



Clinical significance of palliative care assessment in patients referred for urgent intensive care unit admission: A cohort study[☆]



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ABSTRACT

Purpose: To evaluate clinical characteristics of patients with palliative care (PC) and urgent intensive care unit (ICU) referrals in the same hospital admission.

Methods: All urgent ICU referrals at an academic, tertiary hospital, and the co-occurrence and timing of PC assessment were retrieved from a prospectively collected database.

Results: From May 2014 to May 2015, 2476 patients were analyzed and 179 (7%) had co-occurrence of PC assessment and urgent ICU referral in the same hospital admission. Hospital mortality was higher (odds ratio, 8.3; 95% confidence interval, 5.4–12.7) and ICU admission was lower (odds ratio, 0.54; 95% confidence interval, 0.40–0.74) in patients with PC assessment, compared with patients without concurrent PC and ICU referrals. Variables associated with PC assessment were older age, diagnosis of cancer, depressed level of consciousness, nonsurgical admission, lower performance status, physician's subjective prognosis of poor outcome, and length of hospitalization before ICU referral.

Conclusion: In this cohort of patients with urgent ICU referral, clinical characteristics at the moment of ICU referral were associated with co-occurrence of PC assessment in the same hospital admission. These characteristics might guide the development of instruments to enhance early referral of high-risk patients to PC services.

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1. Introduction

The global burden of critical illness is high and is likely to increase as the population ages [1]. In the United States, for instance, it has been estimated that roughly 1 in 5 Americans die using intensive care unit (ICU) services [2]. Moreover, perceptions of inappropriate care in the ICU are reported frequently worldwide [3,4] and much of that care may be seen as nonbeneficial or not consistent with patients' values and preferences [5].

There are several key steps in the evolution of decision making in relation to end-of-life situations in the hospital, from the admission of an at-risk patient to the occurrence of an acute deterioration and its management in the critical care setting [6]. Advanced care planning or palliative care (PC) referral in the wards or during ICU stay may reduce inappropriate ICU admissions and ICU length of stay [7]. In addition, rapid response systems activation during acute deterioration has been associated with modifications in goals of care decisions [8]. However, although it has been suggested that such acute deterioration events could be used as indicators to trigger PC assessment [9], there is little research on the epidemiology of deteriorating patients in the hospital to help discriminating which patients would benefit from such assessment [10,11].

Co-occurrence of PC assessment and urgent ICU referral in the same hospital admission could be used as a marker for high-risk patients that may benefit from goals of care discussions. The aim of this study was to evaluate clinical characteristics at the moment of urgent ICU referral

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that could differentiate patients with concurrent PC and ICU referral from patients with ICU referral only.

2. Methods

2.1. Ethics, consent, and permission

This study was approved, and a waiver for informed consent was granted, by the Hospital das Clínicas da Faculdade de Medicina da Universidade de São Paulo (HCFMUSP) research ethics committee (approval number 638.864).

2.2. Setting

The Central Institute of the HCFMUSP is an academic, tertiary hospital with about 1100 hospital beds and 110 ICU beds, divided in 10 ICUs. The Central Institute is a referral center for acutely ill medical, surgical, and trauma patients and also for elective medical and complex surgery patients, including solid organ transplantation. The ICUs are closed units, staffed by intensivists and medical residents, and all resources are available at a 24/7 schedule. There is also an intermediate care unit at the emergency department, which receives patient from the emergency department and is staffed by emergency medicine physicians and internal medicine residents, with diurnal rounds from Monday to Friday by an intensive care physician. Cardiac (including cardiac surgery) patients are, most of the time, admitted at other facilities in the complex.

The PC team comprises a multidisciplinary team specialized in PC. Palliative care assessments were made after referral by the primary medical team and there was no institutional mechanism to trigger the PC evaluation. Referrals were received from all inpatient units. The PC team was available from Monday to Friday, during work hours. The entire team would meet with the patient/relatives and then collaborated with the attending physicians regarding the most appropriate care for each patient. The PC team did not admit acute patients directly to their service, but, when necessary, after assessment and collaboration with the primary medical team and patient/relatives, it would be possible to transfer the patient to the PC ward or affiliated hospice.

2.3. Study design

All urgent ICU admission referrals at HCFMUSP Central Institute from May 2014 to May 2015 were evaluated. Only the first ICU admission referral was analyzed and patients younger than 16 years were excluded. All data were retrieved from prospectively collected databases that were not designed for the specific purpose of this study.

An *urgent ICU referral* was defined as a nonscheduled request for ICU admission made by the physician, whether or not the patient was actually admitted to the ICU. A *PC assessment* was defined as an evaluation by the PC team, after request by the primary medical team, that occurred in the same hospital admission of the urgent ICU referral. The *ICU admission* was defined as admission to one of the ICUs in a 7-day period after an urgent ICU referral.

The included patients were grouped into the following: (A) patients for whom only urgent ICU admission was requested during the hospital admission (ICU only) and (B) patients for whom urgent ICU admission referral and PC assessment were made during the same hospital admission (ICU and PC), which was further divided into the following: (B.1) patients for whom PC assessment was made before urgent ICU referral (PC before ICU) and (B.2) patients for whom PC assessment was made after urgent ICU referral (PC after ICU).

Patients' characteristics were collected from the ICU request form, an obligatory standardized form for ICU referral that was filled by the physician in charge of the patient at the moment of ICU referral. This form comprises patients' characteristics, such as physiological variables, comorbidities, reason for ICU referral, performance status, and also the

attending physician's subjective prognosis of survival if the patient was to be admitted to the ICU. Characteristics were also retrieved from the PC assessment form, which is filled by the PC team in the first evaluation and during follow-up. Patients were followed up until hospital discharge or death.

Severity of acute illness was measured by the Mortality Probability Model (MPMII0) score [12]. Performance status was measured by a modification of the Katz activities of daily living (ADLs) [13], in which patients were classified as functionally independent (independent for all ADLs), partially dependent (independent for 3–5 ADLs), and severely dependent (capable of performing a maximum of 2 ADLs) and, in those evaluated by the PC team, by the Palliative Performance Scale (PPS) [14]. Physician's subjective prognosis was assessed as a 3-stage categorical variable: probable survival without severe disabilities, survival with severe disabilities, or no survival.

2.4. Statistical analysis

Microsoft Excel 2013 (Microsoft, Redmond, Wash) and Microsoft Access 2013 (Microsoft) were used as database software. Statistical analyses were performed with SPSS 13.0 (SPSS Inc, Chicago, Ill) or EpiInfo 7 for Windows (Centers for Diseases Control and Prevention, Atlanta, Ga). Categorical variables were described as numbers of cases (percent). Continuous variables were described as mean \pm SD or median (interquartile range [IQR]), depending on normality of distribution. Differences in proportions were evaluated with the χ^2 statistics or Fisher exact test, where appropriate. Differences in means and medians were evaluated with analysis of variance test or Mann-Whitney *U* test, where appropriate. Patients transferred to other facilities were excluded from hospital mortality analysis, because their survival status was unknown.

We performed multiple logistic regression to identify variables independently associated with PC assessment. The variables selected were those found to be significantly correlated on univariate analysis. Variables were tested for correlation before they were entered in the model. Physician's subjective prognosis was entered as a dichotomous variable; good outcome (ie, survival without disabilities) vs poor outcome (ie, survival with severe disabilities or no survival), as was performance status (dependent vs independent). Length of hospitalization before ICU referral was divided into quartiles and entered as a categorical variable to ensure linearity. The final covariate model was developed by a stepwise procedure with backward elimination using Wald statistic. Goodness-of-fit was tested by the Hosmer and Lemeshow statistic. A 2-tailed *P* value less than .05 was considered significant in all comparisons.

3. Results

From May 2014 to May 2015, there were 44 291 admissions to the hospital. There were 3115 urgent ICU referrals, of which 639 were excluded (612 repeated requests and 27 requests for patients younger than 16 years), leaving 2476 patients for final analysis. In the period of the study, there were 843 PC assessments (Figure).

3.1. Characteristics of the cohort

There were 179 (7%) patients with ICU and PC assessment in the same hospital admission (ICU and PC) and 2297 (93%) patients with sole ICU referral (ICU only; Table 1). Overall, 1270 (52%) patients were on the wards at the time of ICU referral, median age was 57 (IQR, 42–69) years, and 1378 (55.7%) patients were male. Median MPMII0 score was 0.20 (IQR, 0.09–0.57), and 620 (25%), 678 (27.4%), 242 (9.8%), and 308 (23.1%) patients received vasoactive drugs, underwent invasive mechanical ventilation, were in need of urgent renal replacement therapy, and were in need of monitoring for urgent surgery, respectively. One thousand five hundred fifty-one (62.9%) patients were admitted

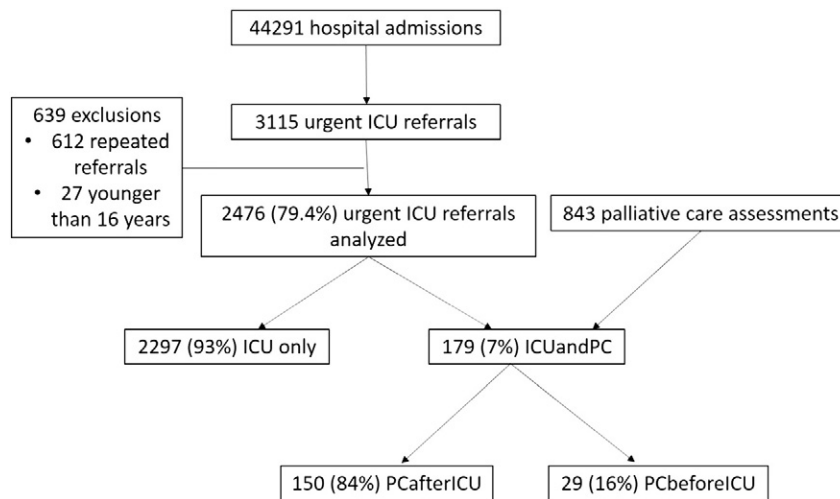


Figure. Flowchart of patients in the study.

to the ICU after referral. Median ICU and hospital length of stay were 6.0 (IQR, 2.0–11.0) and 15.0 (IQR, 7.0–30.0) days, respectively. Hospital mortality was 39.9%, after excluding transferred patients (896 deaths).

3.2. Characteristics of patients with PC assessment

On univariate analysis, ICU and PC patients were older and presented with higher severity of illness, as measured by the MPMII0 and the presence of organ dysfunctions, although there were no differences in the need for life support measures (Table 1). In addition, ICU and PC patients were regarded as more functionally dependent (101 [58%] vs 572 [25.5%]; $P < .001$) and with less chance of survival without disabilities (112 [64.4%] vs 1865 [83%]; $P < .001$).

Clinical characteristics at the moment of ICU referral that were associated with PC assessment on multivariate analysis were age, previous diagnosis of cancer, depressed level of consciousness, nonsurgical or trauma admission, performance status, physician's subjective prognosis, and length of hospitalization before ICU referral (Table 2).

3.3. Details of timing to PC services

Characteristics of the 179 patients with ICU and PC referrals, stratified by timing of PC assessment in reference to ICU referral, are demonstrated in Table 3. Overall, 150 (84%) patients had PC assessment after ICU referral (PC after ICU) and 29 (16%) had PC assessment before ICU referral (PC before ICU). Palliative care before ICU patients were more likely to have pain management as the main reason for PC assessment, had higher PPS scores, and were in the hospital for shorter periods before PC assessment.

3.4. Palliative care assessment and hospital outcomes

When analyzing the whole cohort (2476 patients), ICU and PC patients were less likely to be admitted to the ICU (88 [49.3%] vs 1463 [64.0%]; odds ratio [OR], 0.54; 95% confidence interval [CI], 0.40–0.74). In addition, ICU and PC patients were associated with higher hospital mortality, when compared with ICU only patients (125/151 [82.8%], excluding transferred patients vs 771/2097 [36.8%], excluding transferred patients; OR, 8.3; 95% CI, 5.4–12.7). These ICU and PC patients also had longer hospital and ICU length of stay (Table 1).

Intensive care unit and PC patients were more likely to be transferred to other facilities than ICU only patients (22 [12.3%] vs 170 [7.4%] patients; $P < .001$). When compared with patients discharged alive from the hospital, patients transferred to other facilities were older (median, 58 [IQR, 41–69] vs 54 [IQR, 38–66] years; $P = .012$),

had higher MPMII0 scores (median, 0.20 [IQR, 0.09–0.40] vs 0.13 [IQR, 0.07–0.30]; $P < .001$), were hospitalized for longer period before ICU referral (median, 1 [IQR, 1–10] vs 1 [IQR, 0–4] days; $P = .001$), and were more likely to be referred to the ICU for respiratory distress (87 [45.3%] vs 384 [28.4%] patients; $P < .001$) and for mechanical ventilation support (50 [26%] vs 232 [17.2%] patients; $P = .005$). Moreover, patients transferred to other facilities were less likely to be regarded as functionally independent (122 [64.9%] vs 1043 [78.8%] patients; $P < .001$) or probable survivors without disabilities (142 [74.7%] vs 1203 [91.1%] patients; $P < .001$).

To assess the potential impact of the differential transference proportion on the differential mortality between ICU only and ICU and PC patients, a sensitivity analysis was performed. Because ICU and PC were associated both with higher mortality and a higher transference proportion, it was considered that transference to other facilities would have had an impact on the differential mortality if transferred patients were more likely to survive than nontransferred patients. So, for the sensitivity analysis, it was considered that all patients transferred to other facilities would be alive at the end of the study period. In this analysis, mortality would still be higher for ICU and PC patients (125 [72.3%] vs 771 [34%]; OR, 5.1; 95% CI, 3.6–7.1).

In the subgroup of ICU and PC patients (179 patients), stratified by timing of PC assessment (Table 3), there was no difference in mortality between PC before ICU and PC after ICU patients (OR, 1.73; 95% CI, 0.48–6.25) or in the number of days from PC assessment to death, although physicians were less likely to expect survival without disabilities for PC before ICU patients. Nevertheless, PC before ICU patients were hospitalized for shorter periods (median, 19.0 [IQR, 8.5–26.5] vs 32.0 [IQR, 15.5–52.0] days; $P = .003$) and demonstrated a trend for shorter ICU stay (median, 2.0 [IQR, 1.5–24.0] vs 12.0 [IQR, 5.0–21.0] days; $P = .065$).

4. Discussion

This study has shown that clinical characteristics at the moment of urgent ICU referral were associated with the co-occurrence of PC assessment and ICU admission referral in the same hospital admission. These patients were older, were more likely to have previous diagnosis of cancer and nonsurgical admission, were like to present with depressed level of consciousness, were hospitalized for longer periods before ICU admission request, had lower performance status, and were judged by the physicians to be less likely to survive without severe disabilities.

Previous studies on the role of end-of-life discussions on acutely decompensating patients have demonstrated that up to one third of rapid response systems assessments are associated with end-of-life issues [8,15–17], and that a substantial number of these evaluations led to

Table 1
Characteristics of the cohort of patients with referral for urgent ICU admission (N = 2476)

Characteristic	ICU referral only (n = 2297)	ICU referral and PC assessment (n = 179)	P
Male sex, n (%)	1285 (55.9)	93 (52)	.301
Age (y), median (IQR, 25–75)	56 (41–68)	67 (54–80)	<.001
MPMIII at ICU referral, median (IQR, 25–75)	0.19 (0.09–0.46)	0.37 (0.16–0.60)	<.001
Surgical or trauma admission, n (%)	679 (29.6)	35 (19.6)	.004
Origin of patient at ICU referral, n (%)			
Operating room	61 (2.7)	4 (2.2)	
Surgical or medical wards	767 (33.9)	72 (40.4)	.224
Emergency department	1190 (52.6)	80 (44.9)	
Intermediate care unit	246 (10.9)	22 (12.4)	
Comorbidities, n (%)			
Cancer	34 (1.5)	13 (7.3)	<.001
Cirrhosis	156 (6.8)	17 (9.5)	.171
Chronic kidney disease	291 (12.7)	21 (11.7)	.716
Chronic heart failure	252 (11)	28 (15.6)	.057
Chronic obstructive pulmonary disease	98 (4.3)	12 (6.7)	.127
Dementia	37 (1.6)	7 (3.9)	.025
Immunosuppression	179 (7.8)	18 (10.1)	.281
No known comorbidities	311 (13.5)	8 (5.0)	.001
Length of hospitalization before ICU referral (d), median (IQR, 25–75)	1.0 (0.0–5.0)	3.0 (1.0–11.0)	<.001
Organ dysfunctions at ICU referral, n (%)			
Depressed level of consciousness	837 (36.4)	98 (54.7)	<.001
Respiratory distress	808 (35.2)	74 (41.3)	.097
Shock	722 (31.4)	70 (39.1)	.034
Acute kidney injury	633 (27.6)	63 (35.2)	.029
Life support at ICU referral, n (%)			
Use of vasoactive drugs	569 (24.8)	51 (28.5)	.282
Invasive mechanical ventilation	623 (27.1)	55 (30.7)	.298
Noninvasive mechanical ventilation	220 (9.6)	24 (13.4)	.098
Need for urgent renal replacement therapy	227 (9.9)	15 (8.4)	.514
Urgent surgery monitoring	292 (26.3)	16 (17.2)	.16
Performance status, n (%)			
Functionally independent	1674 (74.5)	73 (42)	
Partially dependent	475 (21.1)	72 (41.4)	
Severely dependent	97 (4.3)	29 (16.7)	<.001
Physician's subjective prognosis at ICU referral, n (%)			
Survival without disabilities	1865 (83)	112 (64.4)	
Survival with severe disabilities	329 (14.6)	55 (31.6)	
No survival	53 (2.4)	7 (4.0)	<.001
Hospital outcomes			
ICU admission, n (%)	1463 (64)	88 (49.2)	<.001
Surgery during hospitalization, n (%)	1016 (44.2)	71 (39.7)	.0236
Length of ICU stay (d), median (IQR, 25–75)	5.0 (2.0–10.5)	10.5 (4.2–21.0)	<.001
Length of hospitalization (d), median (IQR, 25–75)	15.0 (7.0–28.0)	29.0 (15.0–51.0)	<.001
Survival outcome, n (%)			
Alive	1326 (58)	26 (14.5)	
Deceased	771 (33.7)	125 (69.8)	
Transferred to other facilities	170 (7.4)	22 (12.3)	<.001

goals of care discussions and changes. These assessments may help implement a more patient-centered care plan and help optimize allocation of scarce resources [18]. However, the incidence of such discussions is quite variable, in part because of the inherent difficulties on establishing patient's prognosis during acute deterioration [10]. Similarly to others' results [16], our study has found a low rate of PC assessment in acutely decompensating patients. This could be explained, in part, because, contrarily to other studies [7,19,20], there was no formal instrument to trigger the decision for goals of care discussion, although there was a continuing education program on PC within the emergency and critical care departments and with medical residents from different specialties.

Our study differs from previous studies in that it attempted to study the epidemiology of acutely deteriorating patients, trying to identify characteristics at the moment of ICU referral that could recognize a subgroup of patients that were ultimately assessed by a PC team, comprising patients with a high risk of death and possible limitation of medical therapies. We have identified distinct characteristics that could aid clinicians' decision making and may help develop triggers for PC assessments targeting this high-risk group of patients presenting with acute decompensation. Increased awareness and identification of this group of patients may help optimize care and resource allocation even after

those patients are admitted to the ICU, as studies have shown that PC assessment and advance care planning may have impact before or after ICU admission [7].

Table 2
Multivariate logistic regression of variables associated with PC assessment in the cohort of patients with urgent ICU referral (N = 2476)

Variables associated to PC assessment	B	OR	95% CI		P
			Lower	Upper	
Age	0.03	1.03	1.02	1.04	<.001
Previous diagnosis of cancer	1.286	3.62	1.74	7.51	<.001
Depressed level of consciousness	0.713	2.04	1.46	2.86	.001
Surgical or trauma admission	−0.52	0.60	0.40	0.89	.012
Performance status (dependent vs independent)	0.873	2.39	1.69	3.40	<.001
Physician's subjective prognosis (poor outcome vs good outcome)	0.363	1.44	1.00	2.07	.051
Length of hospitalization before ICU referral (quartiles)	0.229	1.26	1.08	1.47	.003

Hosmer and Lemeshow goodness-of-fit test = 0.795.

Table 3
Timing of PC assessment in patients with ICU referral and PC assessment in the same hospitalization (N = 179)

Characteristic	PC assessment after ICU referral (n = 150)	PC assessment before ICU referral (n = 29)	P
Male sex, n (%)	81 (54)	12 (41.4)	.213
Age, median (IQR, 25–75)	66 (53–79)	68 (58–86)	.169
MPMII0 at ICU referral, median (IQR, 25–75)	0.40 (0.16–0.62)	0.40 (0.15–0.56)	.984
PPS, median (IQR, 25–75)	15 (10–30)	30 (20–40)	.001
PPS <30, n (%)	116 (85.3)	15 (55.6)	<.001
Length of hospitalization before ICU referral (d), median (IQR, 25–75)	2.0 (1.0–9.2)	7.0 (3.0–17.0)	.007
Length of hospitalization before PC assessment (d), median (IQR, 25–75)	23.0 (10.8–41.0)	3.0 (1.0–11.0)	<.001
Surgical or trauma admission, n (%)	29 (19.3)	6 (20.7)	.866
Origin of patient at ICU referral, n (%)			
Operating room	3 (2.0)	1 (3.6)	
Surgical or medical wards	57 (38.0)	15 (53.6)	
Emergency department	71 (47.3)	9 (32.1)	
Intermediate care unit	19 (12.7)	3 (10.7)	.398
Most frequent reasons for PC consultation, n (%)			
End-of-life discussion	42 (28)	8 (27.6)	.964
Pain control	4 (2.7)	5 (17.2)	.001
Other symptoms control	15 (10)	4 (13.8)	.544
Family conflicts	28 (18.7)	3 (10.3)	.278
Dehospitalization	14 (9.3)	2 (6.9)	.674
Appropriate PC request, n (%)	127 (84.7)	24 (82.8)	.796
No diagnosis at the moment of PC assessment, n (%)	0 (0)	3 (10.3)	.004
No indication for comfort care only, n (%)	9 (6)	9 (31)	<.001
Organ dysfunctions at ICU referral, n (%)			
Depressed level of consciousness	80 (53.3)	18 (62.1)	.387
Respiratory distress	58 (38.7)	16 (55.2)	.098
Shock	57 (38)	13 (44.8)	.49
Acute kidney injury	54 (36)	9 (31)	.608
Life support at ICU referral, n (%)			
Use of vasoactive drugs	40 (26.7)	11 (37.9)	.219
Invasive mechanical ventilation	49 (32.7)	6 (20.7)	.201
Noninvasive mechanical ventilation	17 (11.3)	7 (24.1)	.064
Need for urgent renal replacement therapy	12 (8)	3 (10.3)	.677
Urgent surgery monitoring	13 (16.9)	3 (18.8)	.857
Physician's subjective prognosis at ICU referral, n (%)			
Survival without disabilities	99 (68.3)	13 (44.8)	
Survival with severe disabilities	44 (30.3)	11 (37.9)	
No survival	2 (1.4)	5 (17.2)	<.001
Length of hospitalization (d), median (IQR, 25–75)	32.0 (15.5–52.0)	19.0 (8.5–26.5)	.003
ICU admission, n (%)	79 (52.7)	9 (31.0)	.033
Length of ICU stay (d), median (IQR, 25–75)	12.0 (5.0–21.0)	2.0 (1.5–24.0)	.065
Transferred to PC ward, n (%)	19 (12.7)	2 (6.9)	.535
Indication for hospice admission, n (%)	45 (30)	8 (27.6)	.794
Survival outcome, n (%)			
Alive	23 (15.3)	3 (10.3)	
Deceased	102 (68)	23 (79.3)	
Transferred to other facilities	19 (12.7)	3 (10.3)	.546
Days from PC assessment to death, median (IQR, 25–75)	5 (2.0–12.0)	7 (4.0–13.0)	.11

This study has strengths and limitations. Data were retrieved from databases that were prospectively collected, but were not designed for the specific purpose of this study, which leads to inherent limitations. In addition, it was a single-center study, although we have analyzed a large number of patients in a tertiary center, comprising 10 different ICUs with diverse admission policies. Moreover, we were not able to retrieve outcome information of patients transferred to other facilities, which could induce bias if patients with PC assessment were somehow more or less likely to be transferred, and if these transferred patients had a differential outcome risk. However, sensitivity analysis demonstrated no evidence that it would have had a significant impact on the results presented.

Although we have analyzed all PC assessments in the period, we were not able to analyze limitations of medical treatment in the group that was not assessed by the PC team and were not able to retrieve information on the reasons for ICU refusal, if, for example, it was related to futility assessment, ICU bed shortage, or other motives. It is possible that some of the patients that were not assessed by the PC team were subjected to goals of care discussion and limitation of medical therapies, which could hamper interpretation of our findings. Nevertheless, comparison of the 2 groups demonstrates that patients that were not assessed by the PC team were, on average, less severely ill, were less

functionally dependent, and had lower hospital mortality rate, which supports the interpretation that patients for whom ICU admission was requested and were also assessed by the PC team were, indeed, at higher risk for unfavorable outcomes.

5. Conclusion

In this cohort of patients with urgent ICU referral, clinical characteristics at the moment of ICU referral were associated with co-occurrence of PC assessment in the same hospital admission. These characteristics might guide the development of instruments to enhance early referral of high-risk patients to PC services.

Authors' contributions

JGRR, MDTC, RTC, and DNF contributed to the designing, acquisition, analysis and interpretation of data, and drafting and revising the manuscript. DJ contributed to interpretation of results, drafting, and critically revising the manuscript. All authors have approved the final version of this manuscript.

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