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Original Article

Comparison of different frailty instruments for prediction of functional decline in older hypertensive outpatients (HYPER-FRAIL pilot study 2)

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ABSTRACT

Background and aims: Few studies have evaluated frailty in older hypertensive individuals and the most appropriate tools to identify frailty in this population have yet to be identified. This study compared the performance of six frailty instruments in the prediction of 1-year functional decline in older hypertensive outpatients.
Methods: The HYPERtension and FRAILty in Older Adults (HYPER-FRAIL) longitudinal pilot study involved hypertensive participants ≥75 years from two geriatric outpatient clinics at Careggi Hospital, Florence, Italy, undergoing identification of frailty with four frailty scales (Fried Frailty Phenotype, Frailty Index [FI], Clinical Frailty Scale [CFS], Frailty Postal Score) and two physical performance tests (Short Physical Performance Battery [SPPB] and gait speed). Prediction of 1-year functional decline (i.e. *a* ≥ 10-point Barthel Index decrease between baseline and follow-up) was examined based on ROC curve analysis and multivariable logistic regression.
Results: Among 116 participants, 24 % reported functional decline. In the ROC curve analyses, FI (AUC=0.76), CFS (AUC=0.77), gait speed (AUC=0.73) and the SPPB (AUC=0.77) achieved the best predictive performance, with FI ≥0.21 and CFS ≥4 showing the highest sensitivity (82 %) and negative predictive value (91 %). Frailty identified with FI, CFS or physical performance tests was associated with an increased risk of 1-year functional decline, independently of baseline functional status and comorbidity burden.
Conclusions: FI, CFS and physical performance tests showed similar predictive ability for functional decline in hypertensive outpatients. The CFS and gait speed might be more suitable for clinical use and may be useful to identify non-frail individuals at lower risk of functional decline.

1. Introduction

Frailty is a geriatric syndrome characterized by a cumulative decline in multiple body systems, which results in the reduction of individuals' physiological functional reserve with increased vulnerability to external stressors [1]. Frailty thus negatively impacts individuals' prognosis, leading to an increased risk of adverse events such as functional decline and disability, hospitalization, nursing home admission and mortality [1–5].

Frailty is common in hypertensive older adults [6] and seems to modify the association between blood pressure (BP) and adverse events [7]. Indeed, recent observational studies suggest that the negative prognostic role of hypertension tends to attenuate or even revert at advanced age and that excessive BP lowering may be detrimental in frail older adults [8–13]. Therefore, identification of frailty represents a cornerstone of hypertension management at old age, as the presence of

Abbreviations: ABPM, ambulatory blood pressure monitoring; AUC, area under curve; BP, blood pressure; CFS, Clinical Frailty Scale; CI, confidence interval; DBP, diastolic blood pressure; FFP, Fried Frailty Phenotype; FI, Frailty Index; FPS, Frailty Postal Score; IQR, interquartile range; OH, orthostatic hypotension; OR, odds ratio; ROC, receiver operating characteristic; SBP, systolic blood pressure; SD, standard deviations; SPPB, Short Physical Performance Battery.

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frailty implies a more prudent treatment approach and less intensive treatment targets. Nevertheless, there has been limited research on frailty in hypertensive individuals, and there is a lack of specific evidence on the relationship between hypertension and frailty [14].

In recent decades, a multitude of frailty instruments has been developed for use in both clinical practice and research contexts. These instruments exhibit various characteristics and levels of complexity, rendering them suitable for different settings and purposes [2,15,16]. The majority of existing frailty instruments are based on two frailty models related to distinct conceptual frameworks: the Fried's model proposes a physical phenotype of frailty [1], while the cumulative deficit model advances that frailty is the accumulation of multiple health deficits and impairments, with the degree of frailty denoted by the proportion of such deficits [17]. Both these models are well validated and widely adopted in research setting, but a "gold standard" for frailty assessment has yet to be identified, especially for its use in clinical practice [15,18]. As regards hypertension, only a limited number of studies have characterized participants in terms of frailty and different criteria have been applied. The Frailty Index based on the cumulative deficits model was used in the SPRINT [19] and in the HYVET study [20], while some authors have considered the Fried Frailty Phenotype or the Clinical Frailty Scale [21,22]. A different approach was adopted in some studies, which applied physical performance tests such as gait speed [12,23] or grip strength [24]. Due to the heterogeneity in the hypertension literature, it is currently unclear which instrument is the most suitable for identifying frailty in older hypertensive individuals. Moreover, most studies focus on the association between BP and mortality or cardiovascular events, while outcomes of core geriatric interest, e.g., decline in functional autonomy, are often overlooked in research and in clinical practice [25].

The present study applied six different frailty instruments to a sample of older hypertensive outpatients, with the goal of comparing their predictive abilities for 1-year functional decline and identifying the instrument with the best prognostic performance.

2. Methods

The HYPERtension and FRAILty in Older Adults (HYPER-FRAIL) longitudinal pilot study was conducted at the Hypertension Clinic and at the Alzheimer' Dementia Evaluation Unit of the Division of Geriatric and Intensive Care Medicine of Careggi University Hospital, Florence, Italy. Patients were screened twice a week between December 2019 and July 2021 and patients aged 75 or older receiving antihypertensive medications were enrolled consecutively. Exclusion criteria included terminal illness (life expectancy <6 months) and refusal of participation by patient and/or his/her legally authorized representative.

All the study participants underwent a comprehensive geriatric assessment including full medical history, physical examination, BP values, functional autonomy, physical performance and cognitive status. Follow-up data were collected between January 2021 and July 2022 by retrieving clinical records and conducting phone interviews with participants and/or their caregivers in case of cognitive impairment. Follow-up data were censored at the time of the interview or at the last date participants were known to be alive.

2.1. Frailty identification

Frailty was identified using four frailty scales and two physical performance tests:

- *Fried Frailty Phenotype* (FFP): it defines frailty as a specific physical phenotype based on five components, namely unintentional weight loss, self-reported exhaustion, weakness, slowness and reduced physical activity [1]. The operational definition of each component is reported in Supplementary Table 1;
- *Frailty Index* (FI): it defines frailty as a cumulative burden of health deficits, including symptoms, diseases, disabilities and other health impairments. It is expressed as a ratio of deficits present out of the total number of variables considered, providing a score on a continuum from 0 (no deficits) to a theoretical maximum of 1 (all items exhibit deficits) [17]. The Italian version validated by Abete and colleagues [26] was applied in the present study (Supplementary Table 2) [27];
- *Clinical Frailty Scale* (CFS): it defines frailty using a 9-point scale based on clinical judgment and functional assessment, with each point corresponding to a written description of frailty degree complemented by a visual chart [28];
- *Frailty Postal Score* (FPS): it is a 6-item questionnaire (Supplementary Table 3) designed for self-administration in older people, which was proven to be accurate in identifying the FFP and predictive of adverse health outcomes in community-dwelling older adults [29];
- *Gait speed* was measured in meters per second over a 4-meter walking distance, allowing the use of a walking aid if typically used by the participant for short distances. Gait speed was shown to modify the association between BP and adverse outcomes [12,23] and can be easily assessed in routine practice.
- *Short Physical Performance Battery* (SPPB): it assesses lower-extremity function using three separate tests, i.e. standing balance, gait speed, and repeated chair stands [30]. A summary performance score is created from the single tests, ranging from 0 to 12, with higher scores indicating better performance. It was found to be highly predictive of several outcomes of geriatric interest including disability, falls, hospitalization and mortality [31].

2.2. Outcome

Functional independence was assessed using the 100-point Barthel Index (score 0–100), with higher scores indicating lower disability [32]. Significant functional decline was defined as a decrease of ≥10 points in the Barthel Index score between baseline and follow-up, which is consistent with available estimates of minimal clinically significant change, adopting both the anchor method [33] and the distribution based method [34].

2.3. Ethics

The HYPER-FRAIL study was carried out in compliance with the Declaration of Helsinki for Human Research. The study was approved by the Local Research Ethics Committee (protocol reference number: 16539_oss). Each participant or his/her legal representative gave written informed consent prior to inclusion in the study.

2.4. Statistical analyses

Data were presented as means with standard deviations (SD) for normally distributed continuous variables, medians and interquartile ranges (IQRs, 25th to 75th percentiles) for non-normally distributed variables, and absolute frequencies with percentages (n,%) for categorical variables. The independent samples *t*-test (parametric) or the Mann–Whitney U test (non-parametric) were used as appropriate for comparisons of continuous variables between groups. For categorical variables, differences between groups were tested using the Chi-square test. Covariates included disease burden - assessed using the Charlson Comorbidity Index [35] - dementia diagnosis, history of falling during the previous year, and use of walking aids. Moreover, all participants underwent office BP measurements, with systolic BP (SBP) and diastolic (DBP) measured twice in the sitting position after 5 min of resting. Orthostatic BP was assessed oscillometrically during a 3-min active stand test in participants who were able to stand and orthostatic hypotension (OH) was diagnosed in the presence of a SBP fall ≥20 mmHg or to SBP <90 mmHg, and/or a DBP fall ≥10 mmHg [36]. 24-hour

ambulatory blood pressure monitoring (ABPM) was performed using a validated oscillometric device (TM-2430, A&D, Tokyo, Japan) with readings obtained automatically at 15-minute intervals during the daytime and at 20-min intervals during the night-time. Mean ambulatory daytime, night-time, and 24-hour SBP and DBP were recorded from the ABPM reports and mean SBP and DBP values were recorded from home BP diaries, if available.

The predictive performance of different frailty instruments was compared using receiver operating characteristic (ROC) curve analysis, using the area under curve (AUC) to estimate the ability of different frailty measures to predict the study outcome (i.e., BI reduction of at least 10 points). The ROC analysis was also applied to define the optimum prognostic cut-offs of different frailty instruments, which were identified as the values corresponding to the optimal combination of sensitivity and 1-specificity. High sensitivity (i.e., probability of the test to predict functional decline when frailty was identified at baseline) was considered to take priority over high specificity, as false negative cases may inappropriately encourage strict BP control in more vulnerable subjects at higher risk of functional decline and BP lowering-related complications.

For frailty instruments showing the best predictive ability, accuracy and predictive values were calculated using MedCalc Software Ltd. Diagnostic test evaluation calculator, https://www.medcalc.org/calc/diagnostic_test.php (Version 22.014 accessed November 4, 2023). To assess prediction of functional decline, after multicollinearity assessment frailty status was included as independent variable in logistic regression models having functional decline as dependent variable and demographics, comorbidity burden (as defined by the Charlson Comorbidity Index), baseline functional status, dementia and follow-up duration as confounders. Associations were presented as odds ratio (OR) with 95 % confidence interval (CI). Statistical significance was set at a p value <0.05. All statistical analyses were performed using SPSS software version 26 (SPSS, Inc., Chicago, IL).

3. Results

The study sample included 120 participants (mean age 81.2 years, SD 4.3, 58 % female), with a median follow-up of 12 months (IQR 9–18). Four participants died during the follow-up and detailed information on their functional trajectories was not available. Among the remaining participants, 28 (24 %) showed functional decline between baseline assessment and follow-up.

Table 1 provides a comparison of baseline clinical characteristics of participants with and without the outcome of interest. Participants with functional decline were more likely to be female, had greater comorbidity burden and a higher prevalence of dementia, while no relevant differences were observed as regards other comorbidities, OH and BP values (except 24 h and night-time DBP on ABPM, which were higher in the functional decline group). The functional decline group also showed higher baseline frailty levels (except by Frailty Postal Score) and worse physical performance, with more frequent use of walking aids. The Barthel Index score was lower at baseline in patients reporting functional decline at follow-up.

In the ROC curve analysis (Table 2 and Supplementary Figures 1&2), the FI (AUC=0.763), the CFS (AUC 0.768) and physical performance tests (SPPB: AUC=0.766; gait speed: AUC=0.730) showed similar predictive ability for functional decline.

Based on the ROC curve analysis, frailty status was defined as follows: FI $\geq$0.21 (sensitivity 82.1 %, specificity 59.1 %), CFS $\geq$4 (sensitivity 82.1 %, specificity 60.2 %), gait speed $\leq$0.85 m/s (sensitivity 75 %, specificity 51.9 %), SPPB $<$10/12 (sensitivity 75 %, specificity 51.4 %). Details for each frailty definition are presented in Table 3. Negative predictive values achieved 91 % for FI and CFS, showing slightly lower values for physical performance tests (88.1–88.5 %). Accuracy, i.e., overall probability that a participant was correctly classified was moderate for all four frailty instruments (64.7–65.5 %). In univariate logistic regression analysis, frailty status was associated with an increased risk of 1-year functional decline, regardless of the frailty instrument applied. This association remained significant in a multivariable logistic regression model adjusted for age, sex, comorbidity burden, and baseline functional status. The association between frailty status and 1-year functional decline was independent of dementia, only when frailty was defined based on the CFS or gait speed (Table 3).

Table 1
Baseline characteristics of the study sample according to functional decline at follow-up.

	Functional decline (n = 28)	No functional decline (n = 88)	p
Age, mean (SD)	82.4 (5)	80.8 (4)	0.107
Female, n (%)	21 (75.0)	46 (52.3)	0.034
Body Mass Index (n = 110), mean (SD)	26.9 (6)	26.4 (4)	0.603
Charlson Comorbidity Index*, median (IQR)	1 (1–3)	1 (0–2)	0.021
Nr. daily medications, median (IQR)	7.5 (5–9)	6 (5–8.75)	0.391
Nr. Antihypertensive medications, median (IQR)	2 (1.25–3)	2 (2–3)	0.904
Diabetes, n (%)	7 (25.0)	19 (21.6)	0.706
Coronary artery disease, n (%)	3 (10.7)	14 (15.9)	0.498
Heart failure, n (%)	2 (7.1)	4 (4.5)	0.589
Stroke/Transient ischemic attack, n (%)	7 (25.0)	19 (21.6)	0.706
Chronic kidney disease, n (%)	13 (46.4)	59 (67.0)	0.050
Dementia, n (%)	17 (60.7)	18 (20.5)	<0.001
MMSE (n = 61), mean score (SD)	20.2 (6)	23.7 (5)	0.020
Depression, n (%)	12 (42.9)	22 (25.0)	0.071
Blood pressure values			
Office SBP, mean (SD)	150.1 (22)	153.4 (21)	0.475
Office DBP, mean (SD)	80.3 (13)	79.1 (13)	0.676
Orthostatic hypotension (n = 114), n (%)	13 (46)	37 (43)	0.752
Home SBP (n = 89), mean (SD)	134.1 (12)	137.6 (12)	0.273
Home DBP (n = 89), mean (SD)	73.4 (9)	73.9 (8)	0.823
24 h SBP (ABPM), mean (SD)	150.8 (13)	145.3 (16)	0.100
24 h DBP (ABPM), mean (SD)	79.7 (11)	75.3 (8)	0.022
Daytime SBP (ABPM), mean (SD)	152.3 (13)	148.1 (16)	0.204
Daytime DBP (ABPM), mean (SD)	81.3 (11)	77.9 (8)	0.085
Night-time SBP (ABPM), mean (SD)	144.1 (21)	135.7 (21)	0.082
Night-time DBP (ABPM), mean (SD)	72.7 (12)	67.1 (9)	0.015
24 h heart rate (ABPM), mean (SD)	69.5 (8)	66.8 (8)	0.125
Functional status, frailty and physical performance			
Barthel Index, median (IQR)	87.5 (71.25–100)	95 (95–100)	0.001
Fried Frailty Phenotype, median score (IQR)	3 (1.25–4)	2 (1–3)	0.011
Frailty Index, mean (SD)	0.37 (0.16)	0.22 (0.15)	<0.001
Clinical Frailty Scale, median (IQR)	5 (4–6)	3 (2–4)	<0.001
Frailty Postal Score, median (IQR)	5.75 (2–8.5)	3.5 (1–6.88)	0.056
Walking aid, n (%)	12 (42.9)	13 (14.8)	0.002
Fall history, n (%)	16 (57.1)	35 (39.8)	0.107
SPPB, median score (IQR)	7 (3.25–9.75)	10 (8–12)	<0.001
Gait speed, mean (SD)	0.65 (0.31)	0.88 (0.28)	<0.001

SD; standard deviation; IQR, interquartile range; MMSE, Mini Mental State Examination; SBP, systolic blood pressure; DBP, diastolic blood pressure; ABPM, ambulatory blood pressure monitoring; ADLs, activities of daily living; SPPB, Short Physical Performance Battery.
**non-age adjusted.*

Table 2
Predictive performance of different frailty instruments for 1-year functional decline (AUCs and 95 % confidence intervals).

	Fried Frailty Phenotype	Frailty Index	Clinical Frailty Scale	Frailty Postal Score	Gait speed	SPPB
FFP	**AUC 0.656** (0.544–0.769)	$p = 0.019$	$p = 0.047$	$p = 0.362$	$p = 0.157$	$p = 0.014$
Frailty Index	–	**AUC 0.763** (0.664–0.862)	$p = 0.845$	$p = 0.003$	$p = 0.547$	$p = 0.948$
CFS	–	–	**AUC 0.768** (0.668–0.869)	$p = 0.009$	$p = 0.499$	$p = 0.938$
FPS	–	–	–	**AUC 0.619** (0.504–0.734)	$p = 0.074$	$p = 0.003$
Gait speed	–	–	–	–	**AUC 0.730** (0.615–0.845)	$p = 0.426$
SPPB	–	–	–	–	–	**AUC 0.766** (0.669–0.862)

AUC, area under the curve; SPPB, Short Physical Performance Battery.
P values refer to AUC comparisons.

Table 3
Sensitivity, specificity, predictive ability, accuracy and odds ratio of different frailty instruments for the prediction of 1-year functional decline.

%	Frailty Index ≥0.21	Clinical Frailty Scale ≥4	Gait speed ≤0.85 m/s	SPPB score <10
Sensitivity	82.1	82.1	75	75
Specificity	59.1	60.2	61.9	61.4
PPV	39	39.7	39.6	38.2
NPV	91.2	91.4	88.1	88.5
Accuracy	64.7	65.5	65.2	64.7
OR (95 % CI)	6.64 (2.31–19.10)	6.96 (2.42–20.04)	4.87 (1.86–12.75)	4.76 (1.83–12.40)
Adj. OR (95 % CI)*	5.42 (1.79–16.45)	5.77 (1.90–17.55)	4.11 (1.53–11.04)	3.80 (1.41–10.28)
Adj. OR (95 % CI)**	4.52 (1.37–14.93)	5.16 (1.55–17.22)	3.17 (1.24–10.54)	3.09 (1.04–9.16)
Adj. OR (95 % CI)§	3.13 (0.91–10.72)	3.57 (1.04–12.20)	3.39 (1.16–9.93)	2.59 (0.88–7.57)

PPV, positive predictive value; NPV, negative predictive value; SPPB, Short Physical Performance Battery; OR, odds ratio; CI, confidence interval.
* adjusted for age and sex.
** adjusted for age, sex, follow-up period (months), Charlson Index (not-age-adjusted) and baseline functional status.
§ adjusted for age, sex, follow-up period (months), Charlson Index (not-age-adjusted) and dementia.

4. Discussion

From a clinical perspective, predicting negative health outcomes is crucial for determining the role of frailty instruments in patient management. Evaluating which frailty instrument better predicts adverse outcomes in older hypertensive patients could assist in deciding the timeliest and appropriate further geriatric assessments and interventions. In the past decade, comparisons of the predictive performance of frailty tools have been described in a number of studies, producing varying results depending on the characteristics of the study populations and the frailty tools used [37–41]. However, studies specifically investigating the predictive role of frailty instruments in older hypertensive patients are lacking [42]. Moreover, existing data primarily focus on investigating and comparing the prognostic ability of frailty instruments in relation to mortality [37,38,43–46], while little consideration has been given to outcomes of core geriatric interest, such as functional independence and decline. Furthermore, data specifically referring to frailty assessment in the context of hypertension management are lacking.

The present study compared the ability of six widely used frailty instruments in predicting 1-year functional decline, with a specific focus on older adults with hypertension. FI and CFS showed similar predictive performance for functional decline (AUC 0.76 and 0.77, respectively), with 81 % sensitivity, 91 % negative predictive value and 65 % accuracy (FI ≥0.21; CFS ≥4). Physical performance tests achieved comparable predictive ability (SPPB: AUC=0.77; gait speed: AUC=0.73) and accuracy (SPPB <10=65 %; gait speed ≤0.85 m/s = 65 %). The discriminative ability of the FFP (AUC=0.656) and of the FPS (AUC=0.619) was very poor. None of the applied instrument showed an excellent predictive performance, implying that other factors exist which influence functional trajectories in older hypertensive individuals. However, frailty status as identified with the FI (≥0.21), the CFS (≥4) or physical performance tests (gait speed ≤0.85 m/s or SPPB <10) significantly increased the risk of 1-year functional decline, independently of baseline functional status and comorbidity burden. Together with available observational data showing that lower blood pressure values carry a higher risk of mortality among frail older subjects [11–13], the present data suggest that the higher disability risk observed in this subgroup is not related to high blood pressure values. Indeed, hypotension and its related adverse events (e.g. fall risk) may even increase the risk of disability progression, warning against an aggressive BP lowering. Conversely, four frailty instrument achieved very high negative predictive value (88–91 %). These results indicate that the use of these frailty instruments for the specific purpose of the prediction of 1-year functional decline could be useful to rule out the outcome when frailty is not identified at baseline. Consistently, data from the TILDA study support the use of frailty instruments for the "rule out" of negative outcomes, showing generally high specificity and low sensitivity of different frailty tools in the prediction of 8-year mortality [41]. It would thus appear reasonable that these instruments would be applied for "rule-out" purposes, i.e., to identify patients at lower risk for functional decline, who may tolerate and probably benefit from a more intensive hypertension treatment approach. While frailer patients deserve more prudent BP lowering, patients who are not identified as frail should not be denied by age a more intensive treatment strategy, if tolerated.

Previous studies support the predictive value of the FI for decline in functional status, even in the long-term [38,47,48]. However, the FI may demand a considerable amount of time to perform and may not be well-suited for routine use in a clinical setting, making it more appropriate as a research tool. In contrast, the CFS is brief and user-friendly, though variable inter-operator agreement has been reported, especially among non-geriatric specialists [49,50]. The latest European Hypertension Society guidelines [51] recommend that the CFS is applied in all hypertensive patients aged 80 or older to identify the degree of frailty before treatment initiation. Moreover, the guidelines encourage repeated on-treatment use of the CFS to monitor patient's frailty status and optimize treatment strategies accordingly. In the present study, the CFS showed the same predictive performance as the FI with similar sensitivity, predictive values and accuracy, thus agreeing that the CFS represents a useful instrument for frailty identification in hypertensive individuals. In particular, the CFS might be helpful to identify patients at lower risk of functional decline, who are likely to benefit from the same treatment approach recommended in younger adults. Therefore, our

data support the recommendations of the 2023 European guidelines regarding the implementation of the CFS in routine management of older hypertensive patients, although there are no data on the concordance of CFS assessment in "real world" clinical practice with the gold standard in research settings.

Previous data indicate an association between reduced gait speed and increased risk of dependency and institutionalization [31,52,53]. Moreover, gait speed was found to be useful to discriminate older participants with and without increased mortality risk due to high BP. Indeed, the association between BP and negative outcomes was shown to be limited or even absent in slow walker and in non-walking individuals [12,13,23]. In the present study, physical performance tests (i.e., gait speed and the SPPB) achieved similar predictive ability and accuracy for functional decline as compared to the FI and the CFS. Moreover, association between frailty status and functional decline was found to be independent of dementia when frailty was defined based on gait speed. These data suggest that gait speed might represent a useful alternative instrument for frailty assessment in hypertensive older adults, particularly for staff with less experience and training in geriatric assessment.

4.1. Limitations

Our results must be interpreted in the context of some study limitations. First, this is a pilot study with a small sample size. Indeed, patients' recruitment was significantly affected by the COVID-19 pandemic, which substantially reduced patients' flow at outpatient clinics during the study period. Second, the study sample included treated hypertensive outpatients, so our findings cannot automatically be extrapolated to more vulnerable populations referred to other clinical settings and to older individuals who are being evaluated before the introduction of antihypertensive therapy. Third, the study was carried out in a geriatric department by investigators with geriatric expertise. The predictive performance of frailty instruments might thus be different when applied by non-geriatric specialists or in the absence of specific training. Finally, the present study restricted the analysis to two physical performance tests and four frailty scales. Therefore, it cannot be excluded that different frailty instruments may have higher predictive performance in older hypertensive patients. Despite these limitations, to the authors' knowledge this is the first study comparing the performance of different frailty instruments in predicting functional decline in older adults with hypertension.

5. Conclusions

The Frailty Index ($\geq$0.21), the Clinical Frailty Scale ($\geq$4) and physical performance tests (gait speed $\leq$0.85 m/s, SPPB $<$10) have similar ability to predict functional decline in older hypertensive outpatients, with high negative predictive value. The Clinical Frailty Scale and gait speed might be more suitable for clinical use and may be useful to identify non-frail hypertensive patients at lower risk of functional decline, who should not be denied a more intensive antihypertensive treatment, if tolerated. Future studies should confirm its predictive properties and investigate related clinical implications, with particular reference to antihypertensive treatment benefits and additional geriatric optimisation strategies once frailty has been identified.

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Declaration of competing interest

The authors declare they have no conflict of interest.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.ejim.2024.05.013.

References

[1] Fried LP, Tangen CM, Walston J, et al. Frailty in older adults: evidence for a phenotype. Journals Gerontol - Ser A Biol Sci Med Sci 2001;56:146–57. https://doi.org/10.1093/gerona/56.3.m146.
[2] Hoogendijk EO, Afilalo J, Ensrud KE, et al. Frailty: implications for clinical practice and public health. Lancet 2019;394:1365–75. https://doi.org/10.1016/S0140-6736(19)31786-6.
[3] Vermeiren S, Vella-Azzopardi R, Beckwée D, et al. Frailty and the prediction of negative health outcomes: a meta-analysis. J Am Med Dir Assoc 2016;17. https://doi.org/10.1016/j.jamda.2016.09.010. 1163.e1-1163.e17.
[4] Kojima G. Frailty as a predictor of hospitalisation among community-dwelling older people: a systematic review and meta-analysis. J Epidemiol Community Health 2016;70:722–9. https://doi.org/10.1136/jech-2015-206978.
[5] Kojima G. Frailty as a predictor of nursing home placement among community-dwelling older adults: a systematic review and meta-analysis. J Geriatr Phys Ther 2018;41:42–8. https://doi.org/10.1519/JPT.0000000000000097.
[6] Vetrano DL, Palmer KM, Galluzzo L, et al. Hypertension and frailty: a systematic review and meta-analysis. BMJ Open 2018;8:1–8. https://doi.org/10.1136/bmjopen-2018-024406.
[7] Zhang XE, Cheng B, Wang Q. Relationship between high blood pressure and cardiovascular outcomes in elderly frail patients: a systematic review and meta-analysis. Geriatr Nurs (Minneap) 2016;37:385–92. https://doi.org/10.1016/j.gerinurse.2016.05.006.
[8] Molander L, Lövheim H, Norman T, et al. Lower systolic blood pressure is associated with greater mortality in people aged 85 and older. J Am Geriatr Soc 2008;56:1853–9. https://doi.org/10.1111/j.1532-5415.2008.01948.x.
[9] Satish S, Freeman DH, Ray L, Goodwin JS. The relationship between blood pressure and mortality in the oldest old. J Am Geriatr Soc 2001;49:367–74. https://doi.org/10.1046/j.1532-5415.2001.49078.x.
[10] Van Bemmel T, Gussekloo J, Westendorp RGJ, Blauw GJ. In a population-based prospective study, no association between high blood pressure and mortality after age 85 years. J Hypertens 2006;24:287–92. https://doi.org/10.1097/01.hjh.0000200513.48441.8e.
[11] Ogliari G, Westendorp RGJ, Muller M, et al. Blood pressure and 10-year mortality risk in the Milan Geriatrics 75+ Cohort Study: role of functional and cognitive status. Age Ageing 2015;44:932–7. https://doi.org/10.1093/ageing/afv141.
[12] Odden MC, Peralta CA, Haan MN, Covinsky KE. Rethinking the association of high blood pressure with mortality in elderly adults. Arch Intern Med 2012;172:1162–8. https://doi.org/10.1001/archinternmed.2012.2555.
[13] Liang Y, Fratiglioni L, Wang R, et al. Effects of biological age on the associations of blood pressure with cardiovascular and non-cardiovascular mortality in old age: a population-based study. Int J Cardiol 2016;220:508–13. https://doi.org/10.1016/j.ijcard.2016.06.118.
[14] Rivasi G, Tortù V, D'Andria MF, et al. Hypertension management in frail older adults: a gap in evidence. J Hypertens 2021;39:400–7. https://doi.org/10.1097/HJH.0000000000002685.
[15] Faller JW, do Nascimento Pereira D, de Souza S, et al. Instruments for the detection of frailty syndrome in older adults: a systematic review. PLoS ONE 2019;14:1–23. https://doi.org/10.1371/journal.pone.0216166.
[16] Afilalo J, Alexander KP, Mack MJ, et al. Frailty assessment in the cardiovascular care of older adults. J Am Coll Cardiol 2014;63:747–62. https://doi.org/10.1016/j.jacc.2013.09.070.
[17] Mitnitski AB, Mogilner AJ, Rockwood K. Accumulation of deficits as a proxy measure of aging. ScientificWorldJournal 2001;1:323–36. https://doi.org/10.1100/tsw.2001.58.
[18] Dent E, Kowal P, Hoogendijk EO. Frailty measurement in research and clinical practice: a review. Eur J Intern Med 2016;31:3–10. https://doi.org/10.1016/j.ejim.2016.03.007.
[19] Williamson JD, Supiano MA, Applegate WB, et al. Intensive vs standard blood pressure control and cardiovascular disease outcomes in adults aged ≥75 years. JAMA 2016;315:2673. https://doi.org/10.1001/jama.2016.7050.
[20] Warwick J, Falaschetti E, Rockwood K, et al. No evidence that frailty modifies the positive impact of antihypertensive treatment in very elderly people: an investigation of the impact of frailty upon treatment effect in the HYpertension in the Very Elderly Trial (HYVET) study, a double-blind, placeb. BMC Med 2015;13:1–8. https://doi.org/10.1186/s12916-015-0328-1.
[21] Benetos A, Bulpitt CJ, Petrovic M, et al. An expert opinion from the european society of hypertension-european union geriatric medicine society working group on the management of hypertension in very old, frail subjects. Hypertension 2016;67:820–5. https://doi.org/10.1161/HYPERTENSIONAHA.115.07020.

[22] Benetos A, Petrovic M, Strandberg T. Hypertension management in older and frail older patients. Circ Res 2019;124:1045–60. https://doi.org/10.1161/CIRCRESAHA.118.313236.
[23] Weidung B, Boström G, Toots A, et al. Blood pressure, gait speed, and mortality in very old individuals: a population-based cohort study. J Am Med Dir Assoc 2015;16:208–14. https://doi.org/10.1016/j.jamda.2014.09.004.
[24] Wu C, Smit E, Peralta CA, et al. Functional status modifies the association of blood pressure with death in elders: health and retirement study. J Am Geriatr Soc 2017;65:1482–9. https://doi.org/10.1111/jgs.14816.
[25] Canavan M, Smyth A, Bosch J, et al. Does lowering blood pressure with antihypertensive therapy preserve independence in activities of daily living? a systematic review. Am J Hypertens 2015;28:273–9. https://doi.org/10.1093/ajh/hpu131.
[26] Abete P, Basile C, Bulli G, et al. The Italian version of the "frailty index" based on deficits in health: a validation study. Aging Clin Exp Res 2017;29:913–26. https://doi.org/10.1007/s40520-017-0793-9.
[27] Basile G, Catalano A, Mandraffino G, et al. Relationship between blood pressure and frailty in older hypertensive outpatients. Aging Clin Exp Res 2017;29:1049–53. https://doi.org/10.1007/s40520-016-0684-5.
[28] Rockwood K, Song X, MacKnight C, et al. A global clinical measure of fitness and frailty in elderly people. Cmaj 2005;173:489–95. https://doi.org/10.1503/cmaj.050051.
[29] Mossello E, Profili F, Di Bari M, et al. Postal screening can identify frailty and predict poor outcomes in older adults: longitudinal data from INTER-FRAIL study. Age Ageing 2016;45:469–74. https://doi.org/10.1093/ageing/afw048.
[30] Guralnik JM, Simonsick EM, Ferrucci L, et al. A short physical performance battery assessing lower extremity function: association with self-reported disability and prediction of mortality and nursing home admission. J Gerontol 1994;49:M85–94. https://doi.org/10.1093/geronj/49.2.M85.
[31] Studenski S, Perera S, Wallace D, et al. Physical performance measures in the clinical setting. J Am Geriatr Soc 2003;51:314–22. https://doi.org/10.1046/j.1532-5415.2003.51104.x.
[32] Mahoney FI, Barthel DW. Functional evaluation: the Barthel index. Md State Med J 1965;14:61–5.
[33] Hsieh Y-W, Wang C-H, Wu S-C, et al. Establishing the minimal clinically important difference of the Barthel index in stroke patients. Neurorehabil Neural Repair 2007;21:233–8. https://doi.org/10.1177/1545968306294729.
[34] Unnanuntana A, Jarusriwanna A, Nepal S. Validity and responsiveness of Barthel index for measuring functional recovery after hemiarthroplasty for femoral neck fracture. Arch Orthop Trauma Surg 2018;138:1671–7. https://doi.org/10.1007/s00402-018-3020-z.
[35] Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. J Chronic Dis 1987;40:373–83. https://doi.org/10.1016/0021-9681(87)90171-8.
[36] Brignole M, Moya A, De Lange FJ, et al. 2018 ESC Guidelines for the diagnosis and management of syncope. Eur Heart J 2018;39:1883–948. https://doi.org/10.1093/eurheartj/ehy037.
[37] Theou O, Brothers TD, Mitnitski A, Rockwood K. Operationalization of frailty using eight commonly used scales and comparison of their ability to predict all-cause mortality. J Am Geriatr Soc 2013;61:1537–51. https://doi.org/10.1111/jgs.12420.
[38] Gonzalez-Colaço Harmand M, Meillon C, Bergua V, et al. Comparing the predictive value of three definitions of frailty: results from the Three-City study. Arch Gerontol Geriatr 2017;72:153–63. https://doi.org/10.1016/j.archger.2017.06.005.
[39] Bongue B, Buisson A, Dupre C, et al. Predictive performance of four frailty screening tools in community-dwelling elderly. BMC Geriatr 2017;17:1–9. https://doi.org/10.1186/s12877-017-0633-y.
[40] Woo J, Leung J, Morley JE. Comparison of frailty indicators based on clinical phenotype and the multiple deficit approach in predicting mortality and physical limitation. J Am Geriatr Soc 2012;60:1478–86. https://doi.org/10.1111/j.1532-5415.2012.04074.x.
[41] Romero-Ortuno R, Hartley P, Kenny RA, O'Halloran AM. Frail by different measures: a comparison of 8-year mortality in The Irish longitudinal study on ageing (TILDA). Eur Geriatr Med 2022;13:279–84. https://doi.org/10.1007/s41999-021-00570-9.
[42] Hu K, Zhou Q, Jiang Y, et al. Association between Frailty and Mortality, Falls, and Hospitalization among Patients with Hypertension: a Systematic Review and Meta-Analysis. Biomed Res Int 2021;2021. https://doi.org/10.1155/2021/2690296.
[43] Kulminski AM, Ukraintseva SV, Kulminskaya IV, et al. Cumulative deficits better characterize susceptibility to death in elderly people than phenotypic frailty: lessons from the cardiovascular health study. J Am Geriatr Soc 2008;56:898–903. https://doi.org/10.1111/j.1532-5415.2008.01656.x.
[44] Rockwood K, Andrew M, Mitnitski A. A comparison of two approaches to measuring frailty in elderly people. Journals Gerontol Ser A Biol Sci Med Sci 2007;62:738–43. https://doi.org/10.1093/gerona/62.7.738.
[45] Mitnitski A, Fallah N, Rockwood MRH, Rockwood K. Transitions in cognitive status in relation to frailty in older adults: a Comparison of three frailty measures. J Nutr Health Aging 2011;15:863–7. https://doi.org/10.1007/s12603-011-0066-9.
[46] Xue QL, JingTian Walston JD, et al. Discrepancy in frailty identification: move beyond predictive validity. Journals Gerontol - Ser A Biol Sci Med Sci 2020;75:387–93. https://doi.org/10.1093/gerona/glz052.
[47] Li JJ, Jiang S, Zhu ML, et al. Comparison of three frailty scales for prediction of adverse outcomes among older adults: a prospective cohort study. J Nutr Heal Aging 2021;25:419–24. https://doi.org/10.1007/s12603-020-1534-x.
[48] Malmstrom TK, Miller DK, Morley JE. A comparison of four frailty models. J Am Geriatr Soc 2014;62:721–6. https://doi.org/10.1111/jgs.12735.
[49] Sze S, Pellicori P, Zhang J, et al. Identification of frailty in chronic heart failure. JACC Hear Fail 2019;7:291–302. https://doi.org/10.1016/j.jchf.2018.11.017.
[50] Surkan M, Rajabali N, Bagshaw SM, et al. Interrater reliability of the clinical frailty scale by geriatrician and intensivist in patients admitted to the intensive care unit. Can Geriatr J 2020;23:223–9. https://doi.org/10.5770/cgj.23.398.
[51] Mancia(Chairperson) G, Kreutz(Co-Chair) R, Brunström M, et al. 2023 ESH Guidelines for the management of arterial hypertension the task force for the management of arterial hypertension of the European Society of Hypertension Endorsed by the European Renal Association (ERA) and the International Society of Hypertensi. J Hypertens Publish Ah 2023:1–198. https://doi.org/10.1097/hjh.0000000000003480.
[52] Woo J, Suzanne CHO, Yu ALM. Dependency, mortality, and institutionalization in Chinese aged 70 and older. J Am Geriatr Soc 1999;47:1257–60.
[53] Viccaro LJ, Perera S, Studenski SA. Is timed up and go better than gait speed in predicting health, function, and falls in older adults? J Am Geriatr Soc 2011;59:887–92. https://doi.org/10.1111/j.1532-5415.2011.03336.x.