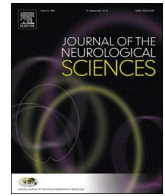




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## Frailty and SARS-CoV-2 infection. A population-based study in a highly endemic village



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### 1. Clinical/scientific note

Frailty is a geriatric state of reduced functional reserve and vulnerability that represent a major public health problem because of its relationship with systemic diseases, increased risk for hospitalization, institutionalization, and all-cause mortality [1]. On the other hand, the SARS-CoV-2 pandemic has affected almost 27 million people worldwide [2]. Therefore, it is likely that many individuals with frailty get exposed to this novel virus. Some reports argued that frail individuals may develop more severe COVID-19 disease [3,4]. However, data is inconsistent as it has also been suggested that there may be a sort of resilience by which certain frail subjects remain asymptomatic [5]. To our knowledge, there are no studies addressing if frail subjects are more prone to acquire SARS-CoV-2 infection in endemic communities, independently of risk factors inherent to aging or other comorbidities.

The Atahualpa Project is an ongoing population-based cohort study designed to assess factors influencing the burden of neurological and cardiovascular diseases in rural Ecuador. We prospectively assessed the frail status in community-dwelling older adults by means of door-to-door surveys conducted every two years, as part of a study attempting to assess prevalence and correlates of frailty in this population [6,7]. The last round of frailty assessment was on December 2019. Taking the unique opportunity of this well-established cohort, we aimed to assess the relationship between previously diagnosed frailty and SARS-CoV-2 infection in the above-mentioned population.

Frailty was evaluated by the use of the Edmonton Frailty Scale (EFS), a validated field instrument that consists of 11 items including cognition, general health status, functional independence, social support, medication use, nutrition, mood, incontinence, and balance/mobility [8]. The maximum score is 17 points, with individuals being classified into robust (0–4 points), pre-frail (5–6 points) and frail ( $\geq 7$  points).

Information on frailty status was evaluated in the light of the results of a door-to-door survey aimed to assess SARS-CoV-2 seropositivity in the population of Atahualpa (study conducted on May 2020), by means of a lateral flow-based antibody testing (BIOHIT Health Care Ltd.,

Cheshire, UK) [9,10]. Multivariate models were fitted to assess the independent association between frailty status and SARS-CoV-2 seropositivity, after adjusting for demographics, cardiovascular risk factors and the presence of SARS-CoV-2-related symptomatology. The study and the informed consent form were approved by the I.R.B. of our Institution.

A total of 319 out of 325 individuals aged  $\geq 60$  years that were actively enrolled in the Atahualpa Project as of May 2020, were included in this study. The remaining six declined the practice of SARS-CoV-2 antibody testing (coverage 98.2%).

The mean age of the 319 participants was  $70.5 \pm 7.8$  years, 187 (59%) were female, 240 (75%) had primary school education only, 12 (4%) were current smokers, 74 (23%) had a body mass index  $\geq 30$  kg/m<sup>2</sup>, 21 (7%) had poor physical activity, 13 (4%) had a poor diet, 134 (42%) had blood pressure  $\geq 140/90$  mmHg, 92 (29%) had fasting glucose  $\geq 126$  mg/dL, 45 (14%) had total cholesterol levels  $\geq 240$  mg/dL, and 130 (41%) had SARS-CoV-2-related symptomatology. According to the EFS, 183 (57%) individuals were robust, 76 (24%) were pre-frail, and the remaining 60 (19%) were frail. A total of 141 (44%) individuals were seropositive to SARS-CoV-2 (including 117 who were reactive to both IgM and IgG, seven to only IgM, and 17 to only IgG). The Kappa coefficient for interrater agreement was 0.91 for seropositivity to SARS-CoV-2.

In univariate analyses, frail and pre-frail individuals were older, more often female, and had more often primary school education only, a body mass index  $\geq 30$  kg/m<sup>2</sup>, worse physical activity, and blood pressure levels  $\geq 140/90$  mmHg than their robust counterparts. In contrast, the single covariate significantly associated with SARS-CoV-2 seropositivity was hypercholesterolemia. Several differences in the above-mentioned covariates were observed when frail, pre-frail and robust individuals were stratified according to whether they have SARS-CoV-2 antibodies or not. However, the single covariate remaining significant at the three different levels of frailty status was the presence of SARS-CoV-2-related symptomatology among seropositive individuals *versus* their seronegative counterparts (Table 1). Also in univariate analysis, there was no association between frailty status and SARS-CoV-

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**Table 1**Characteristics of frail, pre-frail and robust individuals aged  $\geq 60$  years across categories of SARS-CoV-2 serological status (univariate analyses).

	Frail (n = 60)			Pre-frail (n = 76)			Robust (183)		
	SARS-CoV-2 positive (n = 27)	SARS-CoV-2 negative (n = 33)	p value	SARS-CoV-2 positive (n = 38)	SARS-CoV-2 negative (n = 38)	p value	SARS-CoV-2 positive (n = 76)	SARS-CoV-2 negative (n = 107)	p value
Age, years (mean $\pm$ SD)	74 $\pm$ 8.4	78.8 $\pm$ 9.2	0.041*	71.5 $\pm$ 7	70.7 $\pm$ 9.4	0.675	67.9 $\pm$ 5.7	68.8 $\pm$ 5.9	0.304
Female, n (%)	25 (93)	28 (85)	0.353	25 (66)	28 (74)	0.454	34 (45)	48 (45)	0.987
Primary school education, n (%)	26 (96)	26 (79)	0.047*	31 (82)	28 (74)	0.409	55 (72)	73 (68)	0.547
Current smoker, n (%)	0	0	...	1 (3)	0	...	4 (5)	7 (6)	0.719
Body mass index $\geq 30$ kg/m <sup>2</sup> , n (%)	11 (41)	8 (24)	0.172	10 (26)	10 (26)	1.000	13 (17)	21 (20)	0.666
Poor physical activity, n (%)	2 (7)	9 (27)	0.048*	2 (5)	3 (8)	0.644	1 (1)	4 (4)	0.322
Poor diet, n (%)	2 (7)	0	...	0	2 (5)	...	2 (3)	7 (6)	0.228
Blood pressure $\geq 140/90$ mmHg, n (%)	16 (59)	19 (58)	0.895	16 (42)	19 (50)	0.489	24 (32)	41 (38)	0.348
Fasting glucose $\geq 126$ mg/dL, n (%)	12 (44)	10 (30)	0.258	14 (37)	10 (26)	0.324	18 (24)	28 (26)	0.703
Total cholesterol $\geq 240$ mg/dL, n (%)	7 (26)	3 (9)	0.081	11 (29)	4 (11)	0.044*	9 (12)	11 (10)	0.739
SARS-CoV-2 related symptoms, n (%)	16 (59)	7 (21)	0.003*	30 (79)	4 (11)	< 0.001*	64 (84)	9 (8)	< 0.001*

\* Statistically significant result.

**Table 2**

Fully-adjusted logistic regression model showing lack of independent association between frailty status and SARS-CoV-2 seropositivity in community-dwelling older adults living in Atahualpa (rural Ecuador).

Frailty status	Odds ratio	95% C.I.	p value
SARS-CoV-2 seropositivity	1.48	0.72–3.06	0.291
Age	1.09	1.05–1.13	< 0.001*
Female gender	3.58	2.04–6.27	< 0.001*
Primary school education	1.27	0.68–2.36	0.451
Current smoker	0.51	0.60–2.36	0.537
Body mass index $\geq 30$ kg/m <sup>2</sup>	1.83	0.96–3.47	0.066
Poor physical activity	2.39	0.76–7.55	0.135
Poor diet	0.61	0.15–2.40	0.476
Blood pressure $\geq 140/90$ mmHg	1.39	0.82–2.39	0.224
Fasting glucose $\geq 126$ mg/dL	1.56	0.87–2.79	0.137
Total cholesterol $\geq 240$ mg/dL	1.68	0.79–1.56	0.175
SARS-CoV-2-related symptomatology	0.92	0.45–1.91	0.840

\* Statistically significant result.

2 seropositivity ( $p = 0.265$ ). In addition, a fully-adjusted logistic regression model showed no independent association between frailty status and SARS-CoV-2 positivity (Table 2). Covariates remaining significant in this multivariate model were increasing age and being female.

This study shows that frail and pre-frail community-dwelling older adults are not more susceptible to acquire SARS-CoV-2 infection even if living in a highly endemic milieu [10]. Proper interpretation of these results must take into account that study participants were taken from the community and not from long-term care facilities, where the scenario may be different because individuals in the latter do not often engage in strong-moderate physical activity, are often medicated with sedative drugs and live in close – frequently crowded – environments [5]. Further studies are needed to confirm our findings.

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## Declaration of Competing Interest

The authors have no financial interest related to this study.

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