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## Original article

## Physical decline and cognitive impairment in frail hypertensive elders during COVID-19

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## ABSTRACT

**Background:** Hypertension is common in older adults and its incidence increases with age. We investigated the correlation between physical and cognitive impairment in older adults with frailty and hypertension.

**Methods:** We recruited frail hypertensive older adults during the COVID-19 pandemic, between March 2021 and December 2021. Global cognitive function was assessed through the Montreal Cognitive Assessment (MoCA), physical frailty assessment was performed following the Fried criteria, and all patients underwent physical evaluation through 5-meter gait speed test.

**Results:** We enrolled 203 frail hypertensive older adults and we found a significant correlation between MoCA score and gait speed test ( $r: 0.495$ ;  $p < 0.001$ ) in our population. To evaluate the impact of comorbidities and other factors on our results, we applied a linear regression analysis with MoCA score as a dependent variable, observing a significant association with age, diabetes, chronic obstructive pulmonary disease (COPD), and gait speed test.

**Conclusions:** Our study revealed for the first time a significant correlation between physical and cognitive impairment in frail hypertensive elderly subjects.

## 1. Background

Frailty is a biological syndrome of decreased physiological reserves with incremented vulnerability to stressors and its prevalence among older adults has been estimated at ~10% [1]. Hypertension is a prevailing comorbidity in older adults and its incidence increases with age [2,3]. Vascular dementia (VD) and Alzheimer's Disease (AD) are among the main causes of dementia and/or mild cognitive impairment (MCI) in older adults with or without frailty [4]. Despite these shreds of evidence and despite the emerging interest in geriatric conditions, the actual correlation between physical and cognitive impairment in physically frail patients remains unclear.

Cognitive impairment is very common in older populations, and its prevalence increases with age; in fact, dementia is a progressive and

irreversible deterioration of cognitive function that is typical of older adults [5]. Similarly, physical impairment is often diagnosed in older adults [6]. Hence, the importance to correlate these geriatric conditions might be useful to set the best pharmacological, clinical, and interventional approach to reduce adverse outcomes and to improve the quality of life of these subjects.

Thus, in our study we investigated the correlation between physical and cognitive impairment in older adults with frailty and hypertension.

## 2. Methods

## 2.1. Patients and study design

We investigated the relationship between cognitive and physical

**Abbreviations:** CKD, Chronic Kidney Disease; COPD, Chronic Obstructive Pulmonary Disease; AFib, Atrial Fibrillation; MCI, Mild Cognitive Impairment; MMSE, Mini-Mental State Examination; MoCA, Montreal Cognitive Assessment; VD, Vascular Dementia; AD, Alzheimer's Disease.

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impairment in a frail population of hypertensive older adults during the COVID-19 pandemic. We examined frail outpatient subjects (ambulatory care) at ASL Avellino, Italy, between March 2021 and December 2021 (NCT04962841). Inclusion Criteria were: age  $\geq 65$  years; frail status; a previous diagnosis of hypertension; Montreal Cognitive Assessment (MoCA) Score  $< 26$ . Exclusion Criteria were: age  $< 65$  years; absence of frail status; absence of hypertension; left ventricular ejection fraction  $< 25\%$ ; previous myocardial infarction or previous revascularization with primary percutaneous coronary intervention (PPCI) and/or coronary by-pass grafting.

## 2.2. Frailty assessment

Physical frailty assessment was performed following the Fried criteria [7,8]; a diagnosis of frailty status was made with at least three of the following five criteria:

- Weight loss (unintentional loss  $\geq 4.5$  kg in the past year);
- Weakness (handgrip strength in the lowest 20% quintile at baseline, adjusted for sex and body mass index);
- Exhaustion (poor endurance and energy, self-reported);
- Slowness (walking speed under the lowest quintile adjusted for sex and height);
- Low physical activity level (lowest quintile of kilocalories of physical activity during the past week).

All patients underwent physical evaluation through the 5-meter gait speed test [8]. Gait speed is the most common test to measure the time required to walk a short distance at a comfortable pace. Furthermore, it is one of the most used tests to screen frailty and identify high-risk older adults in need of further evaluation. The gait speed test can quantify impairments in lower-extremity muscle function, neurosensory, and cardiopulmonary function [9–12]. Furthermore, a recent paper demonstrated that the brain networks are related with gait control and vary with walking speed; hence, gait control in aging requires a distributed network including regions for emotional control that are recruited in challenging walking conditions [13].

## 2.3. Cognitive evaluation

Global cognitive function was assessed through the MoCA test [8, 14], which is freely available and can be used, reproduced, and distributed by Universities, Foundations, Health Professionals, Hospitals, and Public Health Institutes. We preferred the MoCA test to the Mini-Mental State Examination (MMSE) because the first one has been proved to be more specific to evaluate cognitive domains (attention, concentration, memory, language, calculation, orientation, and executive functions) and is widely considered the gold standard test to detect mild cognitive impairment (MCI) [15,16]. Additionally, MMSE scores have been shown to be influenced by demographic variables such as age and years of education: subjects with higher education levels have better results than subjects with lower levels, and older adults show worst performances in MMSE scores that are age-dependent [17]. Cognitive impairment was defined by MoCA Score  $< 26$ , as previously reported [15,18].

## 2.4. Ethical considerations

The study was carried out following the tenets of the Declaration of Helsinki and Good Clinical Practice guidelines. The study protocol was approved by the Bioethics Committee of Campania Nord. All patients, or their legal representatives, provided informed consent and were informed that they could withdraw from the study at any stage.

## 2.5. Statistical analysis

The sample size was calculated using G\*POWER software, assuming a power of 80% and a two-sided alpha level of 0.05, we found that 140 patients were needed to evaluate the primary endpoint of the study. Descriptive statistics, including frequencies and percentages, were used to describe the categorical variables analyses; continuous variables were expressed as mean  $\pm$  standard deviation (SD). Multiple regression models have been used to explore the relationship between MoCA Score and several covariates. All calculations were computed using SPSS 26. A two-sided p value  $< 0.05$  was considered statistically significant.

## 3. Results

312 consecutive patients were evaluated during the COVID-19 pandemic, of which 73 presented no frailty status and 36 were unwilling to provide clinical information (Figure 1). Therefore, 203 frail older adults were successfully enrolled. All frail patients were administered a MoCA test and performed a 5-meter gait speed test at the beginning of the study. The mean age, sex distribution, BMI, and comorbidities are reported in Table 1. The use of diuretics, angiotensin-converting enzyme inhibitors, beta-blockers, and calcium channel blockers is reported in Table 1, as well.

We found a significant correlation between MoCA score and gait speed test ( $r: 0.495$ ;  $p < 0.001$ , Figure 2).

To evaluate the influence of comorbidities and other factors on our results, we performed a multivariate linear regression analysis with MoCA score as a dependent variable (Table 2). We observed a significant impact of age, diabetes, COPD, and 5-meter gait speed test ( $p < 0.001$ ).

## 4. Discussion

The management of frail patients is a health problem of increasing importance worldwide. A recent study determined that markers of physical performance are linked to the current cognitive status and modestly related to cognitive decline [19]. Nevertheless, the authors of that study did not report data on hypertension in the baseline characteristics of their population. Comorbidities such as hypertension play a key role in increasing the risk of mortality, hospitalization, and disability [20]; hence, the main goal to reduce frailty rates and cognitive decline should focus on the care of underlying chronic diseases that are prevalent in elders [21,22]. Indeed, high blood pressure affects  $\sim 75\%$  of people aged over 70 and frailty adds further complexity to the management of blood pressure modifications in later life [23]. In this scenario, our study evidenced a significant correlation between physical and cognitive impairment in frail hypertensive patients. This result is especially interesting because physical capacity and global cognitive function might influence each other in this population; thus, clinical assessment should be implemented. Interestingly, the majority of our patients were women, which is in agreement with the reports of the REPOSI Study on elderly people [24].

Notably, since our data were collected during the COVID-19 pandemic, we need to reckon that this aspect could have influenced cognitive and physical function in frailty, as recently shown by us and others [25–30].

To further confirm our results, we applied a multivariate linear regression analysis to verify the impact of some covariates, using MoCA as a dependent variable. This analysis revealed a significant impact of diabetes, age, COPD, and 5-meter gait speed test (Table 2).

Several limitations warrant consideration: first, the sample size is relatively small, however, we had performed an *a priori* power analysis and the estimated sample size was 140 patients; second, the results would have benefited from a follow-up. Dedicated studies investigating the mechanisms underlying these effects are necessary, and could involve for instance endothelial dysfunction, inflammation, and oxidative stress; however, these experiments are beyond the scope of this

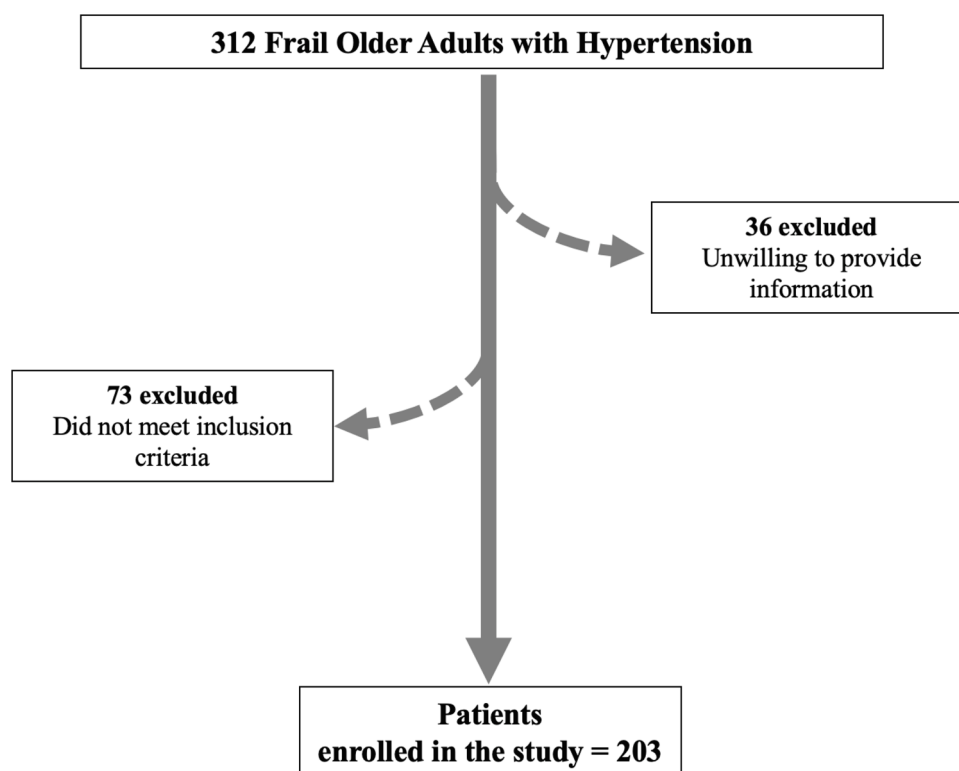
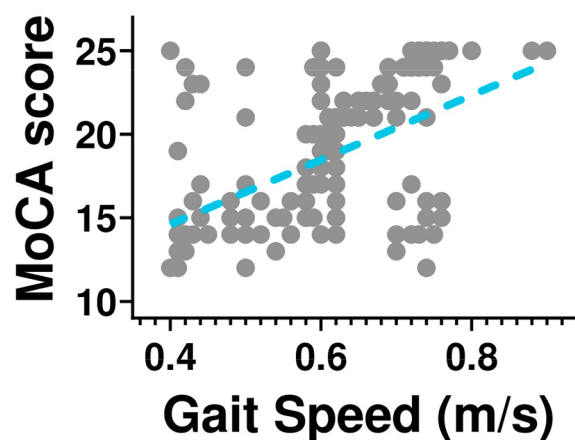


Fig. 1. Study flow chart.

**Table 1**  
Clinical characteristics of our population.

| Parameter                            | Values     |
|--------------------------------------|------------|
| N                                    | 203        |
| Sex (F)                              | 118 (58.5) |
| Age (years)                          | 81.1±7.1   |
| BMI (kg/m <sup>2</sup> )             | 28.8±1.5   |
| SBP (mmHg)                           | 129.5±11.1 |
| DBP (mmHg)                           | 79.3±6.5   |
| Heart rate (bpm)                     | 81.2±7.4   |
| <b>Comorbidities</b>                 |            |
| Diabetes, n (%)                      | 119 (59.0) |
| Hyperlipidemia, n (%)                | 143 (70.5) |
| COPD, n (%)                          | 66 (32.5)  |
| CKD, n (%)                           | 83 (41.0)  |
| Osteoarthritis, n (%)                | 81 (40.0)  |
| AFib, n (%)                          | 47 (23.2)  |
| <b>Laboratory Analyses</b>           |            |
| Plasma glucose (mg/dl)               | 143.4±18.8 |
| Creatinine (mg/dl)                   | 1.0±0.2    |
| <b>Global Cognitive Evaluation</b>   |            |
| MoCA                                 | 18.7±4.2   |
| <b>Fried Criteria</b>                |            |
| Weight Loss, n (%)                   | 84 (41.5)  |
| Exhaustion, n (%)                    | 143 (70.5) |
| Low Physical Activity, n (%)         | 67 (33.0)  |
| Slowness, n (%)                      | 171 (84.0) |
| Weakness, n (%)                      | 134 (66.0) |
| <b>Active Treatments</b>             |            |
| βAR-blockers, n (%)                  | 144 (71.0) |
| ACE-inhibitors, n (%)                | 160 (79.0) |
| Angiotensin Receptor blockers, n (%) | 39 (19.2)  |
| Calcium Channel blockers, n (%)      | 25 (12.3)  |
| Diuretics, n (%)                     | 42 (20.7)  |

Data are expressed as mean ± SD or raw number and percentages. AFib: atrial fibrillation; AR: adrenergic receptors; BMI: body mass index; CKD: chronic kidney disease; COPD: chronic obstructive pulmonary disease; DBP: diastolic blood pressure; SBP: systolic blood pressure.



**Fig. 2.** Correlation between physical decline, assessed through 5-meter gait speed, and Montreal Cognitive Assessment (MoCA) score in our population of hypertensive frail elderly patients ( $r: 0.495$ ;  $p < 0.001$ ).

study.

## Conclusions

Taken together, our results indicate that there is a significant correlation between physical and cognitive impairment in frail hypertensive elderly subjects.

## Ethics approval and consent to participate

The study protocol was approved by the Institutional Bioethics Committee of Campania Nord (#001443). All patients or legal representatives provided written informed consent and were informed that they could withdraw from the study at any stage. The study was carried

**Table 2**

Multivariate linear regression analysis in all patients using MoCA score as a dependent variable.

|                 | B      | Standard Error | P      | 95.0% CI for B |             |
|-----------------|--------|----------------|--------|----------------|-------------|
|                 |        |                |        | Lower Bound    | Upper Bound |
| Age             | -0.185 | 0.040          | <0.001 | -0.264         | -0.106      |
| BMI             | -0.072 | 0.138          | 0.603  | -0.343         | 0.200       |
| SBP             | 0.023  | 0.029          | 0.428  | -0.035         | 0.081       |
| DBP             | -0.019 | 0.036          | 0.596  | -0.090         | 0.052       |
| HR              | 0.028  | 0.027          | 0.300  | -0.025         | 0.080       |
| Diabetes        | -2.789 | 0.495          | <0.001 | -3.765         | -1.813      |
| Hyperlipidemia  | -0.408 | 0.480          | 0.397  | -1.354         | 0.539       |
| COPD            | -1.750 | 0.488          | <0.001 | -2.712         | -0.788      |
| CKD             | -0.399 | 0.571          | 0.485  | -1.525         | 0.726       |
| Osteoarthritis  | 1.123  | 0.574          | 0.052  | -0.008         | 2.255       |
| AFib            | -0.581 | 0.545          | 0.288  | -1.655         | 0.494       |
| Gait speed test | 16.899 | 2.161          | <0.001 | 12.635         | 21.163      |

AFib: atrial fibrillation; AR: adrenergic receptors; BMI: body mass index; CKD: chronic kidney disease; COPD: chronic obstructive pulmonary disease; DBP: diastolic blood pressure; HR: heart rate; SBP: systolic blood pressure.

out following the tenets of the Declaration of Helsinki and Good Clinical Practice guidelines.

### Consent for publication

Not applicable.

### Availability of data and materials

Data are available from the First author upon reasonable request.

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### Authors' contributions

Dr. Mone had full access to all the data in the study and takes full responsibility for the integrity of the data and the accuracy for the data analysis. Study concept and design: PM, AP, GS. Acquisition, analysis, and interpretation of data: PM, AP, AdD, VB, AM, SF, and PDB. Drafting of the manuscript: PM, AP, GS. Critical revision of the manuscript for important intellectual content: AP, MM, ADL, GS. Statistical analysis: PM, AdD, and GS. Administrative, technical, or material support: PM, AP, MM, ADL, GS. Study supervision: PM, GS.

### Declaration of Competing Interest

The authors declare that they have no competing interests.

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