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RESEARCH PAPER

Can ambulatory blood pressure biomarkers predict future falls amongst older people?

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Abstract

Background: While ambulatory blood pressure monitoring (ABPM) biomarkers can predict cardiovascular and cerebrovascular outcomes, little work to date has examined their link with falls. The objective of this study was to examine associations between ABPM biomarkers and further falls in a cohort of older people with recent falls.
Methods: A consecutive series ($n = 118$) of patients≥70 years undergoing falls assessment including 24-hour ABPM were recruited and followed to their next clinical appointment, where incident falls were recorded (minimum follow-up 1 month). ABPM biomarkers included standard deviation for overall systolic blood pressure (sBP), minimum sBP value, sBP values <100 mmHg, sBP dipping (normal dipping>10%, non-dipper 0–10%, reverse dipper <0%) and sBP morning surge (average 2-hour post-awakening sBP minus the lowest night-time sBP). Logistic regression models assessed the relationship between ABPM biomarkers and further falls.
Results: One quarter of participants reported a further fall at mean 7 months' follow-up. Hypotensive episodes were independently associated with further falls, odds ratio 4.52 (95% CI 1.56, 13.11); $P = .006$). Minimum sBP values were also independently associated with further falls, with a 3% reduction in falls for every 1 mmHg increase in sBP (adjusted odds ratio 0.97 (95% CI 0.94, 0.99); $P = .027$)). For every increase in morning surge by 1 mmHg, there was a 6% increase in falls (adjusted odds ratio 1.06 (95% CI 1.02, 1.10); $P = .005$). There was no association between dipping status and further falls.
Discussion: ABPM biomarkers may represent important modifiable risk factors for future falls, and ABPM should be integrated into a comprehensive falls assessment in older patients.

Keywords: blood pressure; hypotension; blood pressure variability; morning surge; blood pressure dipping; orthostatic hypotension; frailty; older people

Key Points

- Hypotensive episodes (systolic BP value <100 mmHg) on ABPM were associated with a greater than four-fold increase in further falls.
- Minimum systolic BP was also associated with further falls, with 3% lower likelihood for a 1 mmHg increase in minimum systolic BP.
- For every increase in the morning surge index on ABPM by 1 mmHg there was a 6% increase in the likelihood of further falls.
- ABPM biomarkers may represent modifiable risk factors for falls and should be integrated into comprehensive falls assessment.

Background

Falls are the most frequent cause of hospital admission in the older person are admitted to hospital [1], and the most frequent cause of accidental death in later life [2]. Falls can have a profound impact on functional status, mood, well-being and quality of life in older people and are frequently a trigger for nursing home admission, development of fear of falling and loss of independence [3–5].

Many falls in later life are preventable; however, but this requires identification and treatment of the underlying cause or causes. It is now increasingly well-recognised that cardiovascular disorders, including blood pressure (BP) dysregulation, cardiac arrhythmia or structural heart disease underpin many unexplained falls in later life [6]. The World Guidelines for falls prevention and management in older adults recommends cardiovascular assessment as part of a comprehensive multifactorial falls risk assessment in older people with falls [7].

As we get older, most likely related to intercurrent illness, insults such as myocardial infarction or the adverse effects of medications, the mechanisms that tightly control our cardiovascular system may become less efficient, particularly the reflexes that control BP [8]. This may be lead to BP Instability, often characterised by orthostatic hypotension (OH), which is usually due to a combination of baroreceptor failure and cardiovascular dysautonomia in later life [9].

Ambulatory blood pressure monitoring (ABPM) may reveal other important biomarkers of future falls risk beyond OH. These may include increased BP variability, a measurement of the oscillation of BP measurements during the ABPM period [10]; hypotensive episodes [11]; the degree of the morning BP surge [12]; presence/absence of nocturnal dipping or reverse dipping [13].

While the association between OH and falls is well-established [14], little work to date has examined the link between falls and these other markers of biomarkers of BP Instability in later life. Given the profound impact falls can have on the older person, it is important to identify potentially modifiable markers of increased falls risk as part of a comprehensive assessment in older people with falls.

Our hypothesis is that ABPM biomarkers, particularly those related to BP instability, including higher BP variability, hypotensive episodes, BP dipping and morning surge, may independently increase the likelihood of falls in older people and may therefore represent a potentially modifiable risk factor. Further, we hypothesise that these abnormalities have a relatively greater impact on falls risk as we get older.

The aim of this study therefore is to examine the association of ABPM biomarkers with future falls in a cohort of patients aged ≥70 years with recent falls attending a specialist falls unit, including a subgroup of patients aged ≥80 years.

Methods

Study design

This study examines the association between ABPM biomarkers and further falls in a cohort of community-dwelling older people with recent falls.

The study site is a large tertiary-referral falls and syncope unit. A consecutive series ($n = 118$) of patients aged ≥70 years who were referred to a specialist falls clinic after a fall, typically within the last 3 months and underwent ABPM as part of a falls assessment were recruited and followed to their next scheduled clinical appointment. Minimum follow-up time was at least 1 month for inclusion. Patients were excluded if they did not attend a follow-up appointment. Recruitment commenced in October 2023 and was completed over one month. Patients were recruited at their follow-up appointment, with ABPM data collected retrospectively. Around 6000 patient reviews are completed annually in the clinic.

Ambulatory blood pressure monitoring

As part of routine clinical care, a 24-hour ABPM (Spacelabs REY90217) was performed. ABPMs were programmed to check BP every 30 minutes during the day and hourly at night. A diary was kept to record symptoms, meal times and sleep times to inform values including morning surge and nocturnal dipping (awakening time used in calculations for these).

The following data of interest was collected (Figure 1):

Average systolic blood pressure (sBP).

Standard deviation (as a marker of BP variability) for average sBP.

Minimum sBP values.

Number of sBP values <100 mmHg during 24-hour period; this cut-off was chosen based on prior work identifying this threshold as a target in patients with syncope [15].

SBP dipping status, i.e. How much BP falls during sleep compared to waking time, calculated as 100 × (awake minus sleep BP/awake BP); defined as normal dipping>10%, non-dipper 0–10%, reverse dipper <0%.

Morning surge index, i.e. How much sBP increases during the period of being asleep to waking up, calculated as the average 2-hour post-awakening sBP minus the lowest nighttime sBP [11].

We focused on sBP in this study as it is well-established that symptoms of orthostatic intolerance, presyncope and OH are primarily dependant on sBP and not diastolic BP [16]. This is reflected in clinical practice in falls units, where treatment strategies are generally based on sBP targets [15].

Additional data

Further data collected at the baseline assessment from clinical notes included:

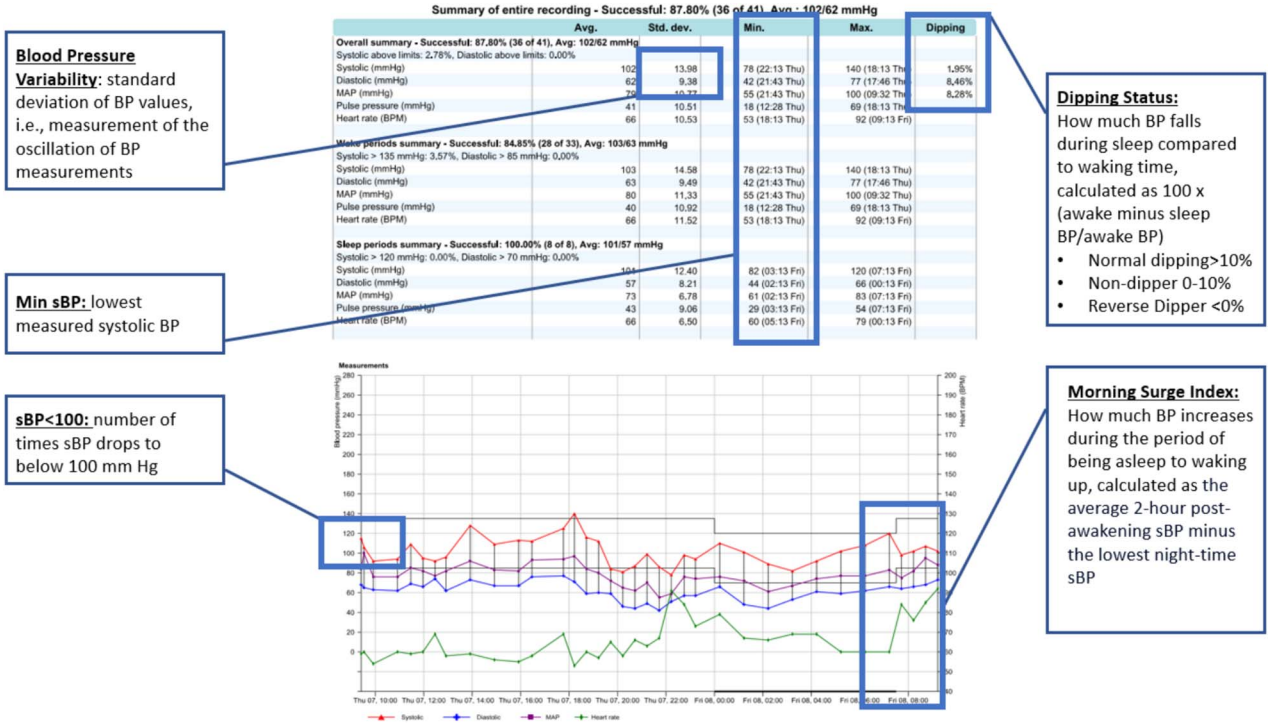

Figure 1. Ambulatory blood pressure monitoring biomarkers. BP, blood pressure; sBP, systolic blood pressure.

Basic demographics (age, sex).

History of heart disease (heart failure, arrythmia, myocardial infarction or other ischaemic heart disease).

Clinical Frailty Scale, an inclusive 9-point scale that uses clinical judgement to summarise the baseline level of fitness or frailty of an older person [17].

Antihypertensive medication use (alpha blockers, aldosterone receptor blockers, angiotensin converting enzyme inhibitors, angiotensin receptor blockers, beta blockers, calcium channel blockers, diuretics, nitrates and/or vasodilators).

Documented diagnosis of OH based on clinical assessment.

Incident falls were recorded and documented at the next scheduled clinical appointment.

Statistical analysis

Binary variables were presented descriptively as proportions, while continuous variables were presented as means if normally distributed or medians, with 95% confidence intervals.

Chi-square tests and *t*-tests were used to assess for differences between binary and continuous variables, respectively. The *F*-test was used to compare standard deviations (as a marker of BP variability) across groups.

Logistic regression models, reporting odds ratios with 95% confidence intervals, were used to assess the relationship between ABPM biomarkers (sBP values <100 mmHg, minimum sBP value, sBP dipping status, morning surge index and overall sBP) and further falls during follow-up (dependant variable). Models were presented fully-adjusted. Models were adjusted for age category (70–75 years, 76–80 years, >80 years), sex, clinical frailty scale score, OH, antihypertensive use, heart disease and follow-up time. Covariates were chosen a prior based on their likelihood of association with future falls. Subgroup analysis was conducted involving only patients aged ≥80 years.

Ethics

The study was approved by the Tallaght/St James's Hospital Research Ethics Committee.

Results

Baseline characteristics are shown in Table 1. Mean follow-up time was 7.1 (95% CI 6.3–7.9) months, with a range from 1 to 30 months. One quarter of participants (29/118) reported a further fall during follow-up.

Overall sBP and BP variability

Participants with further falls had a significantly lower overall sBP (119.6 (95% CI 109.9–129.4) vs. 130.8 (95% CI 126.9–134.7); $P = .0113$) at initial review. In fully adjusted models, there was a 3% lower odds of further falls (adjusted odds ratio 0.97 (95% CI 0.95–0.99); $P = .030$) for every 1 mmHg increase in the overall average sBP. In the ≥80 years subgroup, this reduction was 7% (adjusted odds ratio 0.93 (95% CI 0.86–0.99); $P = .030$).

The adjusted odds ratios for the association between sBP <100 mmHg ($n = 5$), sBP <110 mmHg ($n = 16$) and

Table 1. Baseline characteristics by further falls during follow-up

	Further falls $n = 29$	No further falls $n = 89$
Age in years (mean), 95% CI	79.3 (77.2–81.3)	78.1 (77.1–79.2)
Age categories (proportion), 95% CI		
70–74 years	0.24 (0.11–0.44)	0.33 (0.24–0.43)
75–79 years	0.45 (0.27–0.64)	0.35 (0.27–0.47)
≥80 years	0.31 (0.16–0.51)	0.31 (0.23–0.42)
Female sex (proportion), 95% CI	0.52 (0.33–0.70)	0.49 (0.39–0.60)
Clinical Frailty Scale (mean), 95% CI	3.76 (3.48–4.04)	3.47 (3.32–3.62)
Orthostatic hypotension (proportion)[A], 95% CI	0.79 (0.60–0.91)	0.69 (0.58–0.77)
Number of medications (mean), 95% CI	7.93 (6.56–9.30)	5.66 (5.06–6.26)
Prescribed antihypertensives (proportion)[B], 95% CI	0.70 (0.50–0.80)	0.57 (0.45–0.68)
Heart disease (proportion)[C], 95% CI	0.66 (0.46–0.81)	0.46 (0.36–0.57)
Follow-up in months (mean), 95% CI	7.03 (5.37–8.70)	7.15 (6.19–8.10)

CI, confidence interval. [A]Diagnosis of orthostatic hypotension after clinical assessment; [B]Prescribed alpha blockers, aldosterone receptor blockers, angiotensin converting enzyme inhibitors, angiotensin receptor blockers, beta blockers, calcium channel blockers, diuretics, nitrates and/or vasodilators; [C]Heart failure, arrhythmia, myocardial infarction or other ischaemic heart disease.

Table 2. Adjusted logistic regression model reporting odds ratio with further falls as dependant variable

Dependant variable: further falls	Odds ratio (95% confidence interval)	*P* value
Systolic BP 'Dips' <100 mmHg	4.52 (1.56–13.11)	.005
Age category		
70–75 years	Reference	Reference
76–80 years	1.45 (0.45–4.63)	.532
>80 years	0.86 (0.24–3.13)	.823
Female sex	1.28 (0.50–3.25)	.608
Clinical Frailty Scale	1.86 (0.96–3.62)	.066
Orthostatic hypotension[A]	1.76 (0.57–5.45)	.326
Prescribed antihypertensive medication[B]	1.21 (0.42–3.45)	.728
Heart disease[C]	2.11 (0.75–5.97)	.159
Follow-up (months)	1.02 (0.92–1.14)	.717

Logistic regression models with falls during follow-up (mean 7 months) as dependant variable. [A]Diagnosis of orthostatic hypotension after clinical assessment; [B]Prescribed alpha blockers, aldosterone receptor blockers, angiotensin converting enzyme inhibitors, angiotensin receptor blockers, beta blockers, calcium channel blockers, diuretics, nitrates and/or vasodilators; [C]Heart failure, arrhythmia, myocardial infarction or other ischaemic heart disease.

sBP < 120 mmHg ($n = 38$) and further falls were 3.93 (95% CI 0.41–37.74), 2.89 (95% CI 0.79–10.58) and 0.96 (95% CI 0.35–2.64) respectively.

There was no significant difference in the standard deviation for the mean sBP in patients who did not fall again and those with further falls (15.1 vs. 15.9, $F = 0.9$, $P = .843$).

sBP 'drops'

Over 58% (69/118) of participants had a sBP value <100 mmHg on their ABPM. The incidence of further falls during follow-up in participants with hypotensive episodes was 79% (23/29) compared to 52% (46/89) in those who did not have sBP values <100 mmHg on their ABPM ($X^2 = 6.87$; $P = .009$). See Figure 1.

In logistic regression models with further falls as the dependant variable, hypotensive episodes were independently associated with further falls with an odds ratio of 4.52 (95% CI 1.56–13.11); $P = .006$). See Table 2.

There was no gradient in association related to the number of hypotensive episodes. In similar fully adjusted models, 1–3 hypotensive episodes was associated with future falls at an odds ratio of 7.34 (95% CI 1.94–27.75); $P = 0.003$; $n = 21$ patients) when no hypotensive episodes was the reference point; 4–6 hypotensive episodes was associated with future falls with an odds ratio of 4.25 (95% CI 1.22–14.78); $P = 0.023$; $n = 26$ patients), while >6 hypotensive episodes was not associated with future falls (OR 1.99 (95% CI 0.44–8.92); $P = .370$; $n = 18$ participants).

When examined in the subgroup aged ≥80 years only, there was a stronger independent association between sBP values<100 mmHg and future falls with an odds ratio 28.15 (95% CI 1.61–492.11); $P = .022$).

Minimum sBP

Participants with further falls during follow-up had a significantly lower minimum sBP on their ABPM compared to those who did not fall again (92.1 (95% 87.1–97.1) mmHg in fallers, 100.0 (95% CI 96.0–104.6) mm Hg in non-fallers; $t = 2.07$; $P = .0407$). See Figure 2.

In logistic regression models, minimum sBP values were independently associated with further falls, with a 3% reduction in the odds of falls for every 1 mmHg increase in sBP

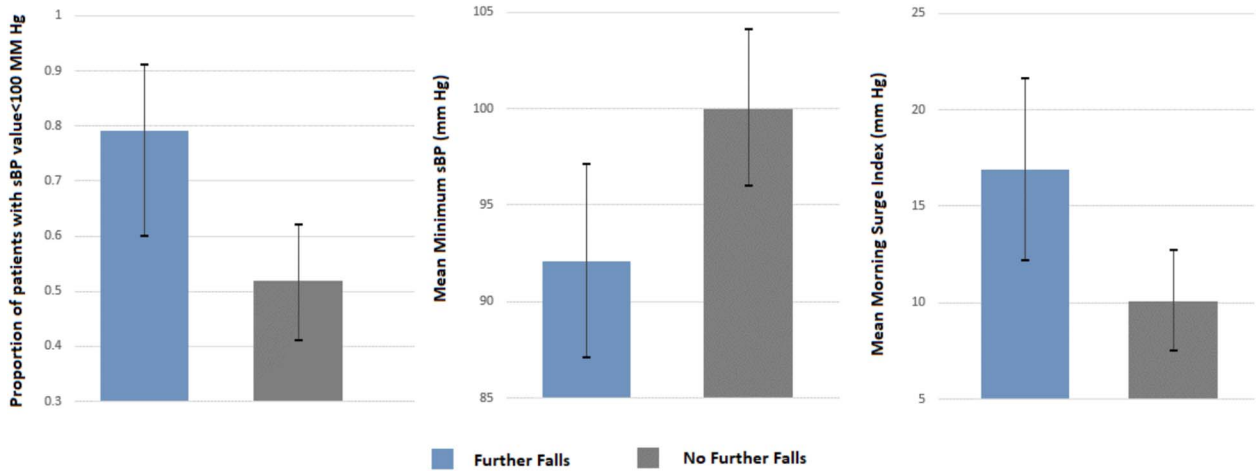

Figure 2. Ambulatory blood pressure biomarkers and further falls. sBP = systolic blood pressure. Data shown are proportion/mean with 95% confidence intervals by further falls. Minimum sBP = lowest systolic blood pressure value during 24-hour ambulatory monitoring; morning surge index = average 2-hour post awakening BP minus the lowest night-time BP.

in fully adjusted models (adjusted odds ratio 0.97 (95% CI 0.94–0.99); $P = 0.027$).

In the subgroup aged ≥80 years, there was a 6% lower odds of falls for every 1 mmHg increase in the minimum sBP value (adjusted odds ratio 0.96 (95% CI 0.88–0.99); $P = .047$).

A minimum sBP value of 80 mmHg had 21% sensitivity 21% and 84% specificity for predicting future falls; minimum sBP of 90 mmHg had 38% sensitivity and 65% specificity and minimum sBP of 100 mmHg had 79% sensitivity and 46% specificity.

sBP dipping

Just over one-third of participants (41/118) were classified as sBP dippers, while over 40% (49/118) were non-dippers and less than a quarter (28/118) were reverse dippers.

There was no significant association between dipping status and further falls, and no significant difference in mean dipping percentage in those with further falls, compared to those who did not fall again (7.13 (95% CI 3.51–10.76) in fallers and 6.15 (95% CI 3.68–8.63) in non-fallers; $t = -0.4090$; $P = .6833$).

Morning surge index

As shown in Figure 2, the mean morning surge was significantly higher in patients with further falls, compared to non-fallers (16.9 (95% CI 12.2–21.6) mmHg vs 10.1 (95% CI 7.5–12.7); $t = -2.59$; $P = .0107$).

In fully adjusted logistic regression models, for every increase in morning surge by 1 mmHg there was a 6% higher odds of recurrent falls (adjusted odds ratio 1.06 (95% CI 1.02–1.10); $P = .005$). There was no significant association between morning surge index and falls in the ≥80 years subgroup (adjusted odds ratio 1.09 (95% CI 0.99–1.20); $P = .073$).

The lowest tertile of morning surge index (≤0 mmHg) had 83% sensitivity and 58% specificity for predicting future falls, the middle tertile (0.1–17.64 mmHg) had 62% sensitivity and 71% specificity and the highest tertile (>17.64 mmHg) had 55% sensitivity and 71% specificity.

Discussion

This study examines whether ABPM biomarkers can predict further falls in a cohort of patients aged ≥70 years, attending a tertiary referral falls unit. At 7 months' follow-up, isolated sBP values<100 mmHg, lower minimum and overall average sBP values and a higher morning surge index were independently associated with further falls. While seen across all age categories in the study, the link between these markers and future falls was particularly strong in the subgroup aged ≥80 years.

While the association between ABPM biomarkers and cardiovascular and cerebrovascular events in later life is now well-established [10, 12, 13], little work to date has examined the prospective association between ABPM biomarkers and future falls.

A single study of over 1000 older people has shown an association between overall BP values on ABPM and future falls [18], while another study of over 150 older patients (mean age 80 years), found that post-prandial hypotension, an additional ABPM biomarker related to BP instability, is more prevalent in those reporting falls [19]. This is the first study however to examine the association of prevalent ABPM biomarkers such as isolated hypotensive events, minimum BP values and morning surge with future falls in a cohort of older patients.

These findings are important because they have the potential to inform clinical care of older people with falls. The ABPM biomarkers we have examined, and therefore, their association with falls are potentially modifiable. The majority

relate to the hypotensive burden experienced by the patient, which is particularly relevant given recent changes to hypertension management guidelines for older people [20]. These changes were informed by the SPRINT study, demonstrating the benefits of tighter BP control [21], despite potential lack of generalisability of the study [22]. Lower BP treatment targets are likely to lead to a higher hypotensive burden; however, this should be considered when addressing BP management in older patients with a history of falls.

While one may anticipate the association between markers of hypotensive burden and falls, the mechanism linking morning BP surge and falls amongst older people is less apparent. Morning surge index is an important risk factor for stroke and heart disease [12] both of which are strongly associated with falls. Also, importantly, impaired baroreflex sensitivity, which can predispose to falls by delaying BP recovery after standing [23], is associated with larger morning surge [24]. Higher morning surge is therefore a marker of inefficiency of the baroreflex to buffer BP changes.

This study also highlights the importance of ABPM in older people with falls, with generally high BP variability, high levels of frailty and over 60% prescribed antihypertensive medication in this study group, demonstrating the difficulties in titrating BP treatment in the absence of ABPM data in this setting [25, 26]. Further, it is also important to consider that two-thirds of patients with hypotensive values on ABPM may not be identified by office-measured BP [27]. ABPM is therefore a readily available tool that can help with BP management in older people with falls but also as a tool to refine falls risk and identify modifiable risk factors in the same cohort.

There are some limitations to this study that should be noted. The sample size is relatively small and from a single clinical centre. Incidence of falls at follow-up is by self-report so may be subject to recall bias. The strengths of the study however are that it is novel, utilises real-world clinical data, includes older people with high levels of frailty and polypharmacy and involves robust follow-up.

In conclusion, this study shows that ABPM biomarkers, particularly those related to BP instability, are independently associated with future falls in a cohort of patients aged ≥70 years with recent falls. Larger interventional studies testing if these biomarkers represent modifiable risk factors for falls in older people are warranted, as these findings may have important implications for BP management as part of comprehensive assessment in older patients with falls.

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