

Frailty and risk of mortality and hospitalization in nursing home residents affected by COVID-19

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Abstract

Coronavirus disease 2019 (COVID-19) is a widespread condition in nursing homes (NHs). However, no research was made regarding frailty in NH residents during COVID-19 pandemic. The aim of this study was to assess whether frailty, assessed by the multidimensional prognostic index (MPI), can predict mortality/hospitalization in COVID-19 NH residents. A Cox's regression analysis was used, reporting the results as hazard ratios (HRs) with 95% confidence intervals (CIs). 1146 NH residents affected by COVID-19 were included (mean age: 86 years; 75.4% females). During the follow-up period, we observed 286 deaths and 239 hospitalizations. Taking those with MPI <0.41 as reference, an MPI \geq 0.50 was associated with a higher risk of death (HR=1.41; 95%CI: 1.07-1.85). Similar results were obtained using the MPI score increase in 0.10 points (HR=1.12; 95%CI: 1.03-1.23). Using hospitalization as outcome, only MPI score as continuous variable was associated with this outcome (HR=1.08; 95%CI: 1.002-1.17). In conclusion, frailty, as assessed by the MPI, was associated with a significant higher risk of mortality and hospitalization in NH residents affected by COVID-19 further indicating the necessity of assessing frailty in NH.

Introduction

Coronavirus disease 2019 (COVID-19) is becoming unstoppable meeting the necessary epidemiological criteria to be declared

a pandemic.¹ Only in 2020, more than 83 million people were affected by COVID-19, with about 2 millions of deaths.¹ The epidemiological data so far indicated that COVID-19 could be considered as a condition typical of older people.²

A particular interest was given to the COVID-19 outbreak in nursing homes (NHs).³⁻⁵ In this setting, in fact, COVID-19 can be considered as a ground zero for several reasons.⁶ First, NHs include people that can be considered per se frail or highly disabled.⁷ Moreover, even if less than 10% of all COVID-19 cases are observed in NH, NH residents and staff accounted for more than one third of the all deaths recorded worldwide.^{8,9}

The multidimensional prognostic index (MPI) is a short- and long-term prognostic mortality index that has been developed and validated in hospitalized and non-hospitalized older patients.¹⁰ The MPI has shown in numerous studies to have very good predictive accuracy and excellent calibration across different settings and clinical situations, being validated and used in over 54,000 older subjects suffering from the most common acute and chronic diseases associated with increased mortality in over 50 national and international scientific studies.¹¹ The MPI is based on information collected through the comprehensive geriatric assessment (CGA) considering different domains.¹²

A version of the MPI has also been developed and validated from the information included in the SVaMA (*Scheda valutazione multidimensionale anziani*), i.e. the official regional CGA tool in Veneto, for the multidimensional assessment of the adult and older persons who require to be admitted to homecare services or NHs.¹³

The data available so far have shown the importance of frailty for prognosis in older individuals with COVID-19,¹⁴⁻¹⁷ but these data are mainly based on community-dwelling and hospitalized older people, whilst COVID-19 is a major problem in NHs.¹⁸ Given this background, the aim of this study was to assess whether frailty, evaluated using the MPI, can predict mortality and hospitalization in NH residents affected by COVID-19.

Materials and Methods

Participants

For the aims of this work, we considered all NH residents in the ULSS 3 'Serenissima', located in an area of 1406 square km in Veneto Region, North-East Italy and with about 650,000 inhabitants. In

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Availability of data and materials: upon reasonable request to the Corresponding author.

Ethics approval and consent to participate: the study was approved by the local Ethical Committee of the ULSS (Unità Locale Socio Sanitaria, i.e., local social and health care system) 3 Serenissima, Venice, Italy.

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this area, 31 NHs hosting approximately 3850 residents are located.

On March, 29th in response to increased local awareness of COVID-19 in NHs, the Veneto Region indicated periodical screening assessments with portable serological tests or nasopharyngeal swabs, every 10 days.¹⁹ The period of which study referred was from 01st March to 16th December 2020.

The study was approved by the local Ethical Committee of the ULSS (Unità Locale Socio Sanitaria, i.e., local social and health care system) 3 Serenissima, Venice, Italy.

COVID-19 diagnosis

A nasopharyngeal swab test with an real-time polymerase chain reaction assays (Copan UTM System, Copan, Italy) for the identification of severe acute respiratory syndrome-related coronavirus 2 infection was administered to all NH residents.

The multidimensional prognostic index

MPI was initially developed in hospital setting¹² and then diffused in other settings, such as primary care¹¹ and NH,²⁰ using adapted versions for these settings. Briefly, in our NHs, the following nine domains, including 55 items, were considered for the construction of the MPI: i) age; ii) sex; iii) main diagnosis; iv) nursing care needs (VIP); v) cognitive status (VCOG), evaluated by the short portable mental status questionnaire (SPMSQ);²¹ vi) pressure sores risk (VPIA), evaluated by the Exton-Smith scale;²² vii) activities of daily living (VADL); and viii) mobility (VMOB) evaluated by the Barthel index;²³ and ix) social support (VSOC).²⁰

For the aims of this work, to calculate the MPI index, we used a weighted sum of each individual domain based on the validation study of the MPI that took as outcome mortality after 1-year.²⁰ The weights used are reported in Table 1.

The *RE*Cursive Partition and *AM*algamation (RECPAM) algorithm²⁴ was used to identify categories of patients at different risks for mortality. This method allows to choose the best points of a continuous variable in determining an outcome, in this case mortality.²² The following cut-offs were estimated for the MPI for mortality prediction: 0-0.41 (low risk), 0.41-0.50 (moderate risk), ≥ 0.50 (severe risk).

Outcomes

The primary outcome of our investigation was mortality. The follow-up period was calculated from the positivity to the nasopharyngeal swab test until the date of death or the last observation made on 16th December 2020. The data regarding mortality are collected routinely as administrative data. Hospitalizations were considered as secondary outcome of our investigation and the time to hospitalization was recorded similarly to time to death. The follow-up period, for both primary and secondary outcome, ranged from 0 to 295 days.

Statistical analysis

Continuous variables were evaluated in term of means and standard deviation (SD), after checking their normality. For categorical relative frequencies (%) were reported. Parametric univariate tests (P-values were referred to Fisher Exact for frequencies and t-Test for means) were used for evaluating possible association according to the MPI groups.

The assessment of the effect of MPI with mortality or hospitalization was made by using a Cox's regression analysis. The results were consequently reported as

hazard ratios (HRs) with their 95% Confidence intervals (95%CI), taking people with a MPI <0.41 as reference. A similar analysis was run modeling MPI as continuous variable (increase in 0.10 points). We also reported the incidence of the outcome of interest, per 1000 persons-days, by MPI groups.

All analyses were performed using the SPSS 21.0 for Windows (SPSS Inc., Chicago, Illinois). All statistical tests were two-tailed and statistical significance was assumed for a P-value <0.05.

Results

Across the 31 NHs included in the territory of ULSS 3 'Serenissima', Venice, Italy, 3850 residents might be hosted. In the period between 01st March and 16th December 2020 and 1233 received a COVID-19 diagnosis in the period of observation. Of them, 87 residents had not sufficient data for the calculation of the MPI, leaving 1146 older NH residents for the aims of this work.

Overall, the 1,146 participants aged a mean of 86 years (SD=8.5, range: 48-105), mainly females (=75.4%). Their mean MPI was 0.42 ± 0.12 (range: 0-1.00). Table 2 summarizes the main baseline characteristics by their MPI categories. No significant differences emerged for the mean age (P=0.29) or for the prevalence of male gender (P=0.41) across the three MPI cate-

gories. People in the MPI ≥ 0.50 category reported significantly higher prevalence in hypokinetic syndrome (P=0.02) than their counterparts with lower MPI values. As expected, people with higher MPI values had worst scores in cognitive, mobility and disability than people with lower scores (P<0.05 for all these comparisons), whilst no significant differences emerged for the social domain (P=0.54) (Table 2).

During the follow-up period, we observed 286 deaths (lethality rate: 25%) and 239 hospitalizations. As reported in Table 2, people in the MPI ≥ 0.50 category reported a significant higher incidence in death mortality than their counterparts, but a similar incidence in hospitalizations (P=0.08).

Figure 1 graphically reported the association between MPI categories and mortality. Taking those with MPI <0.41 as reference (indicating less frail residents) NH residents with an MPI ≥ 0.50 had a significant higher risk of death (HR=1.41; 95%CI: 1.07-1.85; P=0.02). Similar results were evident using MPI as continuous variable since each increase in 0.10 points increased the risk of death of 12% (HR=1.12; 95%CI: 1.03-1.23; P=0.001).

On the contrary, taking those with MPI <0.41 as reference, residents with a value ≥ 0.50 had a similar risk (HR=1.18; 95%CI: 0.88-1.59; P=0.26) of hospitalization, even if each increase in 0.10 points in MPI resulted in a significant higher risk of this outcome (HR=1.08; 95%CI: 1.002-1.17; P=0.03).

Table 1. Estimated domain weights used to compute the multidimensional prognostic index for mortality prediction.

Domain	Category	Weights
Age, years	Continuous	0.00331
Sex	Female (reference)	0
	Male	0.31464
Main diagnosis	Dementia (reference)	0
	Cancer	2.22093
	Hip fracture	-0.65872
	Stroke	0.20318
	Cardiovascular disease	0.38855
	Respiratory disease	0.39394
	Neurological disorder	-0.14409
	Immobilization syndrome	0.43482
Nursing care needs	VIP	0.02741
	Other diagnosis	0.69991
Cognitive status	VCOG	0.01772
Pressure sore risk	VPIA	0.02104
Activities of daily living	VADL	0.01098
Mobility	VMOB	0.02617
Social support	VSOC	0.0007367

VIP, nursing care needs; VCOG, cognitive functions; VPIA, pressure sores risk; VADL, activities of daily living; VMOB, mobility; VSOC, social support network.

Discussion and Conclusions

In this retrospective study, including 1146 older NH residents affected by COVID-19, we found that frailty, as assessed by higher MPI values, was associated with a significant higher risk of mortality. The association between frailty and higher risk of hospitalization was detected only using MPI as continuous variable,

indicating that probably only extreme values are associated with a higher risk for this negative outcome.

In several countries, NHs and long-term care facilities reported a high prevalence of COVID-19 infection, a high rate of hospitalization and mortality, since the infection affected the most vulnerable and frail population in our society.^{25,26} The presence of COVID-19 in NH was defined as a 'ground zero' for COVID-19 epidemic, due to its epi-

demiological and clinical impact.¹⁸ As reported in our research, about 10% of NH residents were affected by COVID-19 infection with a lethality rate of 33%, similar to other works.^{18,25} It is likely that these findings are motivated by numerous reasons.

First, NH residents are typically older adults with high presence of chronic illness, disability and frailty, being particularly susceptible to severe complications and finally mortality from COVID-19.²⁵ Indeed, in the present study over 66% of NH residents showed a moderate or high grade of frailty, as assessed by the MPI. Moreover, we should consider that, differently from a hospital, a NH is someone's home.¹⁸ In this regard, residents may live in close quarters with one another, so it can be quite challenging to move or quarantine residents once they are sick or affected by asymptomatic forms of COVID-19.¹⁸ Moreover, NH staff move from room to room assisting residents, thus providing a further issue in limiting the spread of infections.^{18,25} Due to its epidemiological importance, to stratify prognosis in NH residents can be considered as both clinical and public health priorities, particularly for appropriately caring the individual NH residents and for better using hospital and Intensive Care Unit (ICU) resources.²⁷ In this regard, MPI is associated with a higher risk of hospitalization, too, even if these findings are weaker than those reported for mortality.

The topic of prognostic value of frailty in COVID-19 in older people is of valuable importance. In this regard, the most important study about this topic reported that, among 1564 hospitalized patients, frailer patients (identified as higher clinical frailty

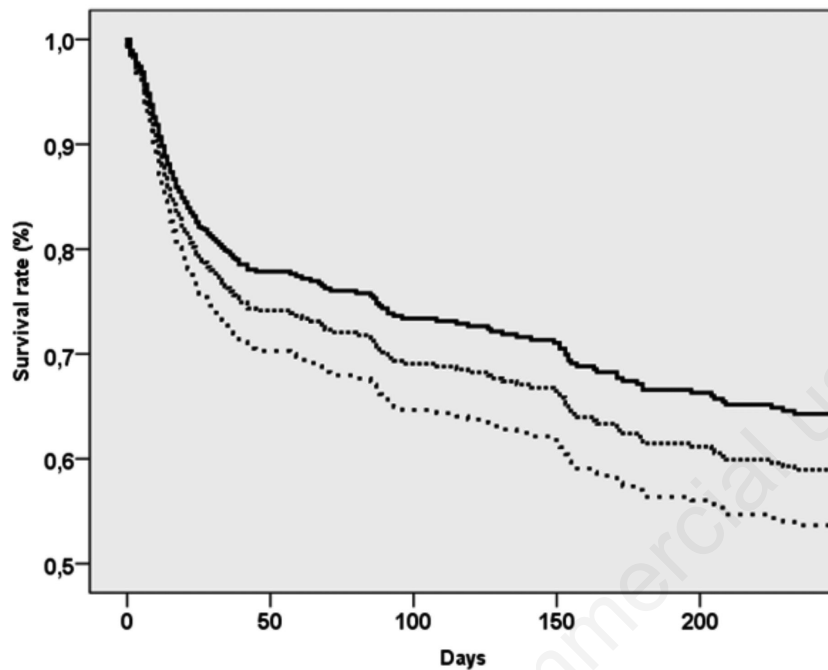


Figure 1. Survival curves by multidimensional prognostic index categories. From the high to low: MPI-SVaMA <0.41; MPI-SVaMA 0.41-0.49; MPI-SVaMA >0.50

Table 2. Descriptive characteristics by multidimensional prognostic index values at the baseline evaluation.

Item	MPI-SVaMA <0.41 (n=571)	MPI-SVaMA 0.41-0.49 (n=288)	MPI-SVaMA >0.50 (n=287)	P-value
Age (mean, SD)	85.4 (8.7)	86.4 (8.1)	85.9 (7.9)	0.29
Male sex (%)	22.9	24.7	27.8	0.41
Dementia (%)	38.9	34.7	40.1	0.45
Hypokinetic syndrome (%)	15.1	19.2	22.9	0.02
VIP (mean, SD)	3.1 (5.8)	2.9 (4.8)	3.0 (5.0)	0.89
VCOG (mean, SD)	6.0 (2.9)	6.8 (2.8)	7.5 (2.7)	0.01
VPIA (mean, SD)	4.4 (5.8)	4.3 (5.6)	4.7 (5.6)	0.73
VADL (mean, SD)	44 (14)	49 (13)	51 (13)	0.02
VMOB (mean, SD)	23 (10)	33 (9)	33 (10)	0.02
VSOC (mean, SD)	239 (11)	239 (6)	239 (7)	0.54
Incidence of death (per 1000 persons-day) (95%CI)	2.9 (2.4-3.5)	3.9 (3.1-4.9)	4.1 (3.3-5.1)	0.01
Incidence of hospitalization (per 1000 persons-day) (95%CI)	2.4 (2.0-2.9)	2.9 (2.3-3.7)	3.1 (2.8-3.8)	0.08

MPI-SVaMA, multidimensional prognostic index-scheda valutazione multidimensionale anziani; SD, standard deviation; VIP, nursing care needs; VCOG, cognitive functions; VPIA, pressure sores risk; VADL, activities of daily living; VMOB, mobility; VSOC, social support network; CI, confidence interval.

scale values) experienced a higher risk of mortality than their counterparts with lower values.¹⁴ Other studies, including more limited sample sizes, substantially confirmed these findings.^{15,16} Even if these studies advanced our knowledge regarding the importance of frailty as prognostic factor in older people affected by COVID-19, these researches included only community-dwelling or hospitalized older people, whilst, as mentioned before, the epidemiological importance of COVID-19 in NH is of critical importance. In this regard, even if less than 10% of all COVID-19 cases are observed in NH, NHs and assisted living facilities residents and staff accounted for more than one third of the all deaths recorded.^{8,9} We believe that our findings could be of importance, *e.g.*, to facilitate clinical decisions on better using the hospital and ICU resources. Our study, in fact, may indicate that frailer people died more frequently, in agreement with the most recent NICE guidelines indicating the need of assessing frailty status before making clinical decisions in older people.

At the same time, our research is one of the first assessing the potential role of MPI (and therefore frailty) in predicting the risk of hospitalization in NH residents. It should be noted that in our experience about a quarter of all NH residents affected by COVID-19 infection are admitted to hospital, even if the hospitalization of frail and very frail older people seem not to be any benefit in survival or quality of life.²⁸ Our research indicated that the propensity of physicians working in NHs is to send to the hospitals very frail people, even if the same people suffered on higher risk of mortality. Altogether, our findings still underline the necessity to better stratify the prognosis of NH residents.

The findings of our study must be interpreted within its limitations. First, the retrospective nature of this research that is, however, common in COVID-19 research since this condition is relatively new. Second, the multidimensional evaluation of the NH residents was not made concomitant to the diagnosis of COVID-19, but before this event with a variable period with the diagnosis of COVID-19 infection that may further affect our results. However, we believe that it can be included among the limitations of a retrospective study. Finally, no information on the therapy used was available, even if this information can reduce mortality in NH residents.²⁹

In conclusion, our study showed that frailty, as assessed by the MPI, was associated with a significant higher risk of mortality among NH residents affected by COVID-19 infection. Extreme values of

MPI are associated with a higher risk of hospitalization. We believe that our findings are of importance for finally introducing prognostic factors derived from comprehensive geriatric assessment in daily clinical practice in NH, a dimension often neglected in geriatric medicine.

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