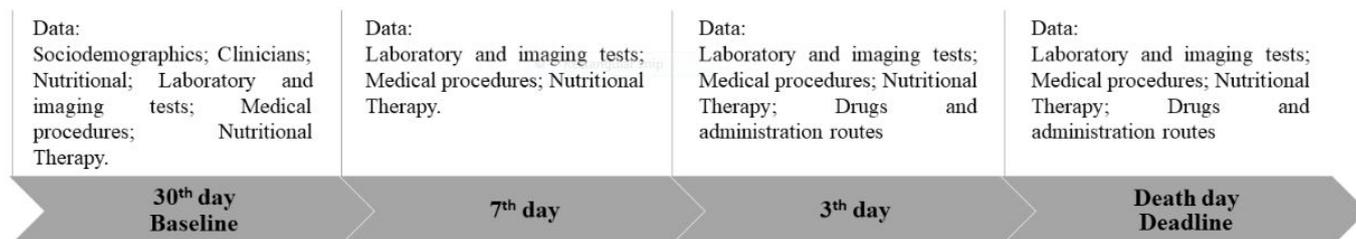
Analyses were performed using Stata Data Analysis and Statistical Software (STATA) version 13.1 (Stata Corp., College Station, Texas, USA). To assess data, the Kolmogorov Smirnov test was applied. For

**Table 1:** Classification of cachexia using the modified Glasgow Prognostic Score.

mGPS	Biomarker		Cachexia Stages
	CRP (mg/L)	Albumin (g/dL)	
0	<10	$\geq 3.5$	Non cachectic
0	<10	<3.5	Malnourished
1	$\geq 10$	$\geq 3.5$	Pre-cachectic
2	$\geq 10$	<3.5	Refractory cachectic

**Note:** mGPS= modified Glasgow Prognostic Score; CRP= C-reactive protein.

Source: Douglas and McMillan (2014).



**Figure 1:** Flowchart of data collection from patients with terminal cancer in the 30 days prior to death.

continuous parametric data, averages, standard deviation, Student's T test and ANOVA were used; for the categorical variables, number of observations and frequency were used, and the Chi-square test was used for proportions. The p-value <0.05 was considered statistically significant.

## Results

The study included 239 patients who, in the majority, were >60 years old (63.2%), female (61.1%) and had the primary tumor site located in the breast (20.1%), followed by GIT (19.7%). The prevalence of nutritional risk was 70.3% and most patients were cachectic (35.4%)

or refractory cachectic (46.9%). One hundred and thirty-one (54.8%) were assisted in the UCUs and 108 (45.2%) in the PCU (Table 2). In most patients, the reason for hospitalization was a decline in their general condition, with no statistically significant difference between the units (data not shown in tables).

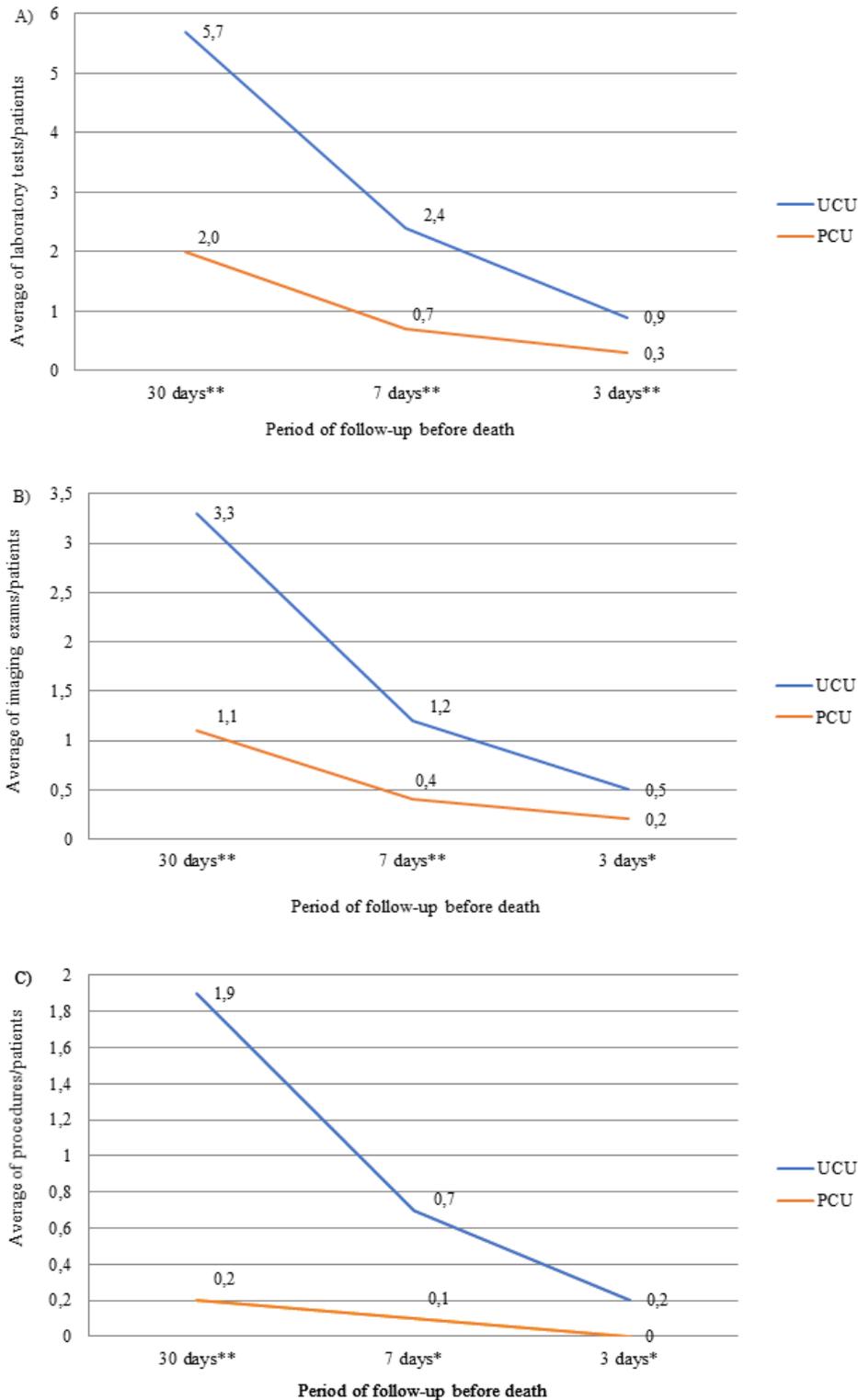
The number of laboratory, imaging tests and procedure performed throughout the follow-up period was greater in patients assisted in the UCUs than in the PCU (Figure 2). The most frequently performed imaging tests were X-ray and CT, and the procedures were QT and blood/platelet transfusion. The frequencies of CT (UCU=4.6% vs. PCU=4.6%)

**Table 2:** Sociodemographic, clinical and nutritional characterization of patients with terminal cancer according to health care units (N=239).

Variables	Total N=239	UCU N=131 (54.8%)	PCU N=108 (45.2%)	p-value <sup>a</sup>
<b>Age (years)</b>				
<60	88 (36.8%)	54 (41.2%)	34 (31.5%)	0.120
≥60	151 (63.2%)	77 (58.8%)	74 (68.5%)	
<b>Sex</b>				
Male	93 (38.9%)	52 (39.7%)	41 (38.0%)	0.785
Female	146 (61.1%)	79 (60.3%)	67 (62.0%)	
<b>Diagnostic</b>				
GIT <sup>b</sup>	47 (19.7%)	21 (16.0%)	26 (24.3%)	0.062
Breast	48 (20.2%)	28 (21.4%)	20 (18.7%)	
Head and neck	31 (13.0%)	13 (9.9%)	18 (16.8%)	
Gynecological <sup>c</sup>	39 (16.4%)	27 (20.6%)	12 (11.2%)	
Lung	25 (10.5%)	14 (10.7%)	11 (10.3%)	
CBT	13 (5.5%)	5 (3.8%)	8 (7.5%)	
Others <sup>d</sup>	36 (14.7%)	23 (17.6%)	13 (11.2%)	
<b>Metastasis</b>				
Local	62 (26.0%)	39 (30.0%)	23 (21.3%)	0.311
Local + distant	177 (74.0%)	92 (70.0%)	85 (78.7%)	
<b>Previous cancer treatment</b>				
No (virgin)	41 (17.2%)	22 (16.9%)	19 (17.6%)	0.206

and QT (UCU=0.9% vs. PCU=0) were only similar between units in the last three days of life. Patients followed in the PCU were less likely to prescribe ONT compared to those followed in the UCU during the entire evaluation period (p-value <0.001). The prescription of ENT was lower in the PCU only in the last 3 days before death (p-value <0.050) (Table 3).

Dipyron remained as the drug with the highest proportion (average of 85%) of prescriptions in the last three days of life in the UCUs, followed by morphine (average of 70%). It should be noted that enoxaparin appeared in the sixth position (average of 38%) and insulin appeared in the ninth position (average of 21%) during the period



**Figure 2:** Average number of prescriptions for laboratory tests (A), imaging tests (B) and procedures (C) in the last month of life by patients with terminal cancer according to health care units (N=239). Note: N=number of observations; UCU=Usual Care Units; PCU= Palliative Care Unit; \*p-value<0.050 and \*\*p-value<0.001 of the Student t test.

**Table 3:** Types of imaging tests and most prescribed procedures in the last month of life for patients with advanced cancer according to health care units (N=239).

Variables	Period of follow up before death								
	30 days			7 days			3 days		
	Total	UCU	PCU	Total	UCU	PCU	Total	UCU	PCU
<b>Imaging exams</b>									
X-ray	135 (56.5%)	<b>88 (67.2%)</b>	<b>47 (43.5%)**</b>	78 (32.6%)	<b>57 (53.5%)</b>	<b>21 (19.4%)**</b>	50 (21.0%)	<b>36 (27.5%)</b>	<b>14 (13.0%)*</b>
CT	80 (33.5%)	<b>54 (41.2%)</b>	<b>26 (24.0%)*</b>	29 (12.1%)	<b>22 (16.8%)</b>	<b>7 (6.5%)*</b>	11 (4.6%)	6 (4.6%)	4 (4.6%)
Ecodoppler	15 (6.3%)	<b>15 (11.4%)</b>	<b>0**</b>	3 (1.3%)	3 (2.3%)	0	0	0	0
Endoscopy	10 (4.2%)	8 (6.1%)	2 (1.8%)	5 (2.1%)	5 (3.8%)	0	0	0	0
Ultrasonography	7 (2.9%)	7 (5.3%)	0	3 (1.3%)	3 (2.3%)	0	0	0	0
Outros <sup>a</sup>	14 (5.8%)	<b>12 (9.2%)</b>	<b>1 (0.9%)*</b>	5 (2.1%)	2 (1.5%)	0	3 (1.3%)	3 (2.3%)	0
<b>Procedure</b>									
Quimiotherapy	31 (13.0%)	<b>29 (22.1%)</b>	<b>2 (1.8%)**</b>	8 (3.3%)	<b>7 (5.3%)</b>	<b>1 (0.9%)*</b>	1 (0.4%)	1 (0.9%)	0
Transfusion	29 (12.1%)	<b>29 (22.1%)</b>	<b>0**</b>	19 (8.0%)	<b>19 (14.5%)</b>	<b>0**</b>	13 (5.4%)	<b>13 (9.9%)</b>	<b>0*</b>
Biopsy	16 (6.7%)	<b>16 (12.2%)</b>	<b>0*</b>	3 (1.3%)	3 (2.3%)	0	0	0	0
Radiotherapy	13 (6.4%)	<b>11 (8.4%)</b>	<b>2 (1.8%)*</b>	5 (2.1%)	5 (3.8%)	0	0	0	0

(Figure 3). The three most prescribed medications in the last three days of life in the PCU were morphine (average of 92%), dipyron (average of 88%), and midazolam (average of 71%) (Figure 4).

According to the analysis of the average frequency of prescription of the four essential drugs, in the last three days of life of patients with advanced cancer, according to the health care units, it was verified that in the UCU there was no prescription of haloperidol and scopolamine. Morphine and midazolam were prescribed in the UCUs, but in a much lower quantity than the PCU (p-value <0.050) (Figure 5).

## Discussion

The present study, about care provided to patients with terminal cancer in a national cancer treatment center, brings some main results. Patients followed-up in the last 30 days prior to death in the PCU underwent fewer laboratory, imaging and procedural tests, had fewer prescriptions for nutritional therapy and more prescriptions for essential drugs for end-of-life care, when compared to those in treatment in the UCUs. Therefore, as was to be expected, at PCU there was a limitation of the use of futile therapies and incapable of meeting the most relevant demands of terminally ill patients. This approach may be related to the fact that teams specialized in palliative care have

greater technical knowledge about prognosis and a careful look at the management of symptoms, promotion of quality of life and death [12].

Even in follow-up at a national referral center for cancer treatment, most patients (54.8%) did not receive assistance from a team specialized in palliative care during the terminal process. World estimates by WHO<sup>5</sup> indicate that more than 56.8 million people demand palliative care but only 12% of this need is met. Brazil has one of the worst offers of palliative care services, accessed by only about 0.3% of people who die annually in the country [13]. In addition to the incipient offer of this type of service, the referral of patients to exclusive palliative care is a difficult task that permeates different barriers, such as those related to health professionals, among which we can mention those related to oncologists. They find referring a patient with advanced cancer to exclusive palliative care a complex task, causing patients to be referred late or never be referred [14].

As expected, we found a high prevalence of nutritional impairment (nutritional risk: 70.3%; cachexia: 82.3%), regardless of the type of care unit. It is irrefutable that the impairment of nutritional status increases as cancer progresses [15]. Previous studies show that nutritional risk may be present in 71% to 100% [16,17] and cachexia in 13.8% to 53.9% of patients with advanced cancer [18].

The high prevalence of laboratory tests, imaging and procedures (chemotherapy and blood/platelet transfusion) performed in the UCUs reflect the therapeutic futility often present in care provided by professionals who are not specialized in palliative care for patients in the process of finitude. Receiving the last dose of chemotherapy within 14 days before death can be defined as an aggressive intervention [19]. Blood transfusion, in turn, involves the expenditure of a finite resource and requires careful evaluation for indication in patients with advanced cancer. However, scientific evidence has shown that patients with

terminal cancer admitted to UCUs are likely to receive treatments with questionable benefits, such as chemotherapy and blood transfusion, towards the end of life, differently from those seen in PCUs [20,21].

The highest prevalence of ONT, ENT and PNT prescription occurred in UCUs. The decision to initiate and maintain Nutritional Therapy in patients with advanced cancer involves prognostic and bioethical issues, as an inadequate prescription can increase discomfort and suffering [22-24]. Kempf et al.<sup>20</sup>, in a study carried out in France,

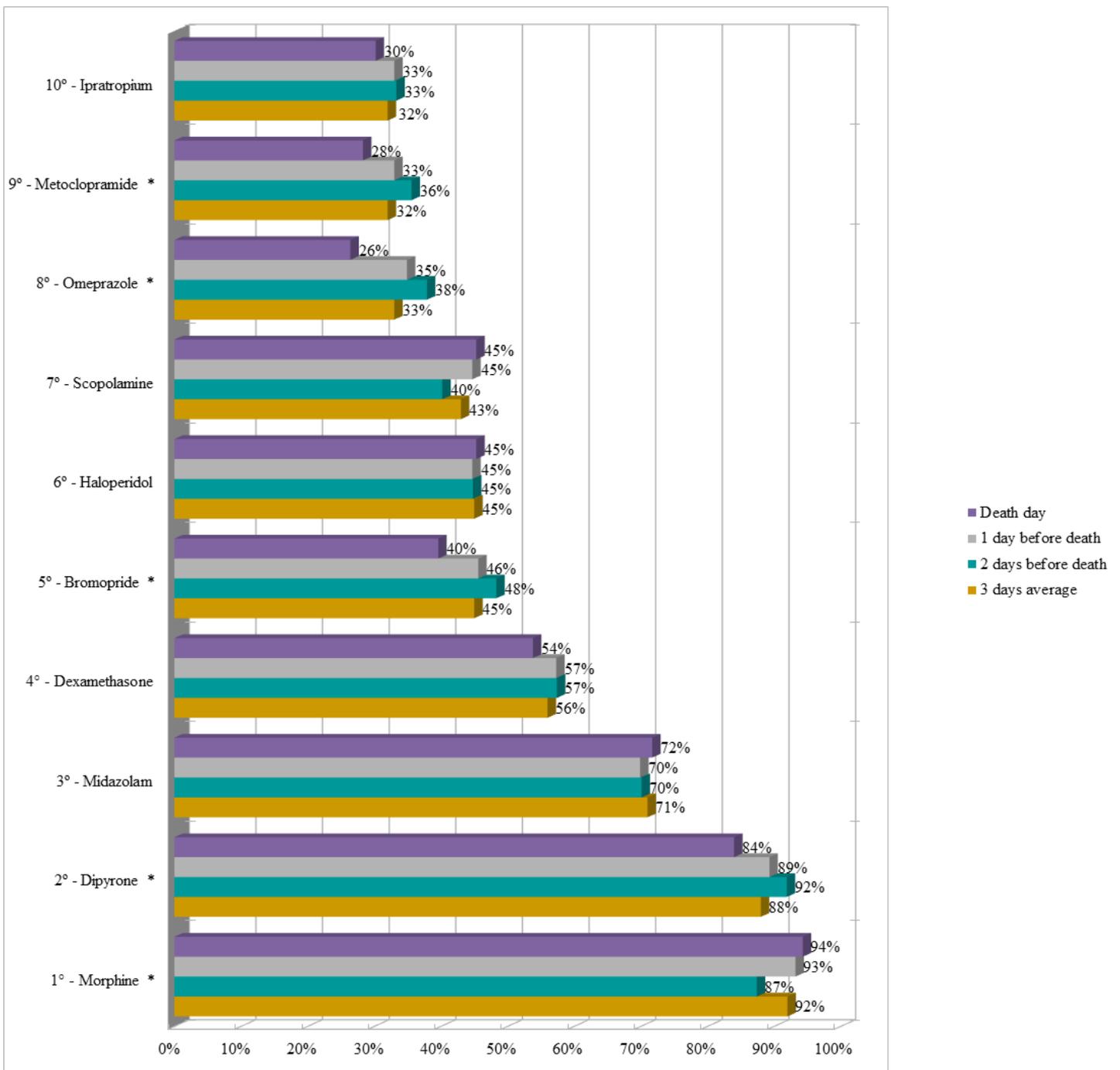


Figure 3: Ranking of the ten most prescribed drugs in the Usual Care Units in the last three days of life of patients with terminal cancer (N=131).

Note: N=number of observations. \*p-value<0.050 of the Chi-square test for proportions.

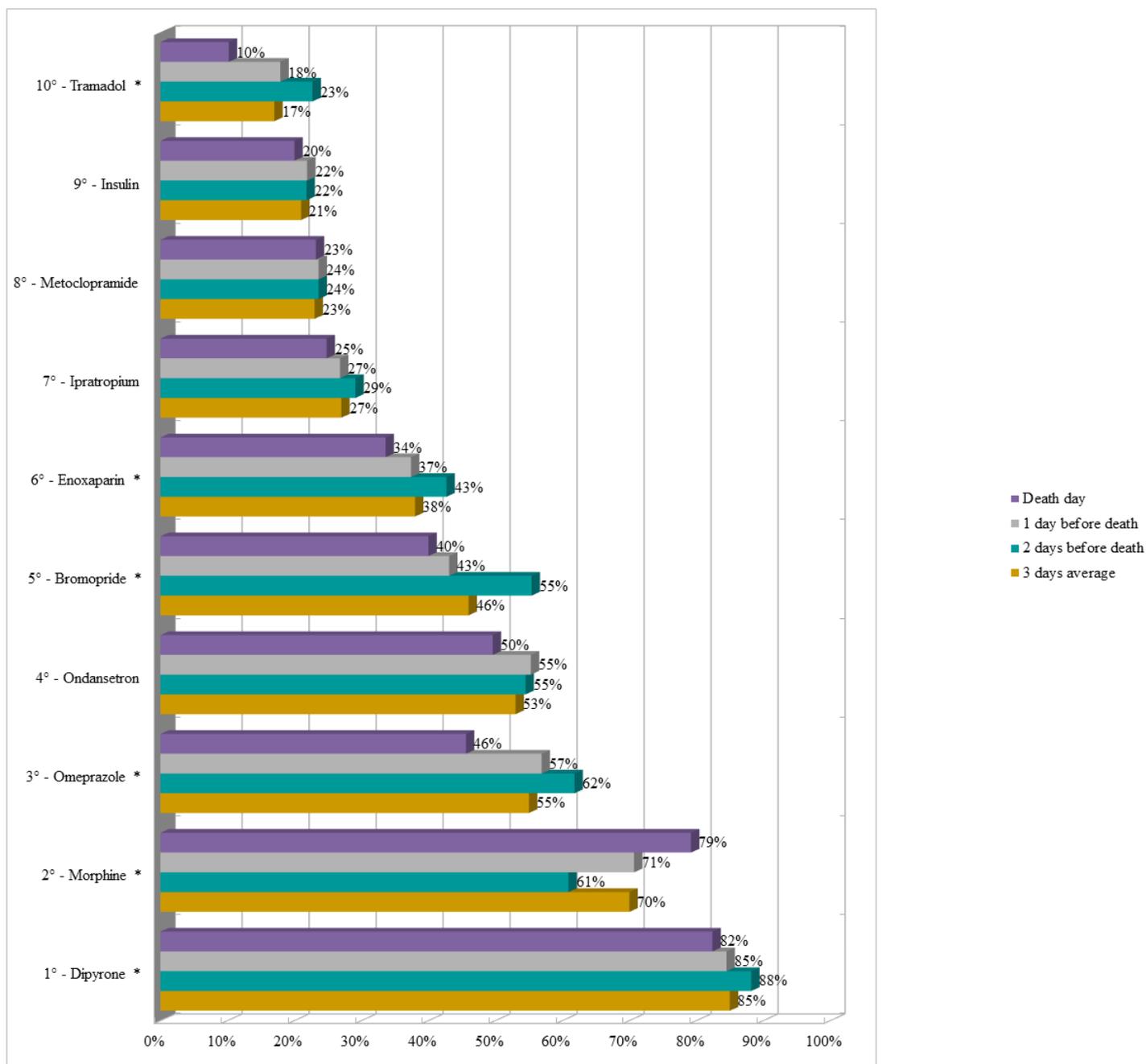


Figure 4: Ranking of the ten most prescribed drugs in the Palliative Care Unit in the last three days of life of patients with terminal cancer (N=108).

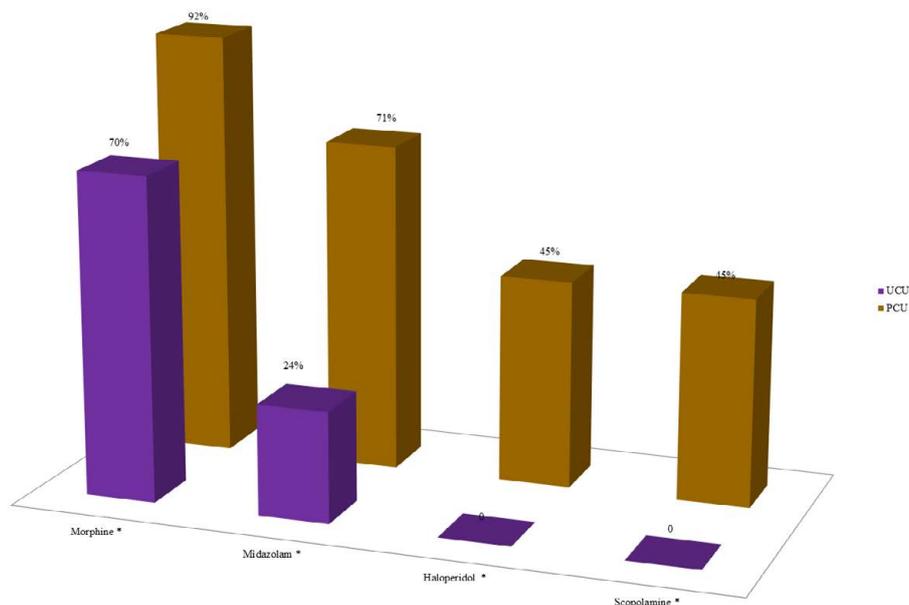
Note: N=number of observations.\*p-value<0.050 of the Chi-square test for proportions.

demonstrated that more than 15% of patients with advanced cancer received ENT and PNT in the last weeks of life, most of them (75.3%) in non-specialized hospitals. It is likely that palliative care providers are more conservative in their conduct related to Nutritional Therapy prescription in the last weeks of life, which may be related to the experience of patient-centered care [25,26].

The quantity and quality of medications used by patients with advanced cancer during their last days of life reflect the quality of care provided. In this context, we observed, for example, the presence of enoxaparin (advised in the institutional protocol for prevention

of venous thromboembolism in prolonged hospitalization) and the absence of haloperidol (indicated in cases of hyperactive delirium) [27] among the 10 drugs. These data suggest the absence of medication reconciliation practice among non-palliative professionals, through the continuity of the prescription of futile medications [28,29].

Another relevant fact regarding the ranking of the 10 most prescribed drugs in UCUs is the absence of sedative drugs such as midazolam. We hypothesize that, this fact, linked to the prescription of morphine, and may indicate the use of opioids to sedate at the end of life, to the detriment of the use of appropriate sedatives, making



**Figure 5:** Analysis of the average frequency of prescription of the four essential drugs, according to Lindqvist et al. 2013, in the last three days of life of patients with terminal cancer according to the health care units (N=239).

Note: N=number of observations; UCU=Usual Care Units; PCU=Palliative Care Unit. \*p-value<0.050 of the Chi-square test for proportions.

it difficult to achieve safe sedation. Morphine is a strong opioid indicated for the treatment of pain and terminal dyspnea, which has a decreased level of consciousness as an adverse effect, characteristic of drug intoxication. Therefore, its use for the purpose of sedation is considered an inappropriate conduct [30]. In addition, the high prescription of omeprazole, ondansetron and bromopride found in UCUs may be related to the increase in symptoms of nausea and vomiting, common in intoxication conditions [31].

According to an international consensus of specialist physicians working in large Palliative Care centers, morphine, midazolam, haloperidol and scopolamine were considered the four essential drugs to control the symptoms prevalent in patients with terminal cancer, especially in the last 48 hours of life. Therefore, they must be available and prescribed in all care units for cancer patients. However, our results showed the absence of prescription of haloperidol and scopolamine and the reduced prescription of morphine and midazolam for patients followed in the UCUs during the last three days of life, when compared to those in the PCU.

Considering, therefore, the high prevalence of distressing symptoms at the end of life of cancer patients [32] and that appropriate drug interventions are essential to reduce suffering, we assume that terminal patients not assisted by a team specialized in palliative care are unlikely to receive adequate comfort for a good death. The development of institutional protocols for terminal patients, whether in the PCU or in the UCUs, could contribute to reversing this reality.

Despite all the evidence brought by this study, some methodological limitations need to be highlighted. Due to the retrospective design, it was not possible to assess the comfort and quality of life and death of the patients who made up the study group. Despite not having been the objective of the proposal, such an evaluation would enrich

our findings. In addition, data collection from medical records can be a source of bias derived from potentially inadequate or insufficient records of information about the care provided to patients in the source document. It is necessary to develop further studies, with an appropriate design to assess other important variables such as symptom control based on the interventions performed.

## Conclusion

The present study demonstrated that the use of health resources in the care of patients with terminal cancer differ between the assessed care units. The assistance provided at the PCU involved a better use of health resources, reflected in the limitation of the use of futile therapies in the context of limited life expectancy, as well as in the prescription of drugs potentially capable of contributing to reduce the burden of symptoms inherent in the terminal phase.

## Funding

This research received no specific grant from any funding agency in the public, commercial, or not for profit sectors.

## Declaration of Conflicts of Interest

The Authors declares that there is no conflict of interest.

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#### Citation:

Freitas RD, Souza-Silva RD, Oliveira LCD (2022) Assistance to Patients with Terminal Cancer in the Last 30 Days Prior to Death: Differences in the Care of the Usual Health Care Units and a Palliative Care Unit. *Cancer Stud Ther J* Volume 7(3): 1-9.