JAMDA 22 (2021) 1235–1241

JAMDA

journal homepage: www.jamda.com

Original Study

Delayed Blood Pressure Recovery After Standing Independently Predicts Fracture in Community-Dwelling Older People

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Keywords:
Orthostatic hypotension
blood pressure
fracture
falls

A B S T R A C T

Objectives: Orthostatic hypotension, characterized by delayed blood pressure (BP) recovery after standing, is a risk factor for falls but the longitudinal relationship with fracture is not yet known. The aim of this study was to examine the prospective risk of fracture associated with delayed BP recovery.
Design: Longitudinal study with 8-year follow-up.
Setting and Participants: More than 3000 (54% female) community-dwelling people aged ≥50 years from a large longitudinal study on ageing.
Methods: Orthostatic BP was measured using a finometer when standing from lying. Delayed BP recovery was defined as systolic BP ≥20 mm Hg lower and/or diastolic BP ≥10 mm Hg from the baseline value at 30, 60, and 90 seconds after standing. Participants with a fracture reported at any of waves 2 to 5 were defined as having incident fracture. Logistic regression models were used to estimate odds ratios (ORs) for the association between delayed BP recovery and incident fracture.
Results: Seven percent (212/3117) of participants sustained a fracture during follow-up. Delayed BP recovery at 30 seconds was a significant predictor of any fracture [OR 1.80, 95% confidence interval (CI) 1.28-2.53] and hip fracture (OR 4.44, 95% CI 2.03-9.71) in fully adjusted models. Delayed BP recovery at 30 seconds did not predict wrist or vertebral fracture. Delayed BP recovery at 60 seconds also predicted any fracture (OR 1.74, 95% CI 1.19-2.54) and hip fracture (OR 4.66, 95% CI 2.12-10.26) whereas delayed BP recovery at 90 seconds predicted any (OR 1.99, 95% CI 1.38-2.87), wrist (OR 1.87, 95% CI 1.19-2.95), and hip fracture (OR 3.39, 95% CI 1.45-7.93) in fully adjusted models.
Conclusion: and Implications: Delayed BP recovery independently predicts fracture in community-dwelling older people, is potentially modifiable, and can be measured in an ambulatory setting. Because of the morbidity and mortality associated with fractures, identification of such risk factors is crucial in order to inform preventative strategies.

Orthostatic hypotension is characterized by delayed recovery of orthostatic blood pressure (BP) to baseline after standing and is defined by consensus guidelines as a persistent drop in systolic BP ≥20 mm Hg or diastolic BP ≥10 mm Hg within 3 minutes.[1]

When we stand, BP drops initially as a result of blood pooling in the legs. Normal physiological mechanisms, involving both sympathetic and parasympathetic responses, work to return BP to pre-standing levels, resulting in increased cardiac output and peripheral vasoconstriction.[2] These mechanisms are complex, however, and if they become less efficient over time, which can occur in the setting of illness and comorbidity, then BP recovery can be prolonged.[3,4] After standing, BP is expected to recover back to the pre-standing value by 30 seconds.[5]

Delayed BP recovery after standing is therefore associated with frailty,[6] heart disease,[7] and other chronic illnesses such as diabetes.[8] Furthermore, individuals with delayed BP recovery also have been shown to have an increased risk of unexplained falls,[9] significant

Financial support was provided by Irish Government, the Atlantic Philanthropies and Irish Life plc. These funders were not involved in the study design, collection, analysis and interpretation of data, writing of the paper or submission for publication. Any views expressed in this report are not necessarily those of the Department of Health and Children or of the Minister for Health.
The authors declare no conflicts of interest.
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https://doi.org/10.1016/j.jamda.2020.12.031
1525-8610/

depressive symptoms,[10] cognitive decline in the setting of coexisting hypertension,[11] and early mortality[12] longitudinally. Dizziness, the primary symptom of orthostatic hypotension, has been shown to independently increase the risk of falls and fracture.[13]

The incidence of fractures in people aged ≥50 years is more than 116 per 10,000 person-years, but this increases markedly after the age of 70 years.[14] Fractures, particularly hip, wrist, and vertebral, can represent a "tipping point" for the older person in terms of subsequent loss of independence and poor outcomes.[15,16] Sustaining a fracture is a profound independent risk factor for subsequent decline in function and mobility and nursing home admission.[17–19] More than 40% of older people develop delirium postoperatively after a hip fracture,[20] and mortality within 12 months after a hip fracture is almost 30%.[21]

It is important therefore to identify modifiable risk factors for incident fracture in order to inform strategies aimed at preventing both the fracture and the cascade of adverse events that can occur afterwards. BP recovery after standing can be readily measured in an ambulatory setting using a finometer after an active stand.[22] It is also potentially modifiable, particularly when due to culprit medications.[23] The aim of this study therefore is to explore the role of delayed BP recovery as a risk factor for incident fracture (hip, wrist, and vertebral) in a large population-representative cohort of community-dwelling older people.

Methods

Study Design

This is a longitudinal study examining the prospective risk of fracture (hip, wrist, or vertebral) associated with delayed BP recovery at 8-year follow-up in a large population-representative sample of older adults.

The TILDA study design has been outlined previously.[24] Briefly, participants were reviewed at 2-yearly intervals (waves 1-5 inclusive). There were 3 components to data collection: a computer-assisted personal interview (CAPI) carried out by social interviewers in the participants' own home; a self-completion questionnaire completed and returned by the participant; and a comprehensive center-based health assessment or a modified home-based health assessment carried out by trained research nurses. The health assessment was conducted at waves 1 and 3 only. We analyzed data from waves 1 to 5, collected between 2009 and 2018.

Participants were included in this study if they were community-dwelling and aged ≥50 years at wave 1, underwent a health assessment at wave 1 including measurement of orthostatic BP by active stand, and completed 8-year follow-up at wave 5. Participants were excluded at wave 1 if they had a pre-existing diagnosis of dementia.

Delayed BP Recovery

Orthostatic BP was measured by active stand using a Finometer Midi as described previously.[22] This allows measurement of finger BP noninvasively on a beat-to-beat basis and is more sensitive for profiling orthostatic BP change than measuring orthostatic brachial artery BP with a sphygmomanometer.[5]

Briefly, participants lay in the supine position for 10 minutes in a quiet room, before standing in a timely manner, and were aided by a research nurse to mobilize as necessary. Baseline BP was measured while supine. After standing, systolic BP, diastolic BP, and heart rate were monitored continuously for a further 120 seconds. Throughout the recording, subjects stood quietly.

Delayed BP recovery was defined as systolic BP ≥20 mm Hg lower than baseline or diastolic BP ≥10 mm Hg from baseline value at 30, 60, and 90 seconds, respectively. Time-point values were 5-second moving averages; that is, the 30-second time point was the average of 27.5 to 32.5 seconds. See Figure 1 for a schematic representation of normal orthostatic BP response, and delayed BP recovery at 30, 60, and 90 seconds after standing.

Fracture

Fracture data were ascertained by self-report. Participants were asked specifically about a prior fracture of the hip, wrist, or vertebra at wave 1. This data point informed the "prior fracture" variable in the study.

At each of waves 2 to 5, participants were further asked about fracture (of hip, wrist, and vertebra) since the last interview. Participants with a fracture reported at any of waves 2-5 were defined as having "incident fracture" during follow-up.

Participants who reported fractures were also asked if the fracture was due to a fall.

Other Measures

Further detailed social and biological data were also collected at wave 1. Educational attainment was obtained by self-report. The CAGE alcohol scale was used to assess for excess alcohol intake. Cardiovascular disease was defined as self-report of angina, congestive cardiac failure, or prior myocardial infarction. History of diabetes and stroke was also obtained by self-report. The Fried Frailty Scale (exhaustion, inactivity, mobility, grip strength, weight loss) was applied to measure frailty status and categorize participants as nonfrail, prefrail, and frail.[25] The Timed Up and Go was used as a measure of gait.[26] A heel ultrasonography was performed to categorize patients as normal bone density, osteopenic (bone mineral density T score < -2.5 standard deviations), or osteoporotic (bone mineral density T score > -2.5 standard deviations).[27]

Medication lists were examined for antidepressant medication [Anatomical Therapeutic Classification (ATC) code N06A], benzodiazepines and Z drugs (ATC code N05BA or N05CF), and antihypertensive medication (ATC code C02, C03, C07, C08, or C09).

Cognitive impairment was defined as a Mini Mental State Examination score <25. Participants were also asked specifically about any falls in the prior 12 months.

Statistical Analysis

Data were analyzed using Stata (version 14.1; StataCorp, College Station, TX). Baseline characteristics of the study sample were presented descriptively. The prevalence of delayed BP recovery at 30, 60, and 90 seconds after standing at wave 1 was compared across groups

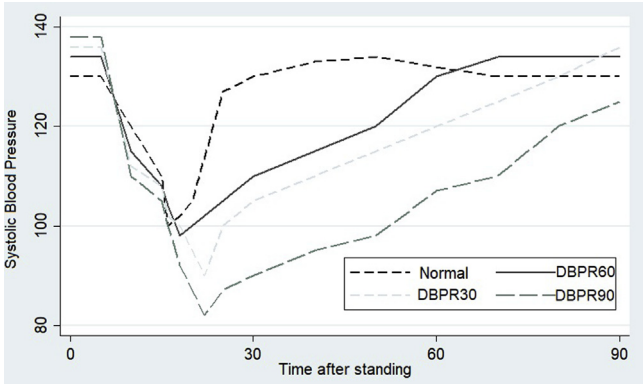

Fig. 1. Schematic representation of delayed BP recovery. DBPR, delayed BP recovery.

with and without incident fracture during follow-up, as well as specifically for groups with and without hip, wrist, and vertebral fracture.

Logistic regression models were used to estimate odds ratios [ORs, with 95% confidence intervals (CIs)] for the association between delayed BP recovery at 30, 60, and 90 seconds after standing and incident fracture (all fractures, hip fractures, wrist fractures, and vertebral fractures). Covariates were chosen a priori, based on their hypothesized role in modifying the relationship between delayed BP recovery and fracture. Model 1 adjusted for age, sex, educational attainment, and CAGE score; model 2 adjusted for model 1 covariates, as well as cardiovascular disease, stroke, osteoporosis status by heel ultrasonography, diabetes, Fried Frailty Scale score, Timed Up and Go score, cognitive impairment (MMSE score <25), antidepressant use, antihypertensive use, benzodiazepine or Z drug use, prior fractures, and falls within the last 12 months.

Regression models were rerun with exclusion of participants who reported a prior fracture at wave 1 in order to ascertain the association between delayed BP recovery and fracture in participants with no prior fracture history (model 3, also adjusted for all model 2 covariates).

A P value $\leq$.05 was considered statistically significant.

Ethics

The TILDA study was approved by the local Faculty of Health Sciences Research Ethics Committee, and all participants gave informed written consent. All experimental procedures adhered to the Declaration of Helsinki.

Results

There were 3117 participants who underwent initial assessment at wave 1 and 8-year follow-up at wave 5. Participants had a mean age of 60.9 (95% CI 60.6-61.1) years, and 54% were female.

Almost 16% (493/3117) of the study sample had delayed BP recovery at 30 seconds after standing, with just more than 11% (352/3117) of the study sample having delayed BP recovery at 60 seconds and just under 11% (328/3117) with delayed BP recovery at 90 seconds after standing.

Differences in baseline characteristics of groups with delayed BP recovery compared to the overall study sample are shown in Table 1. In general, participants with delayed BP recovery were older, more likely to be female, had lower levels of educational attainment and higher

Table 1
Baseline Characteristics (Wave 1) of Study Sample and Groups With Delayed BP Recovery After Standing

	Total Sample (n = 3117)	Del. BP Recovery 30 s (n = 493)	Del. BP Recovery 60 s (n = 352)	Del. BP Recovery 90 s (n = 328)
Mean age, y (95% CI)	60.9 (60.6-61.1)	64.4 (63.7-65.2)**	63.3 (62.5-64.2)**	62.8 (61.9-63.6)**
Female, % (n)	54 (1688)	63 (312)**	65 (227)**	61 (200)**
Mean BMI (95% CI)	28.5 (28.3-28.7)	27.7 (27.3-28.2)	27.6 (27.0-28.1)	27.3 (26.7-27.7)
Educational attainment, % (n)				
Primary	18 (561)	23 (112)*	25 (89)*	25 (81)*
Secondary	42 (1312)	39 (191)	38 (132)	38 (124)
Tertiary	40 (1244)	39 (190)	37 (131)	38 (123)
CAGE Scale, % (n):				
<2	79 (2463)	82 (405)	79 (278)	80 (264)
≥2	13 (412)	12 (57)	14 (49)	12 (38)
Did not complete	8 (242)	6 (31)	7 (25)	8 (26)
Cardiac disease, % (n)*	11 (356)	15 (73)*	15 (52)*	11 (36)
Stroke, % (n)	1 (31)	2 (9)*	2 (8)*	2 (5)
Heel US osteoporosis status, % (n)†				
Normal	54 (1678)	45 (224)**	44 (155)**	47 (154)*
Osteopenia	39 (1206)	42 (206)	45 (160)	42 (138)
Osteoporosis	7 (233)	13 (63)	11 (37)	11 (36)
Mean TUG score in seconds (95% CI)	8.4 (8.4-8.5)	8.9 (8.7-9.1)	8.7 (8.5-8.9)	8.5 (8.3-8.7)
Diabetes, % (n)	6 (183)	8 (39)*	5 (18)	7 (22)
Fried Frailty Scale, % (n)‡				
Nonfrail	75 (2337)	69 (340)**	72 (253)*	76 (249)
Prefrail	24 (757)	29 (143)	26 (93)	23 (75)
Frail	1 (23)	2 (10)	2 (6)	1 (4)
Mean MMSE score (95% CI)	28.8 (28.7-28.9)	28.5 (28.3-28.7)**	28.7 (28.5-28.8)	28.7 (28.6-28.9)
Prescribed antihypertensives, % (n)§	30 (937)	37 (181)*	35 (122)*	30 (100)
Prescribed antidepressants, % (n)‖	6 (179)	9 (45)**	10 (34)*	7 (23)
Prescribed benzodiazepines or Z drugs, % (n)**	4 (127)	7 (36)**	6 (22)*	6 (20)
Previous fracture, % (n)	11 (353)	13 (64)	13 (45)	12 (40)
Fall in last 12 mo, % (n)	19 (593)	24 (119)*	24 (83)*	23 (76)*

BMI, body mass index; CAGE, Cut Down, Angry, Guilty Eye Opener Scale; Del, delayed; MMSE, Mini Mental State Examination; US, ultrasonography.
Delayed BP recovery was based on BP return to normal after standing, when measured continuously during active stand using finometer. It was defined as BP drop from baseline BP of ≥20 mm Hg systolic or ≥10 mm Hg diastolic at respective timepoint (ie, 30, 60, or 90 seconds after standing). Continuous variables are described as means and standard deviations and compared using Student t test. Binary variables are described as percentages with absolute numbers detailed and compared using chi-square test. **P < .001 and *P < .05 for these comparisons.

*Defined as self-report of myocardial infarction, congestive cardiac failure, arrhythmia or angina.

†T score from heel US used to define normal (bone mineral density T score > −1.0 standard deviations), osteopenia (bone mineral density T score < −2.5 standard deviations), or osteoporosis (bone mineral density T score > −2.5 standard deviations).

‡Measured using Fried Frailty Scale (exhaustion, inactivity, mobility, grip strength, and weight loss).

§Prescribed medication with Anatomical Therapeutic Classification (ATC) code C02, C03, C07, C08, or C09.

‖Prescribed medication with ATC code N06A.

**Prescribed medication with ATC code N05BA or N05CF.

rates of heart disease (30- and 60-second groups only), stroke (30- and 60-second groups only), were less likely to have a normal heel ultrasonography and more likely to be prescribed antihypertensives (30- and 60-second groups only), antidepressants (30- and 60-second groups only), and benzodiazepines or Z drugs (30- and 60-second groups only). There was no clinically significant difference in cognitive scores across groups. Participants with delayed BP recovery also had a higher likelihood of a fall within the 12 months prior to initial assessment.

Almost 7% (212/3117) of study participants had a wrist, hip, or vertebral fracture during 8-year follow-up. Almost 5% (142/3117) sustained a wrist fracture; 1% (30/3117) fractured a hip and 2% (49/3117) sustained a fractured vertebra.

Figure 2 shows the prevalence of delayed BP recovery at baseline assessment in those who sustained a fracture during follow-up and those who did not have a fracture. In those who sustained either a wrist, hip, or vertebral fracture, the prevalence of delayed BP recovery was significantly higher at baseline assessment at 30 seconds (27% vs 15%, $P < .001$), 60 seconds (20% vs 11%, $P < .001$), and 90 seconds post standing (19% vs 10%, $P < .001$). Similarly, in those who went on to have a hip or wrist fracture, there was a significantly higher prevalence of delayed BP recovery at 30, 60, and 90 seconds post standing. For those who developed vertebral fractures during follow-up, there was a significantly higher prevalence of delayed BP recovery at 30 and 60 seconds, but not 90 seconds after standing, when compared with those who did not go on to sustain vertebral fractures.

Figure 3 demonstrates BP recovering after standing in participants who suffered a fracture during follow-up compared with those who did not, with significantly delayed recovery demonstrated in those with hip fracture but no wrist or vertebral fracture in fully adjusted models.

Logistic regression models demonstrated that after controlling for relevant covariates, delayed BP recovery at 30 seconds was a significant predictor of any incident fracture (OR 1.80, 95% CI 1.28-2.53; $P < .001$) and of incident hip fracture (OR 4.44, 95% CI 2.03-9.71; $P < .001$). Delayed BP recovery at 30 seconds did not predict incident wrist or vertebral fracture. Findings remained robust after excluding participants who reported a history of prior fracture at initial assessment (Table 2).

Delayed BP recovery at 60 seconds also predicted any incident fracture (OR 1.74, 95% CI 1.19-2.54; $P = .004$) and incident hip fracture (OR 4.66, 95% CI 2.12-10.26); $P < .001$) in fully adjusted models but not wrist or vertebral fracture.

Delayed BP recovery at 90 seconds predicted any incident fracture (OR 1.98, 95% CI 1.36-2.89; $P < .001$), incident wrist fracture (OR 1.87, 95% CI 1.19-2.95; $P = .007$), and incident hip fracture (OR 3.39, 95% CI 1.45-7.93; $P = .005$) but not incident vertebral fracture in fully adjusted models.

Supplementary Table 1 demonstrates the full output from logistic regression models with incident fracture as the dependent variable. Aside from delayed BP recovery, other significant predictors of fracture were female sex and prior fracture while antihypertensive use was associated with lower likelihood of fracture.

Of the 212 participants reporting fracture during follow-up, 75% (160/212) identified a fall as the mechanism for the injury, including 80% of those with hip or wrist fracture and 63% of those with vertebral fracture.

Discussion

This study demonstrates that community-dwelling older adults with delayed BP recovery at 30, 60, and 90 seconds after standing have a significantly higher likelihood of fracture during 8-year follow-up. Delayed BP recovery at 30 and 60 seconds was associated with a greater than 2-fold higher likelihood of incident fracture, after controlling for covariates including heart disease, stroke, antihypertensive use, frailty status, and prior history of falls and fracture.

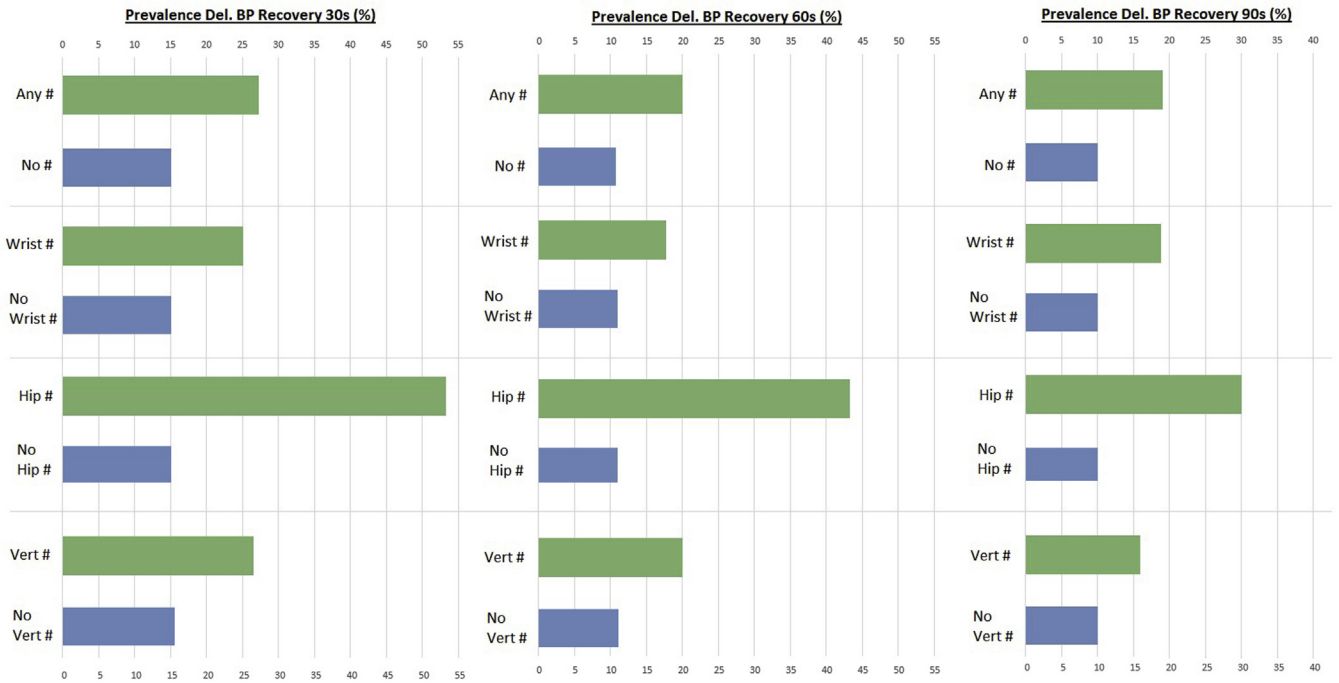

Fig. 2. Delayed BP recovery at 30, 60, and 90 s after standing by incidence of fracture during 8-year follow-up. Delayed BP recovery was based on BP return to baseline after standing, when measured continuously during active stand using finometer. It was defined as BP drop from baseline BP of ≥20 mm Hg systolic or ≥10 mm Hg diastolic at respective time points (ie, 30, 60, or 90 seconds after standing). Del., delayed; #, fracture; Vert, vertebral.

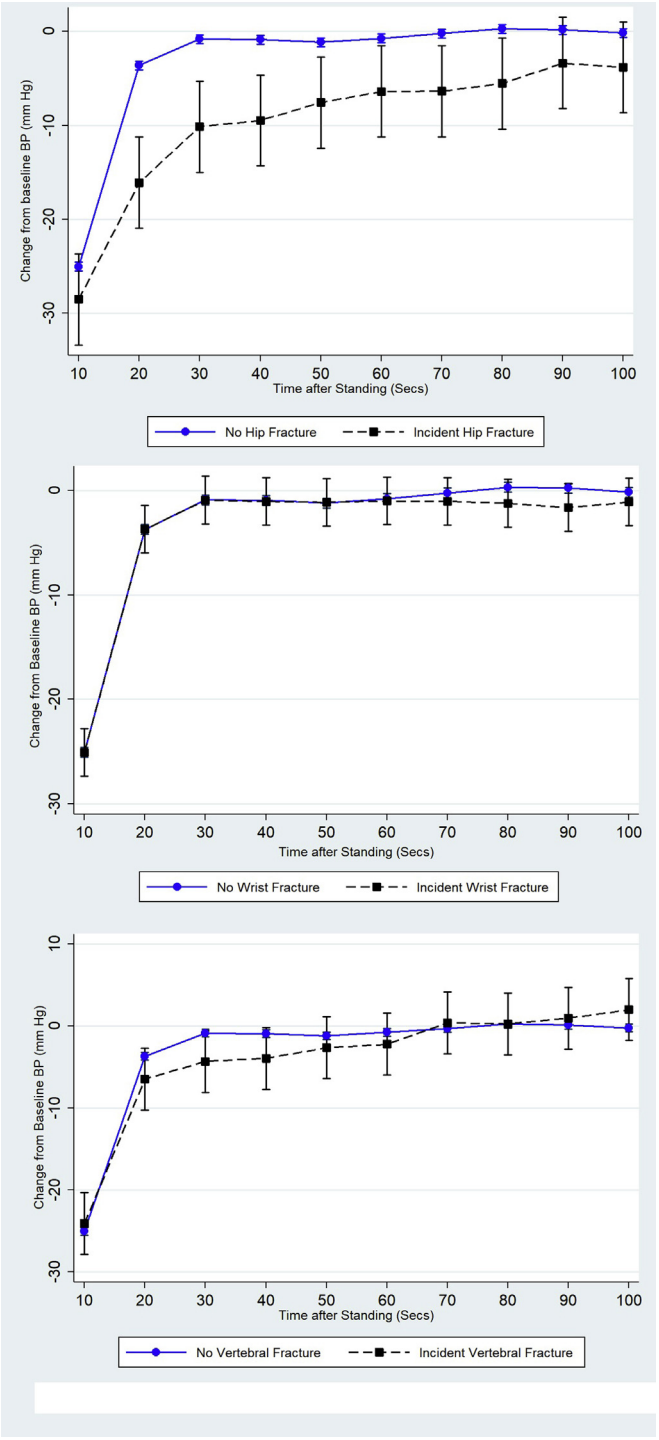

Fig. 3. Systolic BP drop after standing by incidence of hip, wrist, or vertebral fracture. BP trend after standing where 0 = baseline BP before standing, measured continuously during active stand using finometer. Multilevel model adjusted for age, sex, educational attainment, excess alcohol intake, body mass index, cardiovascular disease, stroke, osteoporosis status by heel ultrasonography, diabetes, Fried Frailty Scale, Timed Up and Go, cognitive impairment, antidepressant use, antihypertensive use, benzodiazepine or Z drug use, prior fractures, and falls within the last 12 months.

Findings remained robust after excluding participants with a prior fracture.

When examined by fracture type, delayed BP recovery at 90 seconds was an independent risk factor for both wrist and hip fracture whereas delayed BP recovery at 30 and 60 seconds was an independent risk factor for hip fracture only. Delayed BP recovery did not predict incident vertebral fracture at any time point.

A large prospective study based in Sweden has previously demonstrated an increased risk of low-energy fractures associated with orthostatic hypotension, but this involved a middle-aged sample.[28] Further, initiation of antihypertensive drugs has been shown to increase the risk of hip fracture in older people,[29] whereas a retrospective cohort study in Thailand found that more than one-fifth of falls causing hip fracture in males were due to orthostatic hypotension.[30] However, this is the first longitudinal study to examine the association between orthostatic BP profiles and incident fracture in older people.

It is likely that the mechanism by which delayed BP recovery increases fracture risk is by causing injurious falls or syncope,[9,31] particularly when we consider that there was no association with vertebral fractures, which often occur in the absence of trauma.[32] Eighty percent of participants with hip or wrist fractures reported a fall as the mechanism for the injury. Atraumatic hip fracture is rare,[33] and the association with hip fracture, albeit in the context of relatively low numbers, is particularly strong, with delayed BP recovery at 30 seconds conferring a greater than 4-fold likelihood of hip fracture in the subsequent 8 years.

These findings are important as delayed BP recovery is potentially modifiable, and therefore early identification and management could prevent fracture in later life by preventing injurious falls related to orthostatic hypotension. Initial management strategies include rationalization of culprit medications, particularly antihypertensives and antidepressants,[34] promoting better fluid intake and other conservative measures.[35] Pharmacologic treatment may be used if these initial strategies are insufficient. It is important to note, however, that regression models demonstrated that antihypertensive use was associated with lower likelihood of fracture, and this hints at the complexity involved when managing orthostatic hypotension, especially with coexisting hypertension.[36]

There are some limitations to this study that should be considered. Incident fracture was based on self-report and may therefore be subject to recall bias. It is possible that some fractures may have been missed; however, the study sample is relatively healthy with low rates of cognitive impairment, so it is likely that the number of missed events is low. Heel ultrasonography, used to measure bone mineral density in this study, does not represent the gold standard, and dual-energy X-ray absorptiometry (DXA) is a more reliable measure in a cohort such as this. Nevertheless, it was not practical or feasible to perform DXA on each participant. Furthermore, the number of participants who sustained a fracture was relatively small; in addition detailed biological data were available for each participant, including measures such as heel ultrasonography and continuous orthostatic BP measurements. We did not adjust for the use of assistive devices but instead used the Timed Up and Go. Additionally, although certain classes of BP medications may affect bone mineral density, subgroup analysis based on antihypertensive type was not possible because of participant numbers. We robustly adjusted for competing covariates, such as frailty status and heart disease, however.

Conclusion and Implications

In conclusion, this study demonstrates that delayed BP recovery after standing independently predicts fracture risk, particularly hip fracture, in community-dwelling older people. Given the serious adverse outcomes associated with fracture in later life, identification of potentially modifiable risk factors is crucial. Further dedicated studies are therefore warranted to assess whether early identification and management of delayed BP recovery prevents fracture in later life.

Table 2
Logistic Regression Models With Incident Fracture as Dependent Variable by BP Recovery Status During Active Stand (N = 3177)

Fracture Type	Delayed BP Recovery 30 s			Delayed BP Recovery 60 s			Delayed BP Recovery 90 s		
	Model 1	Model 2	Model 3	Model 1	Model 2	Model 3	Model 1	Model 2	Model 3
Any									
OR (95% CI)	1.85 (1.33-2.58)	1.80 (1.28-2.53)	1.49 (1.00-2.22)	1.80 (1.25-2.60)	1.74 (1.19-2.54)	1.74 (1.13-2.67)	1.99 (1.38-2.87)	1.98 (1.36-2.89)	1.94 (1.26-2.99)
Z	3.66	3.40	1.96	3.17	2.88	2.54	3.67	3.54	3.02
P	<.001	<.001	.049	.002	.004	.011	<.001	<.001	.003
Wrist									
OR (95% CI)	1.36 (0.83-2.23)	1.57 (1.03-2.38)	1.33 (0.80-2.20)	1.47 (0.93-2.33)	1.40 (0.87-2.26)	1.37 (0.78-2.40)	1.96 (1.26-3.05)	1.87 (1.19-2.95)	1.93 (1.14-3.26)
Z	1.20	2.11	1.10	1.64	1.40	1.09	2.98	2.71	2.44
P	.23	.025	.27	.10	.16	.28	.003	.007	.015
Hip									
OR (95% CI)	5.34 (2.21-12.90)	4.44 (2.03-9.71)	4.62 (1.82-11.68)	5.79 (2.45-13.70)	4.66 (2.12-10.26)	5.21 (2.10-12.92)	2.87 (1.29-6.42)	3.39 (1.45-7.93)	3.39 (1.27-9.05)
Z	3.72	3.73	3.23	4.00	3.83	3.56	2.57	2.82	2.44
P	<.001	<.001	.001	<.001	<.001	<.001	.010	.005	.015
Vertebral									
OR (95% CI)	1.76 (0.91-3.42)	1.65 (0.84-3.27)	1.10 (0.48-2.53)	1.82 (0.82-4.02)	1.74 (0.84-3.62)	1.71 (0.76-3.85)	1.55 (0.72-3.36)	1.54 (0.70-3.38)	1.40 (0.57-3.44)
Z	1.68	1.45	0.23	1.47	1.49	1.29	1.12	1.07	0.73
P	.09	.15	.82	.14	.14	.20	.27	.28	.47

Delayed BP recovery was based on BP return to normal after standing, when measured continuously during active stand using finometer. It was defined as BP drop from baseline BP of ≥20 mm Hg systolic or ≥10 mm Hg diastolic at respective timepoint (ie, 30, 60, or 90 seconds after standing).
Model 1 is adjusted for age, sex, educational attainment and CAGE score; model 2 is adjusted for model 1 covariates, as well as cardiac disease, stroke, osteoporosis status by heel ultrasonography, diabetes, Fried Frailty Scale, Timed Up and Go, cognitive impairment, antidepressant use, antihypertensive use, benzodiazepine or Z drug use, prior fractures, and falls within the last 12 months. model 3 adjusts for model 2 covariates but excludes participants who report a prior fracture history at wave 1.

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Supplementary Table 1
Output From Fully Adjusted Logistic Regression Models With Any Incident Fracture as Dependent Variable (N = 3177)

Incident Fracture (Any)	OR (95% CI)	Z	*P*
DBPR 30 s	1.80 (1.28-2.53)	3.40	.001
Age (ref: 50-64 y)			
65-74 y	1.17 (0.83-1.66)	0.89	.37
≥75 y	1.38 (0.77-2.49)	1.08	.28
Female sex	2.08 (1.48-2.92)	4.25	<.001
CAGE Alcohol Scale score (Ref: 0-1)			
CAGE = 2	0.95 (0.60-1.50)	−0.22	.83
Did not complete	0.65 (0.34-1.23)	−1.31	.19
Educational attainment (ref: primary)			
Secondary	0.93 (0.63-1.37)	−0.38	.71
Tertiary	0.78 (0.51-1.17)	−1.21	.23
Body mass index	1.01 (0.98-1.05)	0.94	.35
Cardiovascular disease*	1.01 (0.61-1.65)	0.05	.96
Stroke	1.49 (0.43-5.21)	0.63	.53
Diabetes	0.84 (0.41-1.74)	−0.46	.65
Fried Frailty Status (ref: Nonfrail)†			
Prefrail	1.18 (0.85-1.64)	0.97	.33
Frail	0.97 (0.20-4.61)	−0.04	.97
Heel ultrasonography osteoporosis status (ref: normal)‡			
Osteopenia	1.31 (0.95-1.81)	1.64	.10
Osteoporosis	1.46 (0.88-2.43)	1.46	.15
Timed Up and Go (seconds)	1.01 (0.93-1.11)	0.27	.79
Cognitive impairment§	0.99 (0.40-2.44)	−0.03	.98
Antihypertensive use‖	0.65 (0.45-0.95)	−2.25	.024
Antidepressant use**	1.35 (0.79-2.30)	1.09	.27
Benzodiazepines and Z drugs††	1.47 (0.81-2.68)	1.27	.20
Falls last year	1.14 (0.81-1.61)	0.74	.46
Prior fracture	2.78 (1.96-3.94)	5.76	<.001

CI, confidence interval; DBPR 30 s, delayed blood pressure recovery 30 seconds after standing; CAGE = Cut Down, Angry, Guilty, Eye Opener; OR, odds ratio.
Delayed BP recovery based on BP return to normal after standing, when measured continuously during active stand using finometer. Delayed BP Recovery defined as BP drop from baseline BP of ≥20 mm Hg systolic or ≥10 mm Hg diastolic at 30 seconds after standing.

*Cardiovascular disease was defined as self-report of angina, congestive cardiac failure, or prior myocardial infarction.

†Fried Frailty Scale (exhaustion, inactivity, mobility, grip strength, weight loss) applied to measure frailty status, and categorize participants as nonfrail, prefrail and frail.

‡Heel ultrasonography performed to categorize patients as normal bone density, osteopenic (bone mineral density *T* score < −2.5 standard deviations), or osteoporotic (bone mineral density *T* score > −2.5 standard deviations).

§Cognitive impairment was defined as Mini Mental State Examination Score <25.

‖Prescribed antihypertensive medication (ATC code C02, C03, C07, C08, or C09).

**Prescribed antidepressant medication (ATC code N06A).

††Prescribed benzodiazepines or Z drugs (ATC code N05BA or N05CF).