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Epidemiological profile of deaths from COVID-19 at a reference cardiology hospital and indication for palliative care during the pandemic

Perfil epidemiológico dos óbitos por Covid-19 em hospital de referência cardiológico e a indicação de cuidados paliativos no cenário de pandemia

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ABSTRACT – Background: Palliative care is a set of procedures for patients and families facing terminal or advanced illnesses. Numerous studies have already evaluated the role of palliative care and indications in outpatient or emergency settings. Nonetheless, data referring to the role of palliative care during a pandemic, such as COVID-19, are lacking. This study aimed to analyze the profile of deaths by COVID-19 at a tertiary reference cardiology hospital, and to identify the factors associated with more frequent indication of palliative care during patient management. **Methods:** From March 1 to July 31, 2020, all deaths due to confirmed COVID-19 were analyzed, and their clinical, epidemiological, laboratory and imaging data were obtained. **Results:** Considering the deaths, 26.8% of patients had received palliative care during hospitalization. When the groups were compared (standard care *versus* palliative care), there was a statistically significant difference for age (67.1 ± 12.1 *versus* 73.5 ± 9.1 years), presence of chronic obstructive pulmonary disease (3.2% *versus* 14.7%), and hypoxemia as cause of death (17.2% *versus* 55.9%). **Conclusion:** In this analysis of patients admitted to the emergency room of a tertiary cardiology hospital during the pandemic period, the determining factors for higher indication for palliative care were age and previous chronic obstructive pulmonary disease. The main cause of death was hypoxemia, which was more prevalent in the palliative group.

Keywords: COVID-19; Coronavirus infections; Death/epidemiology; Palliative care; Patient care

RESUMO - Introdução: Os cuidados paliativos consistem em um conjunto de práticas instituídas a pacientes e a seus familiares diante de enfermidades terminais ou avançadas. Diversos estudos já avaliaram seu papel e as indicações nos cenários ambulatoriais ou de emergência. Entretanto, faltam dados na literatura acerca do papel da palição no contexto de pandemia, como a COVID-19. O objetivo deste estudo foi analisar o perfil de óbitos por COVID-19 em um hospital cardiológico terciário de referência e determinar os fatores que estiveram associados à indicação mais frequente de cuidados paliativos na abordagem do cuidado com o paciente. **Métodos:** Foram estudados, entre 1º de março a 31 julho de 2020, todos os casos de óbito no período e infecção comprovada por COVID-19, sendo obtidas informações clínico-epidemiológicas, laboratoriais e de imagem. **Resultados:** Dentre os óbitos, 26,8% receberam abordagem por cuidados paliativos durante a internação. Na comparação entre os grupos (cuidados padrões *versus* abordagem paliativa), houve diferença estatisticamente significativa nos parâmetros idade ($67,1 \pm 12,1$ anos *versus* $73,5 \pm 9,1$ anos), diagnóstico de doença pulmonar obstrutiva crônica (3,2% *versus* 14,7%) e hipoxemia como causa de óbito (17,2% *versus* 55,9%). **Conclusão:** Nesta avaliação de pacientes admitidos em pronto-socorro de hospital terciário cardiológico durante período de pandemia, os fatores determinantes para maior indicação de cuidados paliativos foram idade e doença pulmonar obstrutiva crônica prévia. A principal causa de óbito foi hipoxemia, que foi mais prevalente no grupo paliativo.

Descritores: COVID-19; Infecções por coronavírus; Morte/epidemiologia; Cuidados paliativos; Assistência ao paciente

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INTRODUCTION

In 2002, the World Health Organization (WHO) defined palliative care as multidisciplinary care delivered to patients and their families facing a life-threatening medical condition.^{1,2} Palliative care dates to the 1960s and since then has grown and has been consolidated as a comprehensive health practice. The already indisputable clinical benefits of palliative care, such as optimized control of physical or psychological symptoms, have evolved to alleviate suffering and to promote quality of life for terminally ill patients, avoiding dysthanasia and therapeutic obstinacy.^{3,4}

Across the past decade, there has been an intense worldwide effort to improve the indication for palliative care, as well as management of cases, including the development of tools to help identify patients eligible for palliative care.⁵ After past epidemics of severe acute respiratory syndrome (SARS), influenza and ebola, the significant discussion on the role of palliative care during a pandemic began, focusing on alleviating suffering from often less-known diseases, alongside optimized management of hospital resources, with improved management of health systems, given the chaotic scenario inherent to this scenario.^{6,7}

In December 2019, what would become the 2019 coronavirus disease (COVID-19) pandemic started in the province of Wuhan, China.⁸ As months passed by, with the expansion of the infection and the emergence of the first epidemiological profiles, there was an increased requirement for intensive care in a percentage of COVID-affected patients, particularly for invasive ventilatory support (mechanical ventilation) and administration of supplemental oxygen, leading to overcapacity of health systems, due to the exponential increase of hospital admissions in public and private organizations. In many countries, emergency intensive care beds were opened, and mechanical ventilators and necessary supplies for clinical support of COVID patients were acquired. Early in the pandemic, high fatality rates were also evident among the elderly and patients with multiple comorbidities, who presented a higher incidence of unfavorable outcomes, despite the intensive care and invasive measures implemented.⁹⁻¹¹

In this scenario, the palliative care approach in critically ill patients infected by the severe acute respiratory syndrome virus 2 (SARS-CoV-2) becomes essential to ensure family support and provide comfort to end-of-life patients.^{12,13} Despite its relevance, there is a lack of published data on how palliative care has been used during the pandemic, and which are the criteria for palliative care indication in this setting.

The present study aimed to analyze the profile of deaths from COVID-19 and to determine the factors associated with a more frequent indication of palliative care in the approach to patient care.

METHODS

From March 1 to July 31, 2020, a total of 424 patients were admitted to the emergency room of a tertiary cardio-

logy hospital, which sees patients who seek care outside their area, in the city of São Paulo (SP), with clinical suspicion of COVID-19. Diagnoses were confirmed by a positive reverse transcriptase polymerase chain (RT-PCR) reaction for SARS-CoV-2. We included in the analysis all patients with confirmed diagnosis who died throughout the period of the study.

The study was approved by the local Ethics Committee (opinion 4,238.093; CAAE 33281120.8.1001.5462), and data were acquired from a comprehensive analysis of both paper and electronic medical records. The evaluation of chest computed tomography (CT) scans was based on the presence or absence of typical COVID-19 findings, e.g., presence of unilateral or bilateral ground-glass opacities. The Chi-square test and Fisher's exact test were used for the statistical analysis of categorical variables, and the Mann-Whitney test for continuous variables.

A multidisciplinary team and specialized professionals (palliativists or palliative care physicians) were involved in the decision to indicate palliative care, in addition to meetings with family members or patients themselves, when feasible. Proportional therapeutic goals, as well as care targets, were outlined in these meetings. When palliative care was indicated, a specific form was filled out, which was attached to the cover of the medical chart, with comprehensive clinical information about the decision reached with the family or when feasible with the patient.

RESULTS

Throughout the period of the study, 424 patients with confirmed SARS-CoV-2 infection (positive RT-PCR test) were admitted. Of these, 127 died and comprised the sample analyzed here. Hence, the COVID-19 fatality rate observed among inpatients was 29.9%.

Of the 127 cases analyzed, 34 (26.8%) received palliative care. Regarding the demographic characteristics of the sample (Tables 1 and 2), most patients were male (59.1%), and median age was 71 years. In the standard and palliative care groups, the median age was 69 and 76 years, respectively, with a statistically significant difference ($p=0.001$). Mean body mass index (BMI) was 27.1kg/m^2 . Concerning comorbidities, 78% of patients presented hypertension, 50.4% dyslipidemia, and 49.6% diabetes. Moreover, 22 patients (17.3%) were smokers. Eight patients were diagnosed with COPD, five of them in the group receiving palliative care, with a statistically significant difference between the groups ($p=0.032$). Forty-one patients (32.3%) had some extent of chronic renal failure. Regarding cardiovascular diseases, 54 (42.5%) presented congestive heart failure, and 36 (28.3%) arrhythmias, of which atrial fibrillation and atrial flutter were the most frequent, observed in 34 patients (26.8%). Patients with cardiac implantable electronic devices included 9.4% of the sample, whereas 21 patients (16.5%) presented valvular heart disease.

Table 1. Demographic characteristics and comorbidities of patients

Characteristics and comorbidities	Total (n=127)	Standard (n=93)	Palliative (n=34)	p-value
Age, years	71 (63-77)	69 (61.5-75)	76 (69.75-79.25)	0.001
Female	52 (40.9)	41 (44.1)	11 (32.4)	0.309
BMI, kg/m ²	27.1 (24.5-31.1)	27.2 (24.6-30.8)	25.9 (24.3-32.1)	0.731
Hypertension	99 (78)	70 (75.3)	29 (85.3)	0.334
Diabetes mellitus	63 (49.6)	49 (52.7)	14 (41.2)	0.317
Dyslipidemia	64 (50.4)	51 (54.8)	13 (38.2)	0.112
Smoking	22 (17.3)	20 (21.5)	2 (5.9)	0.061
Chronic obstructive pulmonary disease	8 (6.3)	3 (3.2)	5 (14.7)	0.032
Chronic renal disease	41 (32.3)	31 (33.3)	10 (29.4)	0.831
Congestive heart failure	54 (42.5)	39 (41.9)	15 (44.1)	0.842
Previous transplantation	6 (4.7)	4 (4.3)	2 (5.9)	0.658
Pacemaker	12 (9.4)	6 (6.5)	6 (17.6)	0.083
Valvular heart disease	21 (16.5)	15 (16.1)	6 (17.6)	0.794

Values expressed as median (interquartile range) or n (%).

BMI: body mass index.

Table 2. Clinical features, laboratory tests, echocardiography, and tomography pattern

Test results	Total (n=127)	Standard (n=93)	Palliative (n=34)	p-value
Hemoglobin, g/dL	12.5 (11.0-13.8)	12.4 (11.0-13.7)	13 (10.75-14.6)	0.303
Total leucocytes, cells/mm ³	7,525 (5,860-11,305)	7,960 (6,050-11,430)	6,870 (4,765-9,375)	0.093
Total lymphocytes, cells/mm ³	910 (660-1,390)	920 (627-1,347)	860 (690-1,415)	0.762
C-reactive protein, mg/dL	8.39 (4.3-20.4)	8.85 (3.4-20.8)	7.7 (5.3-19.5)	0.969
Baseline creatinine, mg/dL	1.47 (0.9-2.25)	1.4 (0.9-2.2)	2.6 (1.0-2.4)	0.252
Creatinine highest value, mg/dL	3.1 (2.0-4.5)	3.2 (2.2-4.7)	2.9 (1.8-4.3)	0.19
Troponin highest value, ng/mL	0.1 (0.04-0.62)	0.09 (0.04-0.27)	0.13 (0.5-0.85)	0.376
Dimer-D highest value, ng/mL	2,970 (1,585-6,231)	2,995 (1,604-6,843)	2,487 (1,571-5,467)	0.442
Atrial natriuretic peptide, pg/mL	8,250 (2,540-18,000)	8,335 (1,655-17,875)	7,720 (5,140-18,000)	0.569
Flu-like syndrome	65 (51.2)	49 (52.7)	16 (47.1)	0.689
Arrhythmia	36 (28.3)	26 (28)	10 (29.4)	1
Atrial fibrillation	34 (26.8)	25 (26.9)	9 (26.5)	1
Right bundle branch block	5 (3.9)	4 (6.9)	1 (3.2)	0.654
Left bundle branch block	20 (15.7)	12 (20.3)	8 (25.3)	0.599
Right ventricular dysfunction	41 (32.3)	31 (40.3)	10 (32.3)	0.514
Left ventricular ejection fraction, %	43.5 (31.8-60)	48 (32-60)	39 (2-58)	0.269
Typical pattern on CT scan	79 (62.2)	63 (75.9)	16 (61.5)	0.208

Values expressed as median (interquartile range) or n (%).

Among the patients who underwent chest CT scans to search for typical SARS-CoV-2 pneumonia patterns, 79 (62.2%) showed a typical pattern of bilateral peripheral ground-glass opacity. Among the main electrocardiographic abnormalities, left bundle branch block and right bundle branch block were observed in 15.7% and 3.9% of patients, respectively. Regarding echocardiography findings, patients showed median ejection fraction of 43.5%, and some degree of right ventricular dysfunction was revealed in 32.3% of patients.

As to laboratory tests, hemoglobin showed median values of 12.5g/dL, total leukocytes of 7,525, total lym-

phocytes of 910, C-reactive protein (CRP) of 8.39 and atrial natriuretic peptide (BNP) of 8,250. The median of the highest values of creatinine, troponin and D-dimer during hospitalization were 3.1, 0.1 and 2,970, respectively. None of the laboratory variables analyzed revealed statistically significant differences between the groups.

Analyzing causes of death, 27.6% of deaths were due to hypoxemia, with 17.2% in the standard group and 55.9% in the palliative care group ($p<0.001$). In 29.9% of sample, deaths were due to septic shock, while cardiogenic shock accounted for 16.5% of deaths (Table 3).

Table 3. Causes of death

Cause of death	Total (n=127)	Standard (n=93)	Palliative (n=34)	p-value
Septic shock	38 (29.9)	27 (29.0)	11 (32.4)	0.827
Hypoxemia	35 (27.6)	16 (17.2)	19 (55.9)	<0.001
Cardiogenic shock	21 (16.5)	15 (16.1)	6 (17.6)	0.794
Other causes	8 (6.3)	6 (6.5)	2 (5.9)	1

Values expressed as n (%).

We observed a significant statistical difference between groups (standard care *versus* palliative care) regarding median age, presence of COPD (3.2% *versus* 14.7%), and hypoxemia as cause of death (17.2% *versus* 55.9%).

DISCUSSION

With the worldwide spread of the new coronavirus, several epidemiological profiles of the COVID-19 pandemic have been described in the literature, with emphasis on the province of Wuhan,¹⁰ where the disease was initially reported, the region of Lombardy, in Italy,⁹ and New York, United States.¹¹ There is a lack of published data characterizing the profile of patients for whom palliative care was indicated during the pandemic. To our knowledge, this is the first study with this type of report.

Compared to Wuhan, the present study showed some differences concerning the presence of comorbidities: median of patients presenting hypertension was 48% in Wuhan *versus* 78% in the present study; diabetes patients totaled 31% and 53%, respectively, and chronic kidney disease patients, 4% and 32%, respectively. The similarity between the two studies is found on age of patients (medians 69 and 71) and the presence of chronic obstructive pulmonary disease: 7% and 6%, respectively. Thus, the profile of our study sample showed more clinically severe patients, especially in relation to the presence of cardiovascular risk factors. Such comorbidities are known to increase the frailty index of older patients, causing higher rates of unfavorable outcomes when affected by COVID-19.

A difference in age was found as a factor associated with palliative care, probably because it is related to greater frailty and less functionality in the elderly. The presence of COPD has been described as an independent factor of severity for SARS-CoV-2 infected patients.¹⁴ Its association with patients receiving palliative care and progressing to death was also revealed in this study. A previous diagnosis of COPD, together with other parameters of functionality and severity derived from clinical status and laboratory results, can help reach a decision in relation to providing palliative care in the COVID-19 setting.

Although the relevance of palliative care for patients with advanced heart failure has been well documented,¹⁵ in this study, carried out during the pandemic peak, no association was found between the degree of heart failure and the indication of palliative care in patients who died. This

finding may be related to the bias of the hospital where this study was performed being a reference center for cardiology, leading to a high prevalence of ventricular dysfunction in the study sample, as observed by the reduced median values for left ventricular ejection fraction (43.5%). It is evident that the sample we analyzed, involving cardiac patients, already comprised severe chronic diseases, and regardless of the pandemic, would already deserve outpatient palliative care management, such as congestive heart failure patients with several readmissions, notwithstanding optimized treatment.

It is also relevant that, although acute kidney injury is considered a risk factor for mortality in coronavirus infected patients (as described in the epidemiological profiles cited), it was not associated with indication for palliative care in this service.

In this study, the main causes of death were septic shock, hypoxemia, cardiogenic shock, and mixed septic and cardiogenic shock. Hypoxemia was the leading cause of death in the palliative group (55.9% *versus* 17.2%). This association became evident, since the indication for palliative management occurred for most patients, following the precepts of avoiding needless prolongation of life and invasive measures, such as tracheal intubation and mechanical ventilation. Therefore, the more severe hypoxemia reported in the palliative group would be due to the acceptance of lower oxygen saturation values in this subgroup of patients.

Among the limitations of the present study, because it was a retrospective study, we did not assess patients with any prognostic scales or functionality indices (Karnofsky Performance Scale – KPS, Katz and Lawton). Moreover, the baseline severity of our patients was markedly higher than in the general population, as our sample comprised many patients with heart disease, limiting the generalization of our findings.

CONCLUSION

This study reported the factors most related to the indication of palliative care for patients who died from COVID-19 were older age and presence of chronic obstructive pulmonary disease, in a sample of cardiac patients admitted to the emergency room of a tertiary hospital, during the early months of the pandemic in Brazil. Hypoxemia was the main cause of death, more prevalent in the palliative group. Further research is required to assess the criteria for indicating palliative care and the patients who most benefit from such management during a pandemic.

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None.

DECLARATION OF CONFLICTS OF INTEREST

The authors declare having no conflicts of interest.

CONTRIBUTION OF AUTHORS

Conception and design of the study: LNO and IMF; data collection: MAP, KHV, FHG and MAM; data interpretation: LNO, MAP and KHV; text writing: LNO, MAP and KHV; approval of the final version to be published: FF.

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