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ORIGINAL RESEARCH

Blood Pressure Drop Rate After Standing Up Is Associated With Frailty and Number of Falls in Geriatric Outpatients

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BACKGROUND: The relationship between orthostatic hypotension and clinical outcome in older adults is poorly understood. Blood pressure drop rate (ie, speed of blood pressure drop) may particularly reflect the imposed challenge to the baroreflex and the associated clinical outcome (ie, frailty and number of falls). This study aimed to compare orthostatic blood pressure drop rate and drop magnitude with regard to their association with frailty and number of falls.

METHODS AND RESULTS: Blood pressure was measured continuously during a standardized active stand task in 168 patients (mean age 81.4±7.0; 55.4% female) who visited a geriatric outpatient clinic for cognitive or mobility problems. The association of orthostatic blood pressure drop rate, blood pressure drop magnitude, and baroreflex sensitivity (ie, increase in heart rate divided by systolic blood pressure drop magnitude) with frailty (Fried criteria and 4 frailty markers) and self-reported number of falls was assessed using linear regression models, adjusting for age and sex. Systolic blood pressure drop rate had the strongest association with frailty according to the 4 frailty markers (β 0.30; 95% CI, 0.11–0.49; P=0.003) and number of falls (β 1.09; 95% CI, 0.19–1.20; P=0.018); diastolic blood pressure drop magnitude was most strongly associated with frailty according to the Fried criteria (β 0.37; 95% CI, 0.15–0.60; P<0.001). Baroreflex sensitivity was associated with neither frailty nor number of falls.

CONCLUSIONS: Orthostatic blood pressure drop rate was associated with frailty and falls and may reflect the challenge to the baroreflex rather than drop magnitude.

Key Words: baroreflex ■ blood pressure ■ blood pressure measurement/monitoring ■ falls ■ frailty ■ geriatrics ■ orthostatic hypotension ■

Orthostatic hypotension (OH), defined as a systolic blood pressure (SBP) drop of 20 mm Hg or a diastolic blood pressure (DBP) drop of 10 mm Hg within 3 minutes after standing up, occurs in 5% to 30% of adults above 65 years of age and is associated with impaired physical and cognitive functioning, cardiovascular disease, and mortality.[1-4] However, these associations are poorly understood and may be determined by the blood pressure (BP) challenge imposed to the baroreflex as well as baroreflex sensitivity (ie, heart rate increase relative to BP drop).[5,6]

Continuous beat-to-beat BP was shown to be of additional clinical value compared with intermittent BP measurements.[5,7] The imposed challenge to the baroreflex may be reflected particularly by BP drop rate (ie, the speed of BP drop after standing up), as the baroreflex has a latency to reach its peak potential.[8,9] A large imposed challenge to the baroreflex might result from the baroreflex latency causing a temporary decrease of cardiac output,[10] hypoperfusion of the brain, retina, and muscles,[11] and acute symptoms of dizziness, fainting, blurry vision, and falls.[4] Recurrent brain hypoperfusion

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CLINICAL PERSPECTIVE

What Is New?

- This is the first study assessing the association between orthostatic blood pressure (BP) drop rate with the clinically relevant outcomes frailty and number of falls.

What Are the Clinical Implications?

- The results of this study advocate the use of continuous BP measurements in geriatric outpatients.
- BP drop rate was identified as a clinically relevant parameter.
- BP drop rate might potentially be used to predict frailty and falls related to orthostatic BP drop and to evaluate the efficacy of orthostatic hypotension treatment, which needs to be addressed in further studies.

Nonstandard Abbreviations and Acronyms

BMI	body mass index
BP	blood pressure
BRS	baroreflex sensitivity
COGA	Center of Geriatrics in Amsterdam
DBP	diastolic blood pressure
HR	heart rate
IQR	interquartile range
MMSE	Mini-Mental State Examination
OH	orthostatic hypotension
SBP	systolic blood pressure

may lead to cognitive impairment,[2] mobility limitations, impaired activities of daily living,[1] loss of muscle mass, lower physical activity, and exhaustion, which are reflected by the Fried frailty criteria and the 4 frailty markers.[12] Previous studies reported an association of OH with frailty or falls[7,13–23] but did not assess the association of BP drop rate with frailty or falls.

The objective of this study was to compare BP drop rate after standing up with BP drop magnitude and baroreflex sensitivity with regard to their association with frailty and number of falls in group of geriatric outpatients with a high prevalence of OH. It was hypothesized that BP drop rate is associated with frailty and number of falls.

METHODS

Study Design and Setting

The data that support the findings of this study are available from the corresponding author on reasonable request. Data from 2 patient groups (Bronovo and COGA [Center of Geriatrics in Amsterdam]) were used. The Bronovo patient group included patients referred to the geriatric outpatient clinic of the Bronovo hospital (The Hague, the Netherlands) between March 2011 and January 2012. The COGA patient group included patients referred to the COGA of the VU University Medical Center Amsterdam (Amsterdam, the Netherlands) between January 2014 and December 2015. Patients visiting the outpatient clinic for cognitive or mobility problems after referral by a general practitioner underwent a comprehensive geriatric assessment.

Ethical Approval and Informed Consent

This study was performed in accordance with the Declaration of Helsinki and approved by the local medical ethical committee of the VU University Medical Center Amsterdam (COGA patient group) and the institutional review board of the Leiden University Medical Centre (Bronovo patient group). For both patient groups, informed consent was waived, as the data were collected as part of usual clinical care.

Patient Characteristics

Information about age, sex, height, weight, medical history, medication, living situation, smoking habits, and alcohol consumption was extracted from the medical records. The Mini-Mental State Examination (Par Inc, Lutz, FL) was used to assess cognitive performance.[24] Subdomains assessed by the Mini-Mental State Examination include orientation to time and place, attention, calculation, recall, language, repetition, and complex commands. Multimorbidity was defined as 2 or more of the following diseases diagnosed and described in a patient's medical record by the geriatrician: chronic obstructive pulmonary disease, diabetes mellitus, hypertension, malignancy, myocardial infarction, Parkinson disease, and (osteo)arthritis.

BP Measurement

A subpopulation of patients underwent continuous BP measurements while standing up from a supine to a standing position, depending on the availability of the equipment. Beat-to-beat blood pressure was measured using a finger photoplethysmograph (Nexfin; Bmeye, Amsterdam, the Netherlands). Patients were asked to lie down in a supine position for 5 minutes, after which they were asked to stand up and continue standing for 3 minutes. Standing up was supported by an automatic lift chair (Vario 570, Fitform BV, Best, the Netherlands) in the Bronovo patient group, and performed unsupported in the COGA patient group. The moment of standing was marked in the data. Blood

pressure was also measured intermittently in a supine position and at 1 and 3 minutes after standing up using a sphygmomanometer.

Frailty and Number of Falls

The Fried criteria and the 4 frailty markers were used to assess frailty. The Fried criteria assess unintentional weight loss, exhaustion, physical inactivity, gait speed, and handgrip strength and attribute 1 point for each frailty item (1 point per item, maximum 5 points), more points indicating higher frailty.[12] Patients were considered nonfrail, prefrail, or frail according to the Fried frailty criteria if they scored 0, 1 to 2, or 3 to 5 points, respectively.[12]

The 4 frailty markers assess mobility, incontinence, cognitive function, and activities of daily living (1 point per item, maximum 4 points).[25] Patients were considered nonfrail, prefrail, or frail according to the 4 frailty markers if they scored 0 to 1, 2, or 3 to 4 points, respectively.[25]

Weight loss was defined as a patient-reported loss of more than 3 kg in the previous month or more than 6 kg in the previous 6 months.[26] Exhaustion was assessed by the individual question "I feel as if I am slowed down" answered with "very often" or "nearly all the time" on the Hospital Anxiety and Depression Scale.[26,27] Physically inactive was defined as a patient-reported maximum distance of outdoor walking <20 minutes, only walking indoors, or not walking at all.[26] Gait speed was assessed using the 4-m walk test.[26] Handgrip strength was defined as maximal force in kilograms of 3 performances on each hand, by using hand-held dynamometry (Jamar hand dynamometer; Sammons Preston, Inc, Bolingbrook, IL).[26] Mobility impairment was defined as the patient-reported use of a walking aid or need for assistance with walking.[26] Activities of daily living were assessed using the Katz index excluding the incontinence item, as incontinence is a separate item in the 4 frailty markers.[26,28] Incontinence was defined as the patient-reported incontinence of either bladder or bowel.[26] Cognitive impairment was defined as a score below 24 points on the Mini-Mental State Examination.[26]

Number of falls was assessed by asking patients how many times they fell in the past year.

BP and Heart Rate Signal Analyses

All BP and heart rate (HR) signal analyses were performed using MATLAB R2017b (Mathworks Inc, Natick, MA). Signals were excluded if they were incomplete (baseline <30 seconds or standing time <150 seconds) or very noisy on inspection. Signals were filtered using a 5-second window moving-average filter and split into 3 epochs: resting (60 seconds), transition (7 seconds), and standing (180 seconds). The separation between the transition and standing epochs was manually marked during the test. Baseline was defined as the mean of the 60-second resting epoch. BP drop rate was defined as the largest amplitude of the negative peak in the first derivative of BP; BP drop magnitude was defined as the magnitude of the largest decline in BP compared with the baseline, as demonstrated in a previous study.[5] All BP parameters were assessed both in the 0 to 15- and 15- to 180-second interval after standing up, resulting in 8 BP parameters: $SBP_{drop\_rate\_0\text{-}15}$, $SBP_{drop\_magnitude\_0\text{-}15}$, $DBP_{drop\_rate\_0\text{-}15}$, $DBP_{drop\_magnitude\_0\text{-}15}$, $SBP_{drop\_rate\_15\text{-}180}$, $SBP_{drop\_magnitude\_15\text{-}180}$, $DBP_{drop\_rate\_15\text{-}180}$, $DBP_{drop\_magnitude\_15\text{-}180}$. Positive BP parameters indicate a blood pressure drop, and negative BP parameters indicate a BP increase. Figure 1 demonstrates the computations for the SBP parameters.

Orthostatic heart rate increase ($HR_{max\ increase}$) was defined as the maximum HR within 15 seconds after baseline. Baroreflex sensitivity was defined as $HR_{max\ increase}$ divided by $SBP_{drop\_magnitude\_0\text{-}15}$.

Statistical Analyses

All statistical analyses were conducted with the Statistical Package for the Social Science (IBM SPSS Statistics version 22, IBM Corporation, Chicago, IL). Normally distributed variables were reported using mean and SD, non–normally distributed variables using median and interquartile range. BP and HR parameters were normalized by subtracting the mean and dividing by the SD to enable comparison of effect sizes.

Linear trends in patient characteristics across quartiles of BP parameters were tested using linear regression analysis.

The associations between BP and HR parameters and frailty and number of falls were tested using multiple linear regression models with the BP/HR parameters as independent variables and frailty score and number of falls as dependent variables. For each outcome and BP parameter, 4 models were created. Model 1 adjusts for sex and age. Model 2 additionally adjusts for the complementary BP parameter (eg, $SBP_{drop\_magnitude\_0\text{-}15}$ in the analysis for $SBP_{drop\_rate\_0\text{-}15}$). Model 3 adjusts for age, sex, and baroreflex sensitivity. Model 4 adjusts for age, sex, and baseline blood pressure. *P*-values below 0.05 were considered statistically significant. Differences between frailty categories (nonfrail, prefrail, and frail) were assessed using logistic regression analysis, adjusting for age and sex.

RESULTS

Table presents the characteristics of the 168 geriatric outpatients (59 and 109 from respectively the Bronovo and COGA cohorts) included in the analyses. The

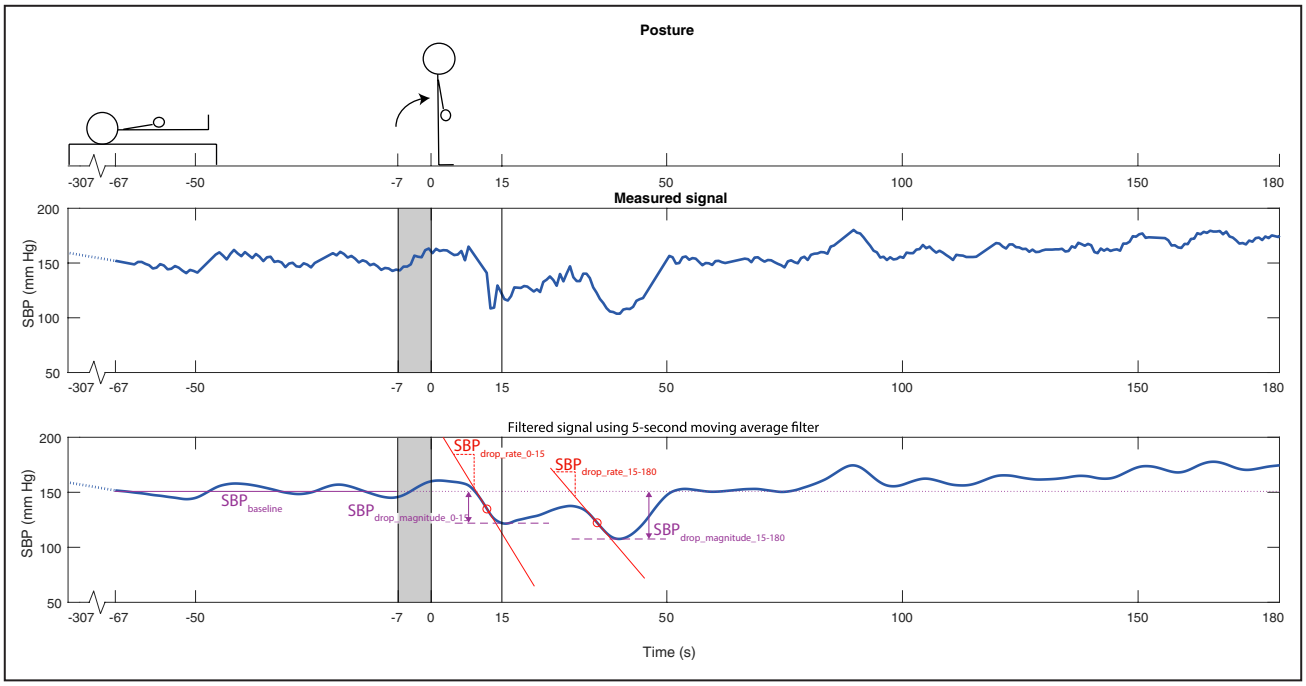

Figure 1. Demonstration of systolic blood pressure (SBP) parameter computation (adapted from Mol et al[5]).
The figure is an example of a systolic blood pressure (SBP) curve. Diastolic blood pressure (DBP) parameters are computed similarly.

mean age of patients was 81.4 years (SD 7.0), 55.4% of the patients were female and 83.5% of the patients were living at home. Mean supine resting SBP and DBP were 139 mm Hg (SD 28.8) and 70.8 mm Hg (SD 13.3), respectively, and 67.1% of the patients had OH as assessed using continuous BP measurement. Mean and median frailty scores according to the Fried criteria and the 4 frailty markers were 1.92 (SD 1.30) and 2.0 (interquartile range 0.0–2.0), respectively, and 35.2% of the population reported at least 1 fall in the past year with a median number of falls of 1 (interquartile range 0–3). Patient characteristics stratified for the different quartiles of all BP parameters are listed in Tables S1 through S8.

Figure 2 shows the association of the BP parameters with frailty and number of falls for models 1 to 4, Tables S9 through S12 list the strengths and confidence intervals of these associations, and Tables S13 and S14 show the association between BP parameters and frailty categories (nonfrail, prefrail, or frail).

The following BP parameters were associated with frailty score according to the Fried criteria: $SBP_{drop\_rate\_0\text{-}15}$ (β 0.27; 95% CI, 0.05–0.48; *P*=0.015), $SBP_{drop\_magnitude\_15\text{-}180}$ (β 0.27; 95% CI, 0.05–0.495; *P*=0.016), and $DBP_{drop\_magnitude\_15\text{-}180}$ (β 0.37; 95% CI 0.15–0.60; *P*<0.001). All other BP parameters showed no association with frailty score according to the Fried criteria.

The following BP parameters were associated with frailty score according to the 4 frailty markers: $SBP_{drop\_rate\_0\text{-}15}$ (β 0.30; 95% CI, 0.11–0.49; *P*=0.003) and $DBP_{drop\_rate\_0\text{-}15}$ (β 0.21; 95% CI, 0.03–0.40; *P*=0.024). All other BP parameters showed no association with frailty score according to the 4 frailty markers.

The following BP parameters were associated with number of falls: $SBP_{drop\_rate\_0\text{-}15}$ (β 1.09; 95% CI, 0.19–1.20; *P*=0.018), $SBP_{drop\_rate\_15\text{-}180}$ (β 1.25; 95% CI, 0.54–1.95; *P*<0.001), and $DBP_{drop\_magnitude\_0\text{-}15}$ (β 0.956; 95% CI, 0.18–1.95; *P*=0.016). All other BP parameters showed no association with number of falls.

Adjusting the results for the complementary BP parameter (eg, adjusting for $SBP_{drop\_magnitude\_0\text{-}15}$ in the analysis for $SBP_{drop\_rate\_0\text{-}15}$) in model 2 did not change the significance of the associations except for the association between $DBP_{drop\_magnitude\_0\text{-}15}$ and number of falls, which did not remain significant. After adjustment for baroreflex sensitivity in model 3, the association between $DBP_{drop\_rate\_0\text{-}15}$ and number of falls became significant, but the association between $DBP_{drop\_magnitude\_0\text{-}15}$ and number of falls lost significance. Furthermore, the association between $DBP_{drop\_rate\_0\text{-}15}$ and the 4 frailty markers lost significance, whereas the association between $DBP_{drop\_rate\_15\text{-}180}$ and the 4 frailty markers became significant. Adjusting for baseline BP did not change the associations except for the association between $DBP_{drop\_rate\_0\text{-}15}$ and frailty according to the Fried criteria, which became significant. The association between $DBP_{drop\_magnitude\_0\text{-}15}$ and number of falls lost statistical significance, whereas the association between

Table. Patient Characteristics

	N	Bronovo (N=59)	N	COGA (N=109)	N	All (N=168)
Sociodemographics						
Age, y, mean (SD)	59	80.8 (7.1)	109	81.7 (7.0)	168	81.4 (7.0)
Female, n (%)	59	33 (55.9)	109	60 (55.0)	168	93 (55.4)
Living at home, n (%)	59	47 (79.7)	105	90 (85.7)	164	137 (83.5)
Health characteristics						
Currently smoking, n (%)	59	9 (15.3)	103	13 (12.6)	162	22 (13.6)
Excessive alcohol use, n (%)*	59	6 (10.2)	72	6 (8.3)	131	12 (9.2)
Multimorbidity, n (%)†	57	20 (35.1)	104	50 (48.1)	161	70 (43.5)
BMI, mean (SD)	58	26.3 (4.9)	105	25.7 (4.5)	163	25.9 (4.6)
MMSE, median (IQR)	59	26.5 (25.0–29.0)	100	26.0 (23.0–28.0)	159	27.0 (24.0–29.0)
No. of medication, median (IQR)	58	5.4 (4.8–7.3)	104	7.0 (4.0–9.0)	162	6.0 (4.0–6.0)
Supine resting blood pressure and heart rate						
SBP, mean (SD), mm Hg	59	148.2 (25.8)	109	132.7 (27.0)	168	138.1 (27.6)
DBP, mean (SD), mm Hg	59	74.3 (15.7)	109	68.6 (11.2)	168	70.6 (13.2)
Pulse pressure, mean (SD), mm Hg	59	73.9 (20.5)	109	64.1 (19.5)	168	67.6 (20.4)
HR, mean (SD), beats/min	59	72.1 (12.5)	109	70.3 (12.0)	168	70.9 (12.2)
Orthostatic blood pressure and heart rate						
OH, n (%)	55	37 (67.3)	109	73 (67.0)	164	110 (67.1)
$SBP_{drop\_rate\_0\text{-}15}$, median (IQR) mm Hg/s	59	4.80 (2.54–7.55)	109	2.53 (0.86–4.97)	168	3.08 (1.39–5.79)
$SBP_{drop\_rate\_15\text{-}180}$, median (IQR) mm Hg/s	59	3.15 (2.06–5.72)	109	2.96 (2.13–4.48)	168	2.98 (2.08–4.81)
$SBP_{drop\_magnitude\_0\text{-}15}$, mean (SD) mm Hg	59	27.8 (23.3)	109	27.6 (24.3)	168	27.6 (23.9)
$SBP_{drop\_magnitude\_15\text{-}180}$, mean (SD) mm Hg	59	24.1 (24.7)	109	26.4 (31.3)	168	25.6 (29.1)
HR increase, mean (SD) beats/min per s	59	12.5 (7.7)	109	14.8 (15.6)	168	12.9 (12.8)
Frailty						
Fried frailty score, mean (SD)	45	1.53 (1.30)	85	2.13 (1.20)	130	1.92 (1.30)
Nonfrail, n (%)	45	13 (28.9)	85	6 (7.1)	130	19 (15.6)
Prefrail, n (%)	45	22 (48.9)	85	46 (54.1)	130	68 (52.3)
Frail, n (%)	45	10 (22.2)	85	33 (38.8)	130	43 (33.1)
Four frailty markers, median (IQR)‡	57	2.0 (0.0–2.0)	91	2.0 (0.0–2.0)	148	2.0 (0.0–2.0)
Nonfrail, n (%)	57	25 (43.9)	91	32 (35.2)	148	57 (38.5)
Prefrail, n (%)	57	23 (40.4)	91	39 (42.9)	148	62 (41.9)
Frail, n (%)	57	9 (15.8)	91	20 (22.0)	148	29 (19.6)
Falls						
Falls in past year, n (%)	59	24 (40.7)	100	32 (32.0)	159	56 (35.2)
Number of falls, median (IQR)	53	1.0 (0.0–2.0)	92	2.0 (0.0–3.0)	145	1.0 (0.0–3.0)

BMI indicates body mass index; COGA, Center of Geriatrics of Amsterdam; DBP, diastolic blood pressure; HR, heart rate; IQR, interquartile range; MMSE, Mini-Mental State Examination; OH, orthostatic hypotension; SBP, systolic blood pressure; $SBP_{drop\_magnitude}$, the difference between baseline SBP and the lowest measured SBP value in the standing intervals at 0 to 15 and 15 to 180 seconds; and SBP_{drop_rate}, the steepness of the steepest negative tangent line in the standing intervals (0–15 and 15–180 seconds).

*Excessive alcohol use was defined as >14 units per week for women and >21 units per week for men.

†Multimorbidity was defined as ≥2 of the following diseases: chronic obstructive pulmonary disease, diabetes mellitus, hypertension, malignancy, myocardial infarction, Parkinson disease, or rheumatoid/(osteo)arthritis.

‡Number of items from the 4 frailty markers present.

$DBP_{drop\_rate\_15\text{-}180}$ and number of falls became statistically significant.

$HR_{max\ increase}$ was negatively associated with the number of falls but not with frailty (β −1.21; 95% CI, −1.92 to −0.49; P<0.001). Baroreflex sensitivity was not significantly associated with either frailty or the number of falls.

DISCUSSION

In a group of geriatric outpatients who underwent continuous BP measurements, orthostatic SBP drop rate was associated with frailty according to the 4 frailty markers and number of falls rather than SBP drop magnitude or DBP drop rate or magnitude, and

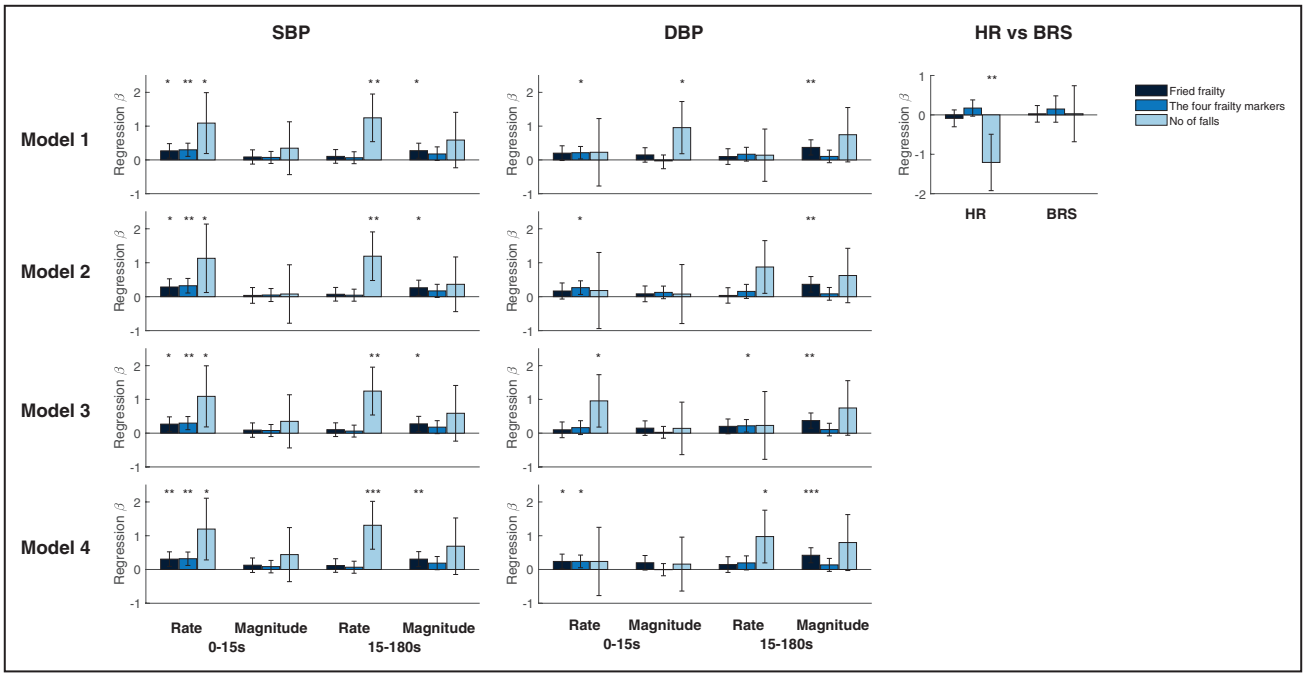

Figure 2. Association between BP, HR, and BRS parameters and frailty and number of falls.
The regression βs of the multiple linear regression analyses are shown with normalized SBP, DBP, HR, and BRS parameters. Model 1 adjusts for age and sex. Model 2 additionally adjusts for the complementary BP parameter (eg, $SBP_{drop\_magnitude\_0\text{-}15}$ in the analysis for $SBP_{drop\_rate\_0\text{-}15}$). Model 3 adjusts for age, sex, and baroreflex sensitivity. Model 4 adjusts for age, sex, and baseline BP. The error bars indicate the 95% CI. Statistical significance is shown as **P*<0.05, ***P*<0.01 and ****P*<0.001, respectively. BP indicates blood pressure; BRS, baroreflex sensitivity; DBP, diastolic blood pressure; HR, heart rate; and SBP, systolic blood pressure.

DBP drop magnitude was most strongly associated with frailty according to the Fried criteria. Baroreflex sensitivity was not associated with frailty or number of falls.

BP Drop Rate Versus Magnitude

The results partly support the hypothesis that BP drop rate rather than BP drop magnitude is associated with frailty and number of falls. No causality can be inferred from these results. A potential explanation for the results is that a rapid BP drop (ie, high BP drop rate) may particularly reflect a challenge to the baroreflex due to an intrinsic baroreflex time delay,[8,9] which might cause a temporary decrease of cardiac output[10] and brain hypoperfusion,[11] which might lead to a poor clinical outcome.[29] Support for causality of this relationship should be sought in further prospective intervention studies investigating the predictive value of SBP drop rate for future frailty and falls. The potential attenuating role of cerebral autoregulation in this relationship should be investigated in further studies using simultaneous measurements of continuous blood pressure and cerebral blood flow using transcranial Doppler measurements during orthostatic challenges. Alternatively, a causative relationship in the opposite direction might play a role, as frailty and previous falls may lead to fear of falls and lower physical activity, resulting in rapid BP drops by general deconditioning and loss of muscle mass.

Mutual adjustment for BP drop rate and magnitude did not change the overall results, indicating the robustness of the associations found. Adjustment for baroreflex sensitivity mainly changed the association of $DBP_{drop\_rate\_0\text{-}15}$ and $DBP_{drop\_magnitude\_0\text{-}15}$ with number of falls to significant and nonsignificant, respectively, suggesting that BP drop rate particularly represents a challenge to the baroreflex irrespective of baroreflex sensitivity.

Baroreflex Sensitivity

No association was found between baroreflex sensitivity and frailty or number of falls. This may indicate that baroreflex sensitivity has no major role in the prevention of frailty and falls or that there was ceiling effect due to a relatively high baroreflex sensitivity in most patients. Alternatively, a more robust measure could be used for baroreflex sensitivity. In the present study, data from a single postural change were available, but baroreflex sensitivity may be measured more robustly using transfer function analysis or the sequence method analysis on blood pressure and heart rate data acquired during rhythmically repeated postural changes.[6,30] The absence of an association of baroreflex sensitivity with frailty and number of falls therefore needs to be further established.

SBP Versus DBP

SBP drop rate was more strongly associated with number of falls and frailty than DBP drop rate, and DBP drop magnitude showed stronger associations than SBP drop magnitude, which might indicate that DBP plays a role in maintaining a minimum level of cerebral perfusion. Cerebral autoregulation might potentially enhance cerebral perfusion depending on the superimposed pulse pressure (ie, the difference between SBP and DPB), as suggested by a study reporting that pulse pressure was positively associated with cortical gray matter volume in patients with atherosclerotic disease whereas DBP was not.[31]

Delayed BP Drops

The strong association of SBP drop rate with number of falls in the 15- to 180-second interval indicates that rapid SBP drops occurring after 15 seconds after standing up are of special clinical relevance. This might be due to a decrease in patient alertness for fall risk (eg, by lightheadedness) after 15 seconds if no symptoms occurred in the first 15 seconds, leading to lower tendency to use fall prevention strategies (eg, leg muscle tensing, crossing the legs, holding a chair). However, this hypothesis needs to be tested in future research.

Fried Criteria Versus the 4 Frailty Markers

In the present study a modified version of the Fried criteria as well as the 4 frailty markers were used. The Fried criteria and the 4 frailty markers represent different constructs, the 4 frailty markers being more subjective than the Fried criteria. This was reflected by the different associations of the BP parameters with 2 of the frailty criteria: DBP drop magnitude in the 15- to 180-second interval had the strongest association with frailty according to the Fried criteria, whereas SBP drop rate in the 0- to 15-second interval had the strongest association with frailty according to the 4 frailty markers. This might indicate that short-term rapid BP drops are particularly related to the perception of orthostatic symptoms and therefore affect subjectively assessed frailty components such as mobility and activities of daily living. More persistent BP drops, on the other hand, might particularly affect more objective frailty components such as gait speed and handgrip strength.

Strength and Limitations

The strength of this study is that it systematically compares the clinical relevance of BP drop rate, BP drop magnitude, and baroreflex sensitivity in a population of geriatric outpatients. Furthermore, it elucidates the value of continuous BP measurements because these are necessary to compute BP drop rate and BP drop magnitude in the 0- to 15-second interval. Limitations include the cross-sectional design of the study, limiting the conclusions that can be drawn about the causal nature of the relationship, and the use of subjectively measured number of falls. The baroreflex sensitivity measure used in the present study did not discriminate between the effect of blood pressure drop and heart rate increase.

Perspectives

The results of this study advocate the use of continuous BP measurements in geriatric outpatients and identify BP drop rate as a clinically relevant parameter to assess in these patients. Potential future applications include the use of BP drop rate to predict frailty and falls related to orthostatic BP drop and to evaluate the efficacy of OH treatment.

CONCLUSIONS

BP drop rate after standing up is associated with frailty and number of falls in geriatric outpatients and may reflect the imposed challenge to the baroreflex rather than BP drop magnitude. The results indicate that BP drop rate is particularly related to clinical outcome.

ARTICLE INFORMATION

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Disclosures

None.

Supplementary Material

Tables S1–S14

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SUPPLEMENTAL MATERIAL

Table S1. Patient characteristics, stratified by quartiles of $SBP_{drop\_rate\_0\text{-}15}$

	First quartile n=42	Second quartile n=42	Third quartile n=42	Fourth quartile n=42	p-value
Age, mean (SD)	82.7 (7.0)	81.4 (6.5)	81.2 (7.1)	80.3 (7.6)	0.03
Female, n (%)	26 (61.9)	20 (47.6)	24 (57.1)	23 (54.8)	0.74
Living home, n (%)	34 (81)	34 (81)	35 (83.3)	34 (81)	0.74
Currently smoking, n (%)	6 (14.3)	5 (11.9)	6 (14.3)	5 (11.9)	0.55
Excessive alcohol use*, n (%)	5 (11.9)	2 (4.8)	5 (11.9)	0 (0)	0.37
Multi-morbidity†, n (%)	17 (40.5)	17 (40.5)	19 (45.2)	17 (40.5)	0.74
BMI, mean (SD)	26.1 (5.7)	25.4 (4.1)	26.0 (4.0)	26.3 (4.5)	0.60
MMSE, median (IQR)	27 (24-28)	27 (25-28)	27 (24-29)	26 (22.3-29)	0.23
No. of medication, median (IQR)	6 (4-9)	6 (4-8)	6 (2.8-8)	6 (4-8.3)	0.29

BMI, body mass index; IQR, interquartile range; MMSE, Mini-Mental State Examination. *Excessive alcohol use was defined as >14 units per week for females and >21 units per week for males. † Multimorbidity was defined as ≥ 2 diseases of the following: chronic obstructive pulmonary disease, diabetes mellitus, hypertension, malignancy, myocardial infarction, Parkinson disease, or rheumatoid/(osteo)arthritis

Table S2. Patient characteristics, stratified by quartiles of $SBP_{drop\_magnitude\_0\text{-}15}$

	First quartile n=42	Second quartile n=42	Third quartile n=42	Fourth quartile n=42	p-value
Age, mean (SD)	80.9 (7.0)	83.5 (6.9)	80.6 (7.8)	80.5 (6.2)	0.63
Female, n (%)	27 (64.3)	19 (45.2)	23 (54.8)	24 (57.1)	0.80
Living home, n (%)	33 (78.6)	31 (73.8)	37 (88.1)	36 (85.7)	0.30
Currently smoking, n (%)	8 (19.1)	4 (9.5)	5 (11.9)	5 (11.9)	0.40
Excessive alcohol use, n (%)	2 (4.8)	3 (7.1)	2(4.8)	5 (11.9)	0.27
Multi-morbidity, n (%)	17(40.5)	16 (38.1)	16 (38.1)	21 (50)	0.35
BMI, mean (SD)	25.4 (5.7)	25.4 (3.9)	26.8 (4.7)	26.1 (4.0)	0.33
MMSE, median (IQR)	26 (22.5-28)	27 (24.5-28)	27 (23.8-29)	28 (25-29)	0.05
No. of medication, median (IQR)	7 (5-11)	6 (4-8.3)	4 (3-8)	6 (5-8)	0.49

BMI, body mass index; IQR, interquartile range; MMSE, Mini-Mental State Examination. *Excessive alcohol use was defined as >14 units per week for females and >21 units per week for males. † Multimorbidity was defined as ≥ 2 diseases of the following: chronic obstructive pulmonary disease, diabetes mellitus, hypertension, malignancy, myocardial infarction, Parkinson disease, or rheumatoid/(osteo)arthritis

Table S3. Patient characteristics, stratified by quartiles of $DBP_{drop\_rate\_0\text{-}15}$

	First quartile n=42	Second quartile n=42	Third quartile n=42	Fourth quartile n=42	p-value
Age, mean (SD)	81.7 (7.1)	81.3 (6.2)	82.4 (7.2)	80.1 (7.6)	0.50
Female, n (%)	24 (57.1)	20 (47.6)	26 (61.9)	23 (54.8)	0.84
Living home, n (%)	33 (78.6)	36 (85.7)	33 (78.6)	35 (83.3)	0.75
Currently smoking, n (%)	5 (11.9)	7 (16.7)	7 (16.7)	3 (7.1)	0.60
Excessive alcohol use, n (%)	5 (11.9)	2 (4.8)	1 (2.4)	4 (9.5)	0.71
Multi-morbidity, n (%)	17 (40.5)	22 (52.4)	16 (38.1)	15 (35.7)	0.50
BMI, mean (SD)	26.4 (6.0)	25.4 (3.9)	26.2 (4.1)	25.8 (4.3)	0.71
MMSE, median (IQR)	26 (24.5-28)	26.5 (24-29)	27 (24-28)	27 (22-29)	0.06
No. of medication, median (IQR)	6 (4-9.3)	6 (5-8)	6 (3.3-8)	6 (3.5-7.5)	0.29

BMI, body mass index; IQR, interquartile range; MMSE, Mini-Mental State Examination. *Excessive alcohol use was defined as >14 units per week for females and >21 units per week for males. † Multimorbidity was defined as ≥ 2 diseases of the following: chronic obstructive pulmonary disease, diabetes mellitus, hypertension, malignancy, myocardial infarction, Parkinson disease, or rheumatoid/(osteo)arthritis

Table S4. Patient characteristics, stratified by quartiles of $DBP_{drop\_magnitude\_0\text{-}15}$

	First quartile n=42	Second quartile n=42	Third quartile n=42	Fourth quartile n=42	p-value
Age, mean (SD)	80.6 (7.1)	80.6 (7.5)	81.3 (6.3)	83.0 (7.1)	0.77
Female, n (%)	25 (59.5)	18 (42.9)	26 (61.9)	24 (57.1)	0.82
Living home, n (%)	34 (81)	29 (69.1)	36 (85.7)	38 (90.5)	0.37
Currently smoking, n (%)	8 (19.1)	5 (11.9)	4 (9.5)	5 (11.9)	0.25
Excessive alcohol use, n (%)	2 (4.8)	3 (7.1)	3 (7.1)	4 (9.5)	0.05
Multi-morbidity, n (%)	18 (42.9)	15 (35.7)	18 (42.9)	19 (45.2)	0.56
BMI, mean (SD)	25.7 (5.6)	25.5 (3.8)	26.1 (4.3)	26.5 (4.7)	0.13
MMSE, median (IQR)	27 (24-28)	27 (22.5-29)	27 (24.3-28.8)	26 (24-29)	0.23
No. of medication, median (IQR)	6.5 (5-9)	5.5 (3.5-7.5)	6.5 (3-8.5)	6 (4.5-8)	0.87

BMI, body mass index; IQR, interquartile range; MMSE, Mini-Mental State Examination. *Excessive alcohol use was defined as >14 units per week for females and >21 units per week for males. † Multimorbidity was defined as ≥ 2 diseases of the following: chronic obstructive pulmonary disease, diabetes mellitus, hypertension, malignancy, myocardial infarction, Parkinson disease, or rheumatoid/(osteo)arthritis

Table S5. Patient characteristics, stratified by quartiles of $SBP_{drop\_rate\_15\text{-}180}$

	First quartile n=42	Second quartile n=42	Third quartile n=42	Fourth quartile n=42	p-value
Age, mean (SD)	82.6 (6.7)	81.6 (4.6)	81.6 (8.2)	79.7 (8.0)	0.07
Female, n (%)	23 (54.8)	23 (54.8)	28 (66.7)	19 (45.2)	0.75
Living home, n (%)	32 (76.2)	35 (83.3)	34 (81)	36 (85.7)	0.16
Currently smoking, n (%)	5 (11.9)	4 (9.5)	7 (16.7)	6 (14.3)	0.40
Excessive alcohol use, n (%)	6 (14.3)	3 (7.1)	1 (2.4)	2 (4.8)	0.17
Multi-morbidity, n (%)	19 (45.2)	19 (45.2)	14 (33.3)	18 (42.9)	0.57
BMI, mean (SD)	25.5 (4.5)	25.4 (4.2)	26.3 (4.6)	26.5 (5.3)	0.09
MMSE, median (IQR)	26 (24-28)	26 (24-28)	25 (22-29)	28 (25.3-29)	0.49
No. of medication, median (IQR)	6 (3-9)	6 (4-8)	6 (3.3-7)	6.5 (4-9)	0.23

BMI, body mass index; IQR, interquartile range; MMSE, Mini-Mental State Examination. *Excessive alcohol use was defined as >14 units per week for females and >21 units per week for males. † Multimorbidity was defined as ≥ 2 diseases of the following: chronic obstructive pulmonary disease, diabetes mellitus, hypertension, malignancy, myocardial infarction, Parkinson disease, or rheumatoid/(osteo)arthritis

Table S6. Patient characteristics, stratified by quartiles of $SBP_{drop\_magnitude\_15\text{-}180}$

	First quartile n=42	Second quartile n=42	Third quartile n=42	Fourth quartile n=42	p-value
Age, mean (SD)	82.8 (7.3)	79.8 (6.4)	83.0 (7.7)	80.0 (6.3)	0.61
Female, n (%)	18 (42.9)	22 (52.4)	26 (61.9)	27 (64.3)	0.03
Living home, n (%)	35 (83.3)	34 (81)	34 (81)	34 (81)	0.23
Currently smoking, n (%)	5 (11.9)	6 (14.3)	4 (9.5)	7 (16.7)	0.60
Excessive alcohol use, n (%)	5 (11.9)	1 (2.4)	3 (7.1)	3 (7.1)	0.68
Multi-morbidity, n (%)	18 (42.9)	17 (40.5)	17 (40.5)	18 (42.9)	1.00
BMI, mean (SD)	25.0 (5.4)	25.2 (4.1)	25.8 (4.2)	27.8 (4.4)	0.09
MMSE, median (IQR)	27 (23.8-28)	27 (23-28.8)	27 (24.5-29)	27 (25-28.8)	NA
No. of medication, median (IQR)	6.5 (3-9)	6 (4-8)	6 (4-8)	7 (4.8-9)	0.60

BMI, body mass index; IQR, interquartile range; MMSE, Mini-Mental State Examination; NA, not applicable.
*Excessive alcohol use was defined as >14 units per week for females and >21 units per week for males.
†Multimorbidity was defined as ≥ 2 diseases of the following: chronic obstructive pulmonary disease, diabetes mellitus, hypertension, malignancy, myocardial infarction, Parkinson disease, or rheumatoid/(osteo)arthritis.

Table S7. Patient characteristics, stratified by quartiles of $DBP_{drop\_rate\_15\text{-}180}$

	First quartile n=42	Second quartile n=42	Third quartile n=42	Fourth quartile n=42	p-value
Age, mean (SD)	83.4 (6.2)	80.6 (6.3)	81.2 (7.4)	80.4 (8.0)	0.21
Female, n (%)	23 (54.8)	19 (45.2)	27 (64.3)	24 (57.1)	0.57
Living home, n (%)	33 (78.6)	31 (73.8)	37 (88.1)	36 (85.7)	0.30
Currently smoking, n (%)	6 (14.3)	7 (16.7)	4 (9.5)	5 (11.9)	0.40
Excessive alcohol use, n (%)	2 (4.8)	6 (14.3)	4 (9.5)	0 (0)	0.60
Multi-morbidity, n (%)	24 (57.1)	19 (45.2)	15 (35.7)	12 (28.6)	0.01
BMI, mean (SD)	25.3 (4.7)	26.4 (4.5)	26.4 (5.7)	25.6 (3.7)	0.79
MMSE, median (IQR)	26 (24-28)	27 (24-28)	27 (23-29)	27.5 (25-29)	0.08
No. of medication, median (IQR)	6 (4.5-8)	6 (3.5-8.5)	6 (4-8.3)	6 (4-8)	0.29

BMI, body mass index; IQR, interquartile range; MMSE, Mini-Mental State Examination. *Excessive alcohol use was defined as >14 units per week for females and >21 units per week for males. † Multimorbidity was defined as ≥ 2 diseases of the following: chronic obstructive pulmonary disease, diabetes mellitus, hypertension, malignancy, myocardial infarction, Parkinson disease, or rheumatoid/(osteo)arthritis

Table S8. Patient characteristics, stratified by quartiles of $DBP_{drop\_magnitude\_15\text{-}180}$

	First quartile n=42	Second quartile n=42	Third quartile n=42	Fourth quartile n=42	p-value
Age, mean (SD)	82.7 (7.5)	81.1 (6.9)	81.4 (6.9)	80.3 (7.0)	0.11
Female, n (%)	19 (45.2)	18 (42.9)	29 (69.1)	27 (64.3)	0.19
Living home, n (%)	33 (78.6)	32 (76.2)	37 (88.1)	35 (83.3)	0.36
Currently smoking, n (%)	6 (14.3)	4 (9.5)	7 (16.7)	5 (11.9)	1.00
Excessive alcohol use, n (%)	4 (9.5)	2 (4.8)	2 (4.8)	4 (9.5)	1.00
Multi-morbidity, n (%)	17 (40.5)	16 (38.1)	23 (54.8)	14 (33.3)	0.93
BMI, mean (SD)	25.3 (5.4)	25.5 (4.0)	26.2 (3.8)	26.8 (5.0)	0.02
MMSE, median (IQR)	27 (24-28)	25 (22-28)	27 (24.3-29)	27 (25-29)	0.74
No. of medication, median (IQR)	6 (4-8.5)	6 (4-8)	7 (4-8.5)	5.5 (4-8)	0.90

BMI, body mass index; IQR, interquartile range; MMSE, Mini-Mental State Examination. *Excessive alcohol use was defined as >14 units per week for females and >21 units per week for males. † Multimorbidity was defined as ≥ 2 diseases of the following: chronic obstructive pulmonary disease, diabetes mellitus, hypertension, malignancy, myocardial infarction, Parkinson disease, or rheumatoid/(osteo)arthritis

Table S9. Association between BP and HR parameters and frailty and number of falls, corrected for age and sex.

	Fried frailty score (n=130)	Four frailty criteria (n=148)	No of falls (n=145)
0 – 15 seconds			
SBP drop rate			
B (95% CI)	0.268 (0.054 – 0.482)	0.299 (0.105 – 0.494)	1.090 (0.188 – 1.992)
p-value	0.015*	0.003**	0.018*
SBP drop magnitude			
B (95% CI)	0.087 (-0.124 – 0.298)	0.073 (-0.105 – 0.251)	0.347 (-0.436 – 1.129)
p-value	0.416	0.421	0.383
DBP drop rate			
B (95% CI)	0.200 (-0.018 – 0.418)	0.213 (0.029 – 0.398)	0.226 (-0.773 – 1.224)
p-value	0.071	0.024*	0.655
DBP drop magnitude			
B (95% CI)	0.147 (-0.067 – 0.361)	-0.029 (-0.203 – 0.146)	0.956 (0.183 – 1.729)
p-value	0.177	0.746	0.016*
15 – 180 seconds			
SBP drop rate			
B (95% CI)	0.104 (-0.099 – 0.306)	0.064 (-0.112 – 0.241)	1.246 (0.540 – 1.951)
p-value	0.312	0.474	0.001**
SBP drop magnitude			
B (95% CI)	0.273 (0.051 – 0.495)	0.176 (-0.015 – 0.368)	0.588 (-0.233 – 1.409)
p-value	0.016*	0.071	0.159
DBP drop rate			
B (95% CI)	0.099 (-0.133 – 0.331)	0.168 (-0.036 – 0.373)	0.140 (-0.634 – 0.914)
p-value	0.400	0.106	0.721
DBP drop magnitude			
B (95% CI)	0.370 (0.145 – 0.595)	0.103 (-0.083 – 0.290)	0.746 (-0.059 – 1.551)
p-value	0.001**	0.276	0.069
Heart rate increase			
B (95% CI)	-0.088 (-0.302 – 0.126)	0.173 (-0.033 – 0.380)	-1.207 (-1.923 – -0.492)
p-value	0.415	0.099	0.001**
Baroreflex sensitivity			
B (95% CI)	0.027 (-0.184 – 0.237)	0.149 (-0.186 – 0.483)	0.029 (-0.682 – 0.740)
p-value	0.801	0.381	0.935

The BP parameters were normalized. SBP, systolic blood pressure; DBP, diastolic blood pressure; B, regression beta; CI, confidence interval. *p< 0.05. **p<0.01.

Table S10. Association between BP parameters and frailty and number of falls, corrected for age, sex and complementary BP parameter (e.g. $SBP_{drop\_magnitude\_0\text{-}15}$ in analysis for $SBP_{drop\_rate\_0\text{-}15}$).

	Fried frailty score (n=130)	Four frailty criteria (n=148)	No of falls (n=145)
0 – 15 seconds			
SBP drop rate			
B (95% CI)	0.285 (0.044 - 0.526)	0.322 (0.108 - 0.537)	1.130 (0.122 – 2.139)
p-value	0.021*	0.004*	0.028*
SBP drop magnitude			
B (95% CI)	0.037 (-0.195 - 0.269)	0.049 (-0.143 – 0.240)	0.078 (-0.782 – 0.939)
p-value	0.752	0.617	0.857
DBP drop rate			
B (95% CI)	0.167 (-0.070 – 0.404)	0.266 (0.066 – 0.467)	0.181 (-0.940 – 1.302)
p-value	0.167	0.010*	0.750
DBP drop magnitude			
B (95% CI)	0.083 (-0.149 – 0.315)	0.126 (-0.060 – 0.312)	0.077 (-0.792 – 0.946)
p-value	0.479	0.184	0.861
15 – 180 seconds			
SBP drop rate			
B (95% CI)	0.071 (-0.130 - 0.272)	0.044 (-0.133 – 0.221)	1.192 (0.476 – 1.908)
p-value	0.484	0.624	0.001**
SBP drop magnitude			
B (95% CI)	0.262 (0.037 - 0.486)	0.170 (-0.024 – 0.364)	0.364 (-0.441 – 1.170)
p-value	0.023*	0.085	0.373
DBP drop rate			
B (95% CI)	0.036 (-0.191 – 0.264)	0.155 (-0.052 – 0.362)	0.874 (0.098 – 1.651)
p-value	0.752	0.140	0.28*
DBP drop magnitude			
B (95% CI)	0.364 (0.135 – 0.593)	0.083 (-0.104 – 0.271)	0.623 (-0.178 – 1.425)
p-value	0.002*	0.382	0.126

The BP parameters were normalized. SBP, systolic blood pressure; DBP, diastolic blood pressure; B, regression beta; CI, confidence interval. *p< 0.05. **p<0.01.

Table S11. Association between BP parameters and frailty and number of falls, corrected for age, sex and baroreflex sensitivity.

	Fried frailty score (n=130)	Four frailty criteria (n=148)	No of falls (n=145)
0 – 15 seconds			
SBP drop rate			
B (95% CI)	0.268 (0.053 – 0.483)	0.298 (0.103 – 0.492)	1.090 (0.185 – 1.995)
p-value	0.015*	0.003*	0.019*
SBP drop magnitude			
B (95% CI)	0.091 (-0.122 – 0.304)	0.079 (-0.100 – 0.257)	0.350 (-0.437 – 1.137)
p-value	0.400	0.385	0.381
DBP drop rate			
B (95% CI)	0.202 (-0.017 – 0.420)	0.218 (0.033-0.403)	0.229 (-0.775 – 1.233)
p-value	0.070	0.021	0.653
DBP drop magnitude			
B (95% CI)	0.149 (-0.066 – 0.364)	0.025 (-0.150 – 0.200)	0.142 (-0.636 – 0.919)
p-value	0.173	0.774	0.719
15 – 180 seconds			
SBP drop rate			
B (95% CI)	0.103 (-0.100 – 0.306)	0.062 (-0.115 – 0.238)	1.246 (0.538-1.955)
p-value	0.316	0.492	0.001**
SBP drop magnitude			
B (95% CI)	0.275 (0.052 – 0.498)	0.178 (-0.014 – 0.370)	0.589 (-0.236 – 1.413)
p-value	0.016*	0.069	0.160
DBP drop rate			
B (95% CI)	0.099 (-0.134 – 0.332)	0.164 (-0.041 – 0.369)	0.956 (0.180 – 1.732)
p-value	0.401	0.117	0.016*
DBP drop magnitude			
B (95% CI)	0.372 (0.147 – 0.598)	0.107 (-0.080 – 0.293)	0.746 (-0.062 – 1.555)
p-value	0.001**	0.262	0.070

The BP parameters were normalized. SBP, systolic blood pressure; DBP, diastolic blood pressure; B, regression beta; CI, confidence interval. *p< 0.05. **p<0.01.

Table S12. Association between BP parameters and frailty and number of falls, corrected for age, sex and baseline blood pressure.

	Fried frailty score (n=130)	Four frailty criteria (n=148)	No of falls (n=145)
0 – 15 seconds			
SBP drop rate			
B (95% CI)	0.307 (0.092-0.523)	0.319 (0.120 – 0.517)	1.197 (0.283 – 2.111)
p-value	0.005**	0.002**	0.011*
SBP drop magnitude			
B (95% CI)	0.127 (-0.088 – 0.341)	0.085 (-0.100 – 0.269)	0.441 (-0.360 – 1.241)
p-value	0.244	0.365	0.279
DBP drop rate			
B (95% CI)	0.238 (0.022 – 0.455)	0.239 (0.052 – 0.427)	0.238 (-0.773 – 1.249)
p-value	0.031*	0.013*	0.642
DBP drop magnitude			
B (95% CI)	0.199 (-0.016 – 0.414)	-0.005 (-0.186 -0.175)	0.159 (-0.639 – 0.958)
p-value	0.069	0.952	0.694
15 – 180 seconds			
SBP drop rate			
B (95% CI)	0.117(-0.084 – 0.319)	0.067 (-0.111 – 0.245)	1.309 (0.600-2.018)
p-value	0.252	0.457	0.000**
SBP drop magnitude			
B (95% CI)	0.307 (0.084 – 0.529)	0.188 (-0.007 – 0.384)	0.689 (-0.148 – 1.526)
p-value	0.007**	0.059	0.106
DBP drop rate			
B (95% CI)	0.145 (-0.087 – 0.378)	0.195 (-0.013 – 0.403)	0.975 (0.195 – 1.756)
p-value	0.218	0.066	0.015*
DBP drop magnitude			
B (95% CI)	0.421 (0.199 – 0.644)	0.136 (-0.056 – 0.328)	0.798 (-0.031 – 1.626)
p-value	0.000**	0.164	0.059

The BP parameters were normalized. SBP, systolic blood pressure; DBP, diastolic blood pressure; B, regression beta; CI, confidence interval. *p< 0.05. **p<0.01.

Table S13. Association between BP parameters and Fried frailty categories, corrected for age and sex.

Fried frailty scale (n=130)	Non-frail vs. frail	Non-frail vs. Pre-frail	Pre-frail vs. frail
0 – 15 seconds			
SBP drop rate			
OR (95% CI)	4.292 (1.305 –14.085)	3.745 (1.172 - 11.905)	1.145 (0.762 - 1.724)
p-value	0.016 *	0.026*	0.515
SBP drop magnitude			
OR (95% CI)	1.297 (0.694 - 2.427)	1.520 (0.895 - 2.710)	0.853 (0.565 - 1.290)
p-value	0.415	0.154	0.452
DBP drop rate			
OR (95% CI)	1.626 (0.709 - 3.731)	1.502 (0.672 - 3.356)	1.082 (0.726 - 1.613)
p-value	0.251	0.321	0.699
DBP drop magnitude			
OR (95% CI)	1.070 (0.580 - 1.972)	1.066 (0.605 - 1.880)	1.003 (0.660 - 1.524)
p-value	0.829	0.824	0.989
15 – 180 seconds			
SBP drop rate			
OR (95% CI)	1.460 (0.735 - 2.899)	1.232 (0.649 - 2.342)	1.185 (0.803 - 1.748)
p-value	0.280	0.524	0.393
SBP drop magnitude			
OR (95% CI)	2.110 (1.093 - 5.319)	1.923 (0.919 - 4.032)	1.253 (0.804 - 1.953)
p-value	0.029*	0.083	0.320
DBP drop rate			
OR (95% CI)	2.457 (0.552 - 10.870)	2.500 (0.571 - 10.870)	0.983(0.639 - 1.513)
p-value	0.238	0.224	0.937
DBP drop magnitude			
OR (95% CI)	2.155 (0.969 - 4.808)	1.563 (0.747 - 3.268)	1.379 (0.852 - 2.237)
p-value	0.060	0.236	0.191

The BP parameters were normalized. SBP, systolic blood pressure; DBP, diastolic blood pressure; OR, odds ratio; CI, confidence interval. ORs relate to the odds of being in the more frail category relative to the less frail category per extra standardized unit of pressure drop rate or magnitude. *p< 0.05; **p<0.01.

Table S14. Association between BP parameters and frailty category according to the 4 frailty criteria, corrected for age and sex.

Fried frailty scale (n=130)	Non-frail vs. frail	Non-frail vs. Pre-frail	Pre-frail vs. frail
0 – 15 seconds			
SBP drop rate			
OR (95% CI)	2.404 (1.274 – 4.545)	1.996 (1.151 - 3.460)	1.203 (0.759 – 1.908)
p-value	0.007*	0.014*	0.430
SBP drop magnitude			
OR (95% CI)	1.098 (0.663 – 1.818)	1.218 (0.832 – 1.783)	0.902 (0.562 – 1.445)
p-value	0.717	0.310	0.666
DBP drop rate			
OR (95% CI)	1.901 (1.094 – 3.311)	1.309 (0.800 – 2.141)	1.454 (0.938 – 2.252)
p-value	0.023*	0.284	0.094
DBP drop magnitude			
OR (95% CI)	0.826 (0.503 – 1.357)	1.016 (0.700 – 1.475)	0.812 (0.509 – 1.295)
p-value	0.449	0.931	0.383
15 – 180 seconds			
SBP drop rate			
OR (95% CI)	1.105 (0.632 - 1.934)	1.232 (0.824- 1.842)	0.898 (0.546 – 1.475)
p-value	0.725	0.310	0.669
SBP drop magnitude			
OR (95% CI)	1.529 (0.883 – 2.646)	1.282 (0.840 – 1.961)	1.192 (0.722 – 1.965)
p-value	0.129	0.250	0.493
DBP drop rate			
OR (95% CI)	2.268 (0.840 – 6.135)	2.667 (1.045 – 6.803)	0.850 (0.518 – 1.400)
p-value	0.106	0.040*	0.522
DBP drop magnitude			
OR (95% CI)	1.226 (0.719 – 2.088)	1.198 (0.799 – 1.795)	1.023 (0.626 – 1.672)
p-value	0.455	0.383	0.928

The BP parameters were normalized. SBP, systolic blood pressure; DBP, diastolic blood pressure; OR, odds ratio; CI, confidence interval. ORs relate to the odds of being in the more frail category relative to the less frail category per extra standardized unit of pressure drop rate or magnitude. *p< 0.05; **p<0.01.

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