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Risk Factors for the Impairment of Ambulation in Older People Hospitalized with COVID-19: A Retrospective Cohort Study

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Abstract: (1) Background: Older people hospitalized with COVID-19 can reduced the capacity to walk. However, the prevalence of impairment of ambulation capacity still need to be established. Objective: To estimate the prevalence and identify the risk factors associated with the impairment of ambulation capacity at hospital discharge of older people with COVID-19. (2) Methods: A retrospective cohort study. Included age > 60 years, both sexes, hospitalized due to COVID-19. Clinical data was collected from the medical records. Ambulation capacity prior to COVID-19 infection was assessed through the patient report from his relatives. Multiple logistic regressions were performed to identify the risk factors associated with the impairment of ambulation at hospital discharge. (3) Results: Data from 429 older people were randomly. Among the 56.4% who were discharged, 57.9% had reduced ambulation capacity. Factors associated with reduced ambulation capacity at discharge were hospital stay higher than 20 days (OR: 3.5) and dependent ambulation capacity prior to COVID-19 (OR: 11.3). (4) Conclusion: More than half of the older people who survived hospitalized due to COVID-19 had reduced ambulation capacity at hospital discharge. Impaired ambulation prior to the infection, and a longer hospital stay were risks factors for reduced ambulation capacity.

Keywords: COVID-19; functional status; hospitalization; older people

1. Introduction

Older people are more vulnerable to suffering adverse effects of hospitalization [1], including the impairment of functional capacity [2]. The greatest vulnerability is associated with the decline of several systems and lower functional reserve because of aging [3–5] in addition to the reduced response to stressful stimuli [3,4]. Therefore, older people are more susceptible to immobility, sepsis and hypoxemia [6]. Thus, hospital admissions can impair several functions of older people, including the ambulation capacity [2].

COVID-19 has affected more than 771.151.224 confirmed cases and caused the death of more than 6.960.783 million worldwide [7]. The highest prevalence of severe cases was found in older people hospitalized with previous comorbidity (obesity, arterial hypertension and diabetes) [8–13]. The treatment of severe COVID-19 requires long periods of hospitalization and bed rest [14,15]. Several studies have shown the negative impact of long hospital stay and immobility on the functional capacity in older people functional impairment [12,16–19]. Thus, the tissue damage in multiple systems directly caused by the cellular invasion of SARS-COV-2 [9], the intense systemic inflammatory response [8], and the adverse effects of the hospitalization can cause a greater

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functional impact on the older people [11]. Muscle inactivity and intensive care interventions, including mechanical ventilation, neuromuscular blocking agents [20] and prone positioning [21] can decrease muscle strength, joint mobility and respiratory capacity [20–22] especially in older people [19].

These structural and functional consequences in critically ill patients can persist even after hospital discharge and are known as post-intensive care syndromes [8], triggering impairments in the performance of daily activities, autonomy and independence, negatively affecting functionality [23,24] and increasing the risk of mortality [25,26].

The longer the stay in the intensive care unit, the greater the risk of physical, cognitive and emotional problems [27]. Approximately 25-45% of critically ill patients' exhibit neuromuscular complications during and after intensive care, including symmetrical flaccid limb paralysis resulting from systemic inflammatory responses [28], associated with the use of steroid medication that can cause significant adverse effects, including immune dysfunction and sarcopenia [16].

Studies showed that approximately 65% of older people hospitalized due to COVID-19 suffer loss of mobility [16,19], but the clinical and sociodemographic factors associated with functional decline and the prevalence of the impairment of ambulation capacity at the hospital discharge have not yet been established.

Thus, the objectives of this study were to estimate the prevalence and identify the factors associated with the worsening of the ambulation capacity at hospital discharge in older people admitted with COVID-19.

2. Materials and Methods

This retrospective study was performed at a referral public hospital for COVID-19 in Sao Paulo, Brazil, and was approved by the local ethics committee (number 4.052.246).

Data were collected from a convenience random sample of the medical records and managed by RedCap. The inclusion criteria were older people aged 60 years or more [29], both sexes and hospitalized with a diagnosis of COVID-19 in the period from April 1, 2020 to November 30, 2020, corresponding to the 1st wave, and from January 1, 2020 to May 31, 2020, 2nd wave. Cases with missing or dubious information in the medical records were excluded.

Sociodemographic data (age, sex and race) and habits (tobacco and alcohol use) were processed. The clinical data consisted of COVID-19 wave (1st and 2nd), hospital outcome (discharge or death), comorbidities (immunosuppression, hematological, neurological, pulmonary, cardiovascular, renal, hepatic, systemic arterial hypertension, diabetes mellitus, obesity and dyslipidemia), length of hospital stay and intensive care unit stay, use of mechanical ventilation. The main outcome was the ambulation capacity before COVID-19 and at the hospital discharge. Ambulation capacity is evaluated and registered at the medical record by the physiotherapy team as a routine. Especially for this study, ambulation capacity prior to COVID-19 infection was assessed through the patient report from his relatives.

Ambulation capacity classification was adapted from Mehrholz et al. [30]. In order to decrease the number of categories, we grouped the following classification:

i. Independent ambulator: Individual can ambulate independently on flat or uneven surfaces, stairs and uneven slopes. This classification includes the categories "independent ambulator only on a flat surface" and "independent ambulator";
ii. Dependent ambulator: Individual requires manual contact of at most one person while ambulating on level surfaces to prevent falls; hand contact consists of continuous or intermittent touch to aid balance or coordination. This classification includes the categories "level III physical assistance-dependent ambulator" and "level I physical assistance-dependent ambulator and supervision-dependent ambulator";
iii. Nonfunctional ambulator: Requires maximum help with the need for assistive technology.

The ambulation capacity at the hospital discharge were divided in two groups, according to their evolution: a) "the same" (ambulation capacity did not change during hospitalization); and b) "worse"

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(independent ambulator previous COVID-19 became dependent or non-functional ambulator; or dependent ambulator previous COVID-19 became non-functional ambulator at the hospital discharge).

Data analysis

Statistical analysis was performed using Stata 16. Data distribution was analyzed through the Shapiro-Wilk statistic. Data did not follow a normal distribution, thus median and interquartile ranges were used for the continuous variables. Frequency (number and percentage) was presented for the nominal variables. The prevalence of the impairment of ambulation capacity at hospital discharge was estimated by confidence interval. Sociodemographic and clinical characteristics were presented according to the ambulation capacity classification before COVID-19. The chi-squared test was used to verify the association between ambulation capacity before COVID-19 and in-hospital death as well as the ambulation capacity evolution (the same or worse) at hospital discharge.

Bivariate logistic regression analysis was calculated for each independent variable with the impairment of ambulation capacity at hospital discharge. For the multivariate regression model, sociodemographic and clinical variables with p<0.20 were included and a correlation matrix was performed to one of the pair of highly correlated variables for the multivariate regression (length of hospital stay and length of intensive care unit stay). Finally, a multivariate regression model adjusted for sex, race, tobacco use, obesity, dyslipidemia and neurological diseases was built to identify possible predictors for reduced ambulation capacity at the hospital discharge. We adopted a significance level of 0.05.

3. Results

3.1. Older people Hospitalized with COVID-19

Data from 429 older people hospitalized with COVID-19 were randomly collected from the medical records. Mean age of the older people included in this study was 68 (63-74) years, most were male (60.1%, n=258), 32.0% (n=136) were brown and 33.6% (n=143) were black. Before COVID-19 infection, 67.4% (n=289) of the older people were classified as independent ambulators, 15.8% (n=68) as dependent ambulators and 16.8% (n=72) as non-functional ambulators.

In hospital death occurred in 187 (43.6%) of patients. Patients who died during hospitalization had worse ambulation capacity prior to COVID-19 (OR: 2.6; CI95% 1.7 – 4.9 p<0.001).

Among the 242 (56.4%) who were discharged, 42.1% (n=102) maintained the same level of ambulation as before COVID-19 and 57.9% (n=140) suffered reduced ambulation capacity (Flowchart 1). Hence, the prevalence of the impairment of ambulation capacity at the hospital discharge was 57.9% (CI95%: 51.4 - 64.1%).

Age, race, tobacco use, neurological diseases, use of invasive mechanical ventilation, in-hospital death and wave had an association with the classification of ambulation capacity prior to COVID-19 (Table 1).

Table 1. Sociodemographic and clinical characteristics of the older people according to their functionality at the pre-admission assessment.

Sociodemographic and clinical characteristics		Ability to walk before hospital admission				
		Independent Ambulator n= 289 (67.4%)	Dependent Ambulator n= 68 (15.8%)	Non-functional Ambulator n= 72 (16.8%)	Total n = 429 (100%)	p^{x2}
Age (years)	60-69	172 (69.9)	32 (13.0)	42 (17.1)	246	***0.046***
	70-79	95 (68.8)	24 (17.4)	19 (13.8)	138	
	80 or older	22 (48.9)	12 (26.7)	11 (24.4)	45	
Sex	Woman	113 (66.1)	27 (15.8)	31 (18.1)	171	*0.828*
	Man	176 (66.2)	41 (15.9)	41 (15.9)	258	
Race	White	91 (52.3)	20 (13.7)	35 (24.0)	146	***0.015***

	Brown	88 (64.7)	26 (19.1)	22 (16.2)	139	
	Black	108 (75.5)	21 (14.7)	14 (9.8)	143	
Habits	Tobacco	62 (67.5)	12 (15.2)	5 (6.3)	79	***0.016***
	Alcoholic Beverage	8 (72.7)	2 (18.2)	1 (9.1)	11	*0.782*
Comorbidity	Immunosuppression	30 (69.8)	9 (20.9)	4 (9.3)	43	*0.299*
	Hematologic	3 (75.0)	1 (25.0)	-	4	*0.629*
	Neurologic	10 (41.7)	8 (33.3)	6 (25.0)	24	***0.015***
	Pulmonary	20 (65.3)	5 (17.9)	5 (16.8)	30	*0.992*
	Cardiovascular	62 (63.26)	17 (17.35)	16 (19.39)	95	*0.818*
	Renal	8 (80.0)	2 (20.0)	-	10	*0.355*
	Hepatic	4 (80.0)	1 (20.0)	-	5	*0.599*
	Systemic Arterial Hypertension	153 (67.7)	40 (17.7)	33 (14.6)	226	*0.302*
	Diabetes Mellitus	111 (70.3)	29 (18.3)	18 (11.4)	158	*0.060*
	Obesity	49 (68.1)	15 (20.8)	8 (11.1)	72	*0.221*
	Dyslipidemia	37 (77.1)	6 (12.5)	5 (10.4)	48	*0.190*
Hospitalization (> 20 days)		118 (66.3)	36 (22.2)	24 (13.5)	178	*0.059*
Intensive care unit (> 11 days)		135 (65.2)	38 (18.4)	34 (16.4)	207	*0.332*
Invasive mechanical ventilation		265 (65.59)	57 (14.11)	82 (20.30)	404	***0.001***
In-hospital death		106 (64.17)	31 (13.37)	50 (22.46)	187	*0.684* ***<0.001***
COVID-19 wave	1st	107 (59.1)	22 (12.2)	52 (28.7)	181	
	2nd	182 (73.4)	46 (18.5)	20 (8.1)	248	***<0.001***

Abbreviation: x^2 = *chi square.*

3.2. Ambulation capacity at hospital discharge

Table 2 shows that 105 (24.5%) individuals classified as independent and 35 (8.2%) individuals classified as dependent ambulator prior to COVID-19 had reduced ambulation capacity at hospital discharge. There was a significant difference between the level of ambulation capacity before COVID-19 and at hospital discharge ($\chi 2 = 50.69$, df = 6, $p < 0.001$), as shown in Table 2 below. In hospital deaths in the independent ambulators, dependent ambulators and non-functional ambulators were 36.7% (n=106), 45.6% (n=31) and 69.4% (n=50), respectively. The proprotion of reduced ambulation capacity of the independent ambulators and dependent ambulators were 36.3% (n=105), and 51.;5% (n=35), respectively. Non-functional ambulators did not change their ambulation capacity at the hospital discharge.

Table 2. Ambulatory capacity before COVID-19, in-hospital death and reduced ambulation capacity at hospital discharge.

Ability to walk before hospitalization	**In-hospital Death n = 187 (43.6%)**	**At Hospital Discharge n = 252 (57,4%)**		**Total**	
		Same ambulation capacity n = 102 (23.81%)	**Worse ambulation capacity n = 140 (32.6%)**	**n = 429**	**p**
Independent Ambulator (n=289)	106 (24.7)	78 (18.2)	105 (24.5)	289 (67.4)	*<0.001*x^2
Dependent Ambulator (n=68)	31 (7.2)	2 (0.5)	35 (8.2)	68 (15.9)	
Non-Functional Ambulator (n=72)	50 (11.7)	22 (5.1)	--	72 (16.8)	

Abbreviation: χ^2 = *chi square.*

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Table 3 shows the demographic and clinical characteristics of the older people who were discharged from the hospital (n=242). The median age of the survivors was 67 years (63-73 interquartile range), and 52.9% (n=128) were male. Most of the older people (57.9%, 95% CI: 51.4 - 64.1%) had reduced ambulation capacity at the hospital discharge. Table 3 also presents the distribution and bivariate regression of demographic and clinical characteristics related to the ambulation capacity change at hospital discharge. The factors associated with reduced ambulation capacity were male sex, brown or black race, neurological disease, dyslipidemia, obesity, length of hospital stay higher than 20, intensive care stay higher than 11 days, being dependent or non-functional ambulator prior to COVID-19 and hospitalization during the second wave.

Table 3. Distribution and bivariate regression for the ambulation capacity change at hospital discharge (n=242).

Demographic and clinical characteristics		**Ambulation capacity at hospital discharge**			
		Same n= 102 (42.1%)	**Worse n= 140 (57.9%)**	**OR (CI95%)**	***p***
Age (years)	**60-69**	61 (42.9)	81 (57.1)	Ref	
	70-79	35 (44.3)	44 (55.7)	1.0 (0.5 - 1.6)	*0.847*
	80 years or older	6 (28.6)	15 (71.4)	1.8 (0.7 - 5.1)	*0.217*
Sex	Women	57 (50.0)	57 (50.0)	Ref	
	Man	45 (35.2)	83 (64.8)	**1.8 (1.1 - 3.1)**	***0.020***
Color/Race	White	47 (58.8)	33 (41.2)	Ref	
	Brown	27 (33.3)	54 (66.7)	**2.8 (1.5 - 5.4)**	***0.001***
	Black	27 (34.6)	51 (65.4)	**2.7 (1.4 – 5.1)**	***0.003***
Habits	Tobacco	13 (30.9)	29 (69.1)	**1.7 (0.8 - 3.5)**	***0.124***
	Alcoholic beverage	–	4 (100.0)	---	---
Comorbidities	Immunosuppression	9 (36.0)	16 (64.0)	1.3 (0.6 - 3.1)	*0.512*
	Hematologic	1 (50.0)	1 (50.0)	0.7 (0.1 - 11.7)	*0.822*
	Neurologic	3 (721.4)	11 (78.6)	**2.8 (0.7 - 10.3)**	***0.120***
	Pulmonary	9 (56.3)	7 (43.7)	0.5 (0.2 - 1.5)	*0.243*
	Cardiovascular	29 (46.0)	34 (54.0)	0.8 (0.4 - 1.4)	*0.468*
	Renal	2 (33.3)	4 (66.7)	1.5 (0.3 - 8.2)	*0.660*
	Hepatic	1 (33.3)	2 (66.7)	1.4 (0.1 - 16.3)	*0.757*
	Systemic Arterial Hypertension	62 (44.9)	76 (55.1)	0.7 (0.4 - 1.3)	*0.314*
	Diabetes Mellitus	42 (42.4)	57 (57.6)	1.0 (0.6 - 1.6)	*0.942*
	Obesity	12 (30.8)	27 (69.2)	**1.8 (0.8 - 3.7)**	***0.119***
	Dyslipidemia	4 (19.1)	17 (80.9)	**3.4 (1.1 - 10.4)**	***0.033***
Hospitalization (> 20 days)		32 (28.3)	81 (71.7)	**2.9 (1.7 – 5.0)**	***<0.001***
Intensive care unit (> 11 days)		29 (19.0)	71 (71.0)	**1.9 (1.1 – 3.4)**	***0.027***
Invasive mechanical ventilation		91 (43.1)	120 (56.9)	0.6 (0.3 – 1.5)	*0.211*
Ambulation capacity before COVID-19	Independent Ambulator	78 (42.6)	105 (57.4)	Ref	
	Dependent Ambulator	2 (5.4)	35 (94.6)	**13.0 (3.0 - 55.6)**	***0.001***
2nd wave		28 (26.4)	106 (73.6)	**5.2 (3.0 - 9.1)**	***<0.001***

Abbreviation: ref = reference; OR = odds ratio; CI = 95% confidence interval; p = probability of significance.

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Table 4 shows the predictors for reduced ambulation capacity at hospital discharge. The worsening of the ambulation capacity was independent of sex, race, tobacco use, obesity, dyslipidemia and neurological diseases, but was associated with hospital stay higher than 20 days (OR: 3.5; CI95%: 1.7 - 7.3; p = 0.001), being dependent ambulator before COVID-19 (OR: 11.3; CI95%: 1.4 - 52.7; p=0.002) and hospitalization at the 2nd wave (OR: 4.8; CI95%: 2.1 - 11.1; p<0.001).

Table 4. Logistic regression adjusted for the ambulation capacity evolution at hospital discharge (n= 214).

Demographic and clinical characteristics		Ambulation capacity at hospital discharge OR ($CI_{95\%}$) *p*	
Gender	Male	1.7 (0.9 – 3.6)	*0.114*
Color/Race	White	Ref	
	Brown	1.7 (0.7 – 4.4)	*0.203*
	Black	1.1 (0.4 – 2.7)	*0.925*
Tobacco Use		0.7 (0.3 - 1.9)	*0.603*
Obesity		1.2 (0.4 - 3.4)	*0.770*
Dyslipidemias		1.3 (0.3 - 5.6)	*0.741*
Neurological Diseases		3.8 (0.3 - 46.9)	*0.293*
Hospitalization > 20 days		**3.5 (1.7 – 7.3)**	***0.001***
Ambulation capacity before hospital admission	Independent Ambulator	Ref	
	Dependent Ambulator	**11.3 (1.4 - 52.7)**	***0.002***
2nd wave		**4.8 (2.1 – 11.1)**	***<0.001***

Abbreviation: OR = odds ratio; CI = 95% confidence interval.

4. Discussion

The prevalence of the worsening in the ambulation capacity of older adults hospitalized due to severe COVID-19 was 57.9%. The factors associated with the worsening in the ambulation capacity at hospital discharge were hospital stay higher than 20 days, worse ambulation capacity before COVID-19, and hospitalization at the 2nd wave.

Our findings concerning the worsening in ambulation capacity are consistent with studies in which acute post-covid-19 patients presented with alterations in musculoskeletal and cardiorespiratory function [27,31]. Welch et al. [14] point out that a decline in muscle trophism and function may be common in patients with COVID-19. However, our in-hospital mortality (43.6%) was higher than previously reported (20% to 31%) [8,19,32]. This finding may be related to our data collection site, which was a referral hospital for severe and moderate cases of COVID-19, where only patients with significant clinical worsening were transferred to, often requiring mechanical ventilation.

Our results showed that older adults with hospital stay higher than 20 days presented higher chance to suffer worsening in their ambulation capacity. In our study, the older adults stayed longer in the hospital (median 17 days) than in other studies (with a median hospital stay of 12 days) [10,13]. Indeed, higher serum concentrations of inflammatory cytokines are seen in patients with COVID-19 who require intensive care [14,33] and stay longer in the hospital. This has negative consequences on muscle protein synthesis resulting in a state of anabolic resistance, which requires a higher protein intake to stimulate muscle protein synthesis [14,27].

Worse ambulation capacity prior to COVID-19 (OR: 11.3) was also a predictor of reduced function at discharge. Our results corroborate a study that followed the functional trajectory of older adults among the people who had a mild to moderate disability before admission to the intensive

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care unit. In this study, 39.5% developed a severe disability, and of those who had a severe disability prior to their stay in the intensive care unit, one-third had an intra-hospital death [32,34].

Our results showed that older adults hospitalized during the 2nd wave had a greater influence on the worsening in ambulation capacity (OR: 4.8). We speculate that this finding could be related to the fact that there was a greater number of dependent and non-functional ambulators requiring hospitalization in this period, because of the 1st wave. According to a study conducted by Moura et al. [35] the analysis between the first and second waves in Brazil showed that there was a swift increase rate of cases and deaths in the 2nd wave, and despite social distancing measures being required, they were not respected, inevitably the contamination rate turned out to be higher, which may explain the occurrence of more individuals with worse ambulation capacity prior to COVID-19.

Therefore, older adults with worse ambulation capacity prior to COVID-19 had a worse ambulation prognosis at hospital discharge as well as a higher prevalence of death. A longer hospitalization can cause functional losses, especially in older adults with comorbidities and the need for sedation [19,36], another study showed that frailty and age over 80 years were the main factors associated with functional decline after hospital discharge due to chronic obstructive pulmonary disease [3].

According to Stam et al. [37], post-intensive care effects could be the next public health crisis to face, as at least 20% of patients with COVID-19 require supportive care in intensive care units and approximately 50% of all patients at different ages tend to develop post-intensive care syndrome.

It is known that older adults have exacerbated responses to SARS-COV-2 infection, with muscle damage related to the intensification of myokines' (muscle cytokines) production, resulting in an increased viral invasion of the peripheral and musculoskeletal nervous system with a heightened muscle inflammatory process, which causes symptoms such as fatigue, weakness, muscle atrophy and myalgia [38]. Individuals post-hospitalized due to COVID-19 who were in critical condition are likely to be at greater risk of developing post-Covid syndrome [39] with the persistence of several signs and symptoms, such as chronic pain, that can further affect the recovery process and thus require a longer rehabilitation time [22,27].

Our results reinforce the importance of performing functional assessment and intervention of older adults during hospitalization, especially with regard to the ability to walk. The literature shows that gait speed is an indicator of future adverse health events in the older adult [27]. In addition, hospitalization itself is considered an aggravating factor for functionality, with a negative impact on mobility and daily activities [40].

Finally, only a few studies with a small number of participants have evaluated the impairment of ambulation in adults and older adults hospitalized with COVID-19 [32,40]. Our study contributes to fill this gap in the literature and seeks to understand the functional impact of COVID-19 on the older adult, helping to devise new interventions for post-COVID-19 prevention and rehabilitation related to this population.

5. Conclusions

The older patients who died during hospitalization due to COVID-19 had greater gait impairment prior to hospitalization, and more than half of those who were discharged had worsened gait impairment. The main factors associated with impaired ambulation after hospitalization were a hospital stay longer than 20 days, having impaired gait prior to admission, and being infected by the 2nd wave of COVID-19. Our results suggest the need for interventions aiming to reduce ambulation impairment in hospitalized older people with severe COVID-19, in order to decrease the risk of longer term functional impairment in this population.

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Informed Consent Statement: Informed consent was obtained from all subjects involved in the study.

Conflicts of Interest: The authors declare no conflict of interest.

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