

Twenty-four-hour ambulatory blood pressure monitoring in very elderly patients

Comparison of in-hospital versus home follow-up results

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Abstract

Elevated blood pressure (BP) is frequently diagnosed in very elderly hospitalized patients. Accurate diagnosis of hypertension is challenging in the hospital environment, due to the "white coat effect," and both overtreatment and undertreatment can adversely affect clinical outcome. Twenty-four-hour ambulatory blood pressure monitoring (ABPM) has the potential to avoid the "white coat effect" and accurately guide the management of hypertension. However, effects of the hospital environment on ABPM are unknown in the very elderly. We set out to enroll 45 patients, age ≥70 years, with elevated conventional BP during hospitalization in this observational study. It was prespecified by protocol to assess initially the difference between 24-hour BP during hospital-admission and home follow-up. Subsequent analysis should investigate the change in anxiety (Hospital Anxiety and Depression Scale-A [HADS-A]) after discharge, the correlation with change in 24-hour BP after discharge, and the prevalence of orthostatic hypertension. Thirty-one patients were included in the final analysis (age 83.5±4.4 years; 71% female). Twenty-four-hour BP decreased significantly after hospital discharge (systolic from 133.5 ± 15.6 to 126.2 ± 14.4 mm Hg [millimeter of mercury], P = .008; diastolic from 71.0 ± 9.0 to 68.3 ± 8.6 mm Hg, P = .046). Anxiety level (HADS-A) decreased significantly after discharge, from 7.5 (interguartile range [IQR]: 4.0-13.8) to 5.0 (IQR: 4.0-8.0, P=.012). The change in anxiety was a predictor of change in systolic BP after discharge (F[1,20]=5.9, P=.025). Sixty-one percent of the patients had significant orthostatic hypotension during hospital stay. In conclusion, 24-hour BP in very elderly patients is lower in the home environment than during hospitalization. This phenomenon seems to be directly linked to a lower anxiety-level at home. Reassessing hypertension at home may decrease the need for (intensified) antihypertensive medical therapy in a substantial number of patients. This is particularly important in the very elderly, who have a high prevalence of symptomatic and asymptomatic orthostatic hypotension, making them prone to hazardous effects of antihypertensive therapy.

Abbreviations: ABPM = ambulatory blood pressure monitoring, BP = blood pressure, HADS = Hospital Anxiety and Depression Scale, IQR = interquartile range, mm Hg = millimeter of mercury, SD = standard deviation.

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1. Introduction

Elevated blood pressure (BP) is frequently diagnosed in patients hospitalized for reasons other than hypertension, especially in the very elderly.^[1] Accurate diagnosis of hypertension during hospitalization using conventional techniques is challenging, due to the "white coat effect"^[2] and both overtreatment and undertreatment can adversely affect clinical outcome.^[3,4] Twenty-four-hour ambulatory blood pressure monitoring (ABPM) during hospitalization has the potential to avoid the "white coat effect" and accurately guide antihypertensive therapy. However, data on environmental effects on ABPM are scarce and inconsistent. For example, 1 study found that, following heart transplant, patients had lower ABPM at home than during hospital admission.^[5] Another study found that in-hospital ABPM of randomly selected patients was similar to ABPM of patients in a home environment.^[6] Therefore, ABPM was suggested to be a promising method for diagnosing previously unknown arterial hypertension and for optimizing antihypertensive therapy in hospitalized patients. The present study examined environmental effects on ABPM in the very elderly to test the hypothesis that ABPM results differ between hospital and home environments.

2. Methods

2.1. Patients and study design

Patients at the Department of Internal Medicine, Community Hospital Zollikerberg, from October 2013 until May 2015, who were hospitalized for reasons other than hypertension, were assessed for eligibility. All clinically stable patients, aged ≥ 70 years, with elevated BP (conventional systolic BP [SBP] \geq 140 mm Hg [millimeter of mercury] and/or diastolic BP [DBP] ≥90 mm Hg in more than 3 consecutive readings) were eligible. Patients were deemed to be clinically stable by the treating physician. Key criteria were: acute phase of disease completed (discharge date defined); no perturbing pain; in case of infection, subsiding inflammatory markers; and stable medical therapy established. Exclusion criteria were: indication for immediate antihypertensive treatment (i.e., hypertensive emergencies and urgencies); admitted with stroke or acute coronary syndrome; start or change of antihypertensive medication within 2 weeks before enrollment; and not discharged directly to home. All antihypertensive drugs had to remain unchanged, from hospital discharge until home follow-up of ABPM.

It was prespecified by protocol to assess the difference between in-hospital ABPM and home follow-up. Subsequent analysis should investigate the change in anxiety after discharge, the correlation with ABPM after discharge, and the prevalence of orthostatic hypertension.

The study was approved by the regional Internal Review Board, and all work was conducted in accordance with the Declaration of Helsinki. Written informed consent was given by all patients before participation.

2.2. Procedures

2.2.1. Assessment of antihypertensive therapy. To assure a stable dose of drugs that might interfere with patient's BP drug charts on hospital admission, at the time of in-hospital ABPM and home follow-up, ABPM were thoroughly reviewed.

2.2.2. Assessment of conventional blood pressure and orthostatic hypotension. Before the ABPM was obtained, conventional BP was assessed using a validated oscillometric BP monitoring device (Omron 705IT HEM-759-E; Omron Corporation, Kyoto, Japan).^[7] Clinostatic BP was measured 3 times in a sitting position, with 1-minute intervals between measurements. After 5-minute rest in a supine position, sitting BP was reassessed, immediately followed by 3 BP measurements in a standing position, with 1-minute intervals between measurements. Current European Society of Hypertension/ European Society of Cardiology (ESH/ESC) guidelines were used to define orthostatic hypotension: >20 mm Hg decrease in SBP or >10 mm Hg decrease in DBP within 3 minutes of the transition from supine to standing position.^[8]

To validate our data, the evolution of conventional BP from hospitalization to home follow-up was assessed in a subset of 15 patients.

2.2.3. Twenty-four-hour ABPM. The first ABPM was performed during the hospital stay; the second was obtained within 3 weeks after discharge. The same validated and calibrated oscillometric ABPM device was used for both measurements (Spacelabs 90217; SpaceLabs Medical Inc., Redmond, Washington).^[9] A cuff of appropriate size was placed on the upper arm, and the settings were: measurement every 15 minutes during daytime (8.00 AM until 10.00 PM), and every 30 minutes during

nighttime. The device displayed "off" to avoid a biofeedback effect. Patients were instructed to undertake their usual activities during hospital and home recordings, and to keep the ABPM arm at rest during each measurement. The quality criteria were: \geq 80% successful readings during >10 daytime hours and >7 nighttime hours. The following BP values were considered as invalid: SBP < 50 or >250 mm Hg; DBP < 30 or >150 mm Hg. Hypertension was defined based on ESH/ESC guidelines: 24-hour average systolic ABPM \geq 130 mm Hg and/or diastolic ABPM \geq 80 mm Hg; nighttime SBP \geq 120 mm Hg and/or DBP \geq 70 mm Hg; or daytime SBP \geq 135 mm Hg and/or DBP \geq 85 mm Hg.^[8]

In addition, variability of BP was assessed by analyzing the standard deviations (SD) and the variation of coefficients, as reported previously.^[10] Of particular interest was the comparison of BP-variability during hospitalization and at home follow-up (24-hour period, daytime and nighttime).

2.2.4. Level of anxiety and pain, and burden of comorbidities. The level of anxiety was assessed with the Hospital Anxiety and Depression Scale (HADS),^[11] and pain was rated 0 to 10 (no pain to severe pain), at the time of initial and follow-up ABPM. The Charlson comorbitiy index was used to determine the burden of comorbities among the study population, as previously described: no comorbidities (score = 0), low (score 1–2), moderate (3–4), and high burden (\geq 5).^[12]

2.2.5. Statistical analysis. A sample size of 40 patients was calculated to have 80% power to detect an effect size of 0.46, using a paired t test with a 0.05 2-sided significance level.^[5,13] Assuming a dropout rate of ~10%, it was planned to enroll 45 patients. All variables were expressed as mean \pm SD, or as median accompanied by interquartile range (IQR), if the Shapiro-Wilk test indicated a nonnormal distribution of data. Initial versus follow-up measurements for the same participant were compared using paired t tests for numerical data, Mann-Whitney tests for ordinal data (scores), and χ^2 test or Fisher exact test for nominal data. The effect of the level of gender and anxiety on BP was evaluated using univariable linear regression analysis, incorporating changes in HADS-A score and systolic ABPM from inhospital to follow-up. Further multivariate regression was not performed, due to the small number of patients. Statistical analyses were performed using SPSS 22.0 (SPSS, Inc., Chicago, IL). A P value <.05 was considered statistically significant.

3. Results

3.1. Baseline characteristics

Forty-five patients, \geq 70 years of age, with elevated BP or known hypertension, but hospitalized for other reasons, were prospectively enrolled in the present study. Fourteen of the initial 45 patients were excluded from the final analysis, because their antihypertensive therapy was changed after hospital discharge (6 patients), the ABPM did not meet the quality criteria (4 patients), they were not directly discharged to home (2 patients), or they declined follow-up ABPM (2 patients).

Of the 31 patients included in the final analysis, mean age was 83.5 ± 4.4 years, and 71% were women (Table 1). A large majority had a Charlson comorbidity index <3, indicating a low burden of comorbidities. Twenty-one patients had a history of hypertension, and all patients were on a stable medical therapy without changes in antihypertensive therapy between hospital admission, in-hospital ABPM, and home follow-up ABPM (Table 2). On average, patients stayed in the hospital for 9.0 ± 4.0 days.

Table 1

Patient baseline characteristics and reasons for hospital admission.

	All patients (n=31)
Age, mean (SD)	83.5 (4.4)
Female sex, no., %	22 (71)
Hypertension, no., %	22 (71)
Diabetes mellitus, no., %	5 (16)
Hypercholesterolaemia, no., %	4 (13)
Coronary artery disease, no., %	5 (16)
Active smoker, no., %	3 (10)
History of heart failure, no., %	2 (7)
Cerebrovascular disease, no., %	5 (16)
Peripheral arterial disease, no., %	4 (13)
Chronic kidney disease*, no., %	10 (32)
Chronic pulmonary disease, no., %	3 (10)
Obesity [†] , no., %	4 (13)
History of cancer, no., %	4 (13)
Dementia, no., %	3 (10)
Charlson comorbidity index, no., %	
None (0)	9 (29)
Low (1-2)	17 (55)
Moderate (3-4)	4 (13)
High (≥5)	1 (3)
Orthostatic symptoms (past y), no., %	13 (42)
Previous falls (past y), no., %	1 (3)
Reason for hospital admission	
Infectious disease, no., %	12 (39)
Musculoskeletal disease, no., %	6 (19)
Gastroenterological disease, no., %	5 (16)
Cerebrovascular disease, no., %	5 (16)
Orthopaedic surgery, no., %	2 (7)
Endocrinological disease, no., %	1 (3)

No. = number, SD = standard deviation.

^{*} Chronic kidney disease stage \geq 3 (kidney disease outcomes quality initiative).

[†] BMI \geq 30 g/m².

Table 2	
Medication	use.

	All patients (n=31)
Antihypertensive medication, no., %	23 (74)
Angiotensin system-blocking medication	
Angiotensin receptor blocker, no., %	14 (45)
ACE-inhibitor, no., %	5 (16)
Calcium channel blockers, no., %	11 (36)
β-Blocker, no., %	9 (29)
Aldosterone receptor antagonists, no., %	1 (3)
Any diuretic, no., %	11 (36)
α -Blocker	1 (3)
Aspirin, no., %	14 (45)
Psychotropic medication, no., %	9 (29)
Analgetics, no., %	9 (29)
Acetaminophen, no., %	4 (13)
NSAID, no., %	2 (6)
Opioid, no., %	8 (26)

ACE-inhibitor = angiotensin-converting-enzyme inhibitor, no. = number, NSAID = nonsteroidal antiinflammatory drug.

3.2. Twenty-four-hour ABPM

ABPM was performed on average 4.0 ± 3.1 days before discharge and 16.0 ± 6.7 days after discharge. The average 24-hour systolic and diastolic ABPM decreased significantly after hospital discharge (SBP from 133.5 ± 15.6 to 126.2 ± 14.4 mm Hg, P=.008; DBP from 71.0 ± 9.0 to 68.3 ± 8.6 mm Hg, P=.046; Fig. 1, Table 3). The same pattern was found for systolic and diastolic ABPM during daytime and nighttime. Univariate linear regression analysis indicated that gender might be a predictor of decreased systolic ABPM at home follow-up (F[1,29]=7,6, P=.01). Further multivariate regression was not performed, due to the small number of patients.

Based on ESH/ESC criteria, 24 patients were classified as hypertensive during hospital admission, but only 17 met these criteria during home follow-up (P=.012). Thus, 7 of the 24 patients (29.2%) were misclassified as hypertensive based on in-hospital ABPM. Diagnostic performance for in-hospital ABPM was: sensitivity=94.4%, (95% confidence interval, 72.7–99.9); specificity=46.2% (19.2–74.9); positive predictive value=70.8 (59.2–80.3); and negative predictive value=85.7% (45.0–97.8).

The variability of SBP and DBP for the 24-hour period as well as during day- and nighttime are shown in the online appendix (online table 1, http://links.lww.com/MD/B819). There were no significant differences in BP variations during hospitalization and home follow-up.

3.3. Conventional BP during hospital admission and home follow-up

Based on conventional BP measurements during hospitalization, 9 patients (29.0%) had a sitting SBP > 160 mm Hg (Table 3). Nineteen patients (61.3%) met the criteria for orthostatic hypotension (supine to standing change in SBP=20.4 \pm 26.9 mm Hg, *P* < .001), and 12 of those 19 (63.2%) reported symptomatic orthostatic hypotension. Figure 2 shows an illustrative case.

Data on the evolution of conventional BP from hospitalization to home follow-up is available for a subset of 15 patients. BP decreased significantly after hospital discharge (SBP from 151.8 ± 16.7 to 137.1 ± 25.0 mm Hg, P = .03; DBP from 78.7 ± 10.7 to 70.4 ± 15.6 mm Hg, P = .06; Table 3).

3.4. Anxiety and pain levels

Average anxiety level decreased significantly after discharge, from an average HADS-A score of 8.3 ± 5.3 to 5.9 ± 3.5 (P=.011). The change in the average HADS-D score (6.5 ± 4.5 vs 6.0 ± 3.50) was not significant (P=.74). Results of univariate linear regression indicated that decreased anxiety during followup was a predictor of decreased systolic ABPM (F[1,20]=5.9, P=.025). Further multivariate regression was not performed, due to the small number of patients. No differences were found in the average level of pain during hospital stay and follow-up (1.2 ± 1.6 and 1.1 ± 1.5 , respectively, P=.49).

4. Discussion

Results of this prospective study show that 24-hour BP in very elderly patients was lower in the home environment than during hospitalization; level of anxiety decreased significantly after discharge; the change in anxiety after discharge was directly linked with the change in BP after discharge; in-hospital ABPM misclassified around 1/3 of patients as hypertensive; and very elderly patients had a high prevalence of severe orthostatic hypotension, 1/3 of these patients were asymptomatic.





Table 3

Hemodynamics.

	In-hospital	Follow-up	Р
Twenty-four-hour ABPM			
Systolic blood pressure-24-hour, mean (SD)	133.5 (15.6)	126.2 (14.4)	.008
Systolic blood pressure-daytime, mean (SD)	134.3 (15.8)	127.4 (14.7)	.015
Systolic blood pressure-nighttime, mean (SD)	129.8 (18.5)	122.5 (16.6)	.019
Diastolic blood pressure-24-hour, mean (SD)	71.0 (9.0)	68.3 (8.6)	.046
Diastolic blood pressure-daytime, mean (SD)	72.1 (9.2)	69.5 (9.0)	.084
Diastolic blood pressure—nighttime, mean (SD)	67.0 (10.4)	63.8 (9.9)	.012
Conventional blood pressure			
Sitting systolic blood pressure, mean (SD)	148.6 (19.0)	_	-
Evolution of sitting systolic blood pressure, mean (SD) st	151.8 (16.7)	137.1 (25.0)	.03
Evolution of sitting diastolic blood pressure, mean (SD) st	78.7 (10.7)	70.4 (15.6)	.06
Sitting systolic blood pressure >160 mm Hg, no., %	9 (29)	_	-
Supine systolic blood pressure, mean (SD)	154.6 (15.2)	_	-
Supine systolic blood pressure >160 mm Hg, no., %	9 (29)	_	-
Systolic BP change, supine to standing, (SD)	20.4 (26.9)	_	-
Diastolic BP change, supine to standing, (SD)	4.6 (15.0)	_	-
Orthostatic hypotension, no., $\%^{\dagger}$	19 (61)	_	-
Symptomatic orthostatic hypotension, no., %	12 (39)	-	-

ABPM = ambulatory blood pressure monitoring, no. = number, SD = standard deviation.

Data on evolution of conventional BP from hospitalization to home follow-up is available for a subset of 15 patients.

[†] Orthostatic hypotension was defined as >20 mm Hg decline in systolic BP or >10 mm Hg decline in diastolic BP going from supine to standing within 3 minutes.



Figure 2. Conventional in-hospital blood pressure (BP) assessment (panel A) and sequential 24-hour ambulatory blood pressure monitoring (ABPM) in-hospital (panel B) and 10 days after discharge (panel C) in an 83-year-old man, initially admitted with influenza. Twenty-four-hour ABPM in panel B, (panel C) daytime: white time-zone; nighttime: gray time-zone. Notably, the patient has severe, but asymptomatic orthostatic hypotension (supine to standing change in systolic BP (SBP)/ diastolic BP (DBP)=40/22 mm Hg). The average 24-hour ABPM revealed a change in SBP/DBP between in-hospital and home follow-up of -29/3 mm Hg. ABPM = ambulatory blood pressure monitoring, BP = blood pressure, mm Hg = millimeter of mercury.

4.1. Disparity in ABPM during hospital admission and home follow-up

The present study found significantly lower conventional BP and ABPM in the home environment following discharge than during hospitalization. This pattern was consistent for all ABPM parameters: SBP and DBP over 24 hours, daytime and nighttime measurements. Higher BP during hospitalization is consistent with the "white coat effect", and has been described thoroughly for conventional BP.^[2,14-16] However, data for ABPM is scarce and conflicting. Similar to our results, the "white coat effect" of ABPM was described for heart transplant patients.^[5] Conflicting results of another previous study might be related to the older mean age of our study population (84 vs 58 years).^[6] Profound differences of hemodynamics have been reported in older subjects, related to the dramatic increase in prevalence of hypertension with age, from ~60% in patients in their 60s and 70s to as high as 90% in octogenarians.^[8,17] Increasing age is associated with increasing arterial stiffness, resulting in higher SBP and pulse pressure, as well as higher pulse wave velocity, an independent predictor of myocardial infarction, stroke, and overall cardiovascular disease.^[18–22] These changes along with other age-related pathophysiological changes, such as metabolic changes, neurohormonal disorders, a proinflammatory state, and endothelial dysfunction, all contribute to high prevalence of isolated systolic hypertension, impaired BP variability, and orthostatic hypotension.^[22] In the present study, the majority of patients (61%) met the criteria of orthostatic hypotension. It is noteworthy that more than 1/3 of these patients reported no symptoms during these episodes, highlighting the deceitful character of orthostatic hypotension, a pathology which is closely linked to poor cardiovascular outcome.^[23,24] It is conceivable that age-related changes in hemodynamics contribute to the environmental effects on ABPM, but ultimately remain a matter of debate.

We found a higher level of anxiety during hospital stay compared to home follow-up, which in turn was significantly correlated with higher levels of ABPM. Previous studies demonstrated a link between the level of anxiety and hypertension,^[25–27] and Paterniti et al^[28] confirmed this relationship for the elderly. Although our results do not prove a causal relationship, anxiety might induce hypertension via stimulation of sympathetic activity, similar to the "white coat effect."^[29,30] Regardless of the mechanism, our findings demonstrate an environmental effect (hospital vs home) on 24-hour ABPM in the very elderly, and suggest that anxiety is an important contributing factor.

4.2. Value of in-hospital ABPM

Similar to conventional BP measurements, 24-hour ABPM appears to be influenced by in-hospital versus in-home location, that is, a "white coat effect." This environmental effect should be taken into account in interpreting results of in-hospital ABPM. Nearly 1/3 of the patients who were labeled as hypertensive based on in-hospital data in our study had normal ABPM results at home. The positive predictive value of in-hospital ABPM compared to in-home ABPM was only 70.8% for identifying hypertensive patients. Thus, in-hospital ABPM should be used with caution in guiding antihypertensive therapy. Theoretically, ABPM at home after discharge might obviate the need for (intensified) antihypertensive treatment in a substantial number of patients. However, from a practical point of view, especially if the in-hospital BP is consistently >160/100 mm Hg, we

recommend carefully monitored intensification of antihypertensive therapy. This treatment should be thoroughly reevaluated following discharge. Reevaluation is very important in elderly patients, who have high prevalence of comorbidities and orthostatic hypotension, and are particularly susceptible to hazardous effects of antihypertensive therapy.

Despite the environmental effect, in-hospital ABPM demonstrated good diagnostic performance for identifying normotensive patients (negative predictive value = 85.7%). Therefore, if a patient has consistently elevated conventional BP, but normal ABPM during their hospital stay, it would be reasonable to defer the start or intensification of antihypertensive therapy until inhome reassessment.

4.3. Gender and the disparity in ABPM during hospital admission and home follow-up

Univariate regression analysis indicated that gender might be a predictor of decreased systolic ABPM at home follow-up. To the best of our knowledge, there is no appropriately powered study investigating environmental and gender effects on ABPM in a similar setup as in our study.

Literature on the effect of gender in white coat hypertension is conflicting, reporting no gender difference in the "white coat effect" after adjustment for other factors^[31] or supporting our finding even after adjustment for other factors.^[32] It is sensible to consider our results as hypothesis generating. Further, larger scale trials are warranted and hopefully will shed light on the important topic of gender differences and the white coat effect, especially in the growing population of octogenarians.

4.4. Study limitations

The present study was mainly limited by its small sample size, which limited the power of the analyses. Due to its observational approach, the conclusions should be considered as hypothesis generating. Although a bias by order-effect cannot be ruled out, the effect in ABPM is small and cannot explain the differences between in-hospital and in-home ABPM.^[33] Finally, 24-hour ABPM was not performed before hospital admission, because enrolled patients were not electively scheduled for hospital admission.

Furthermore, we did not include a control arm of normotensive elderly patients to the study design. This limitation is mainly attributed to the design of present study as a "pilot study" to gain information for future larger scale studies on this topic.

A substantial proportion of patients (\sim 30%) were excluded from final analysis, based on predetermined criteria. This highlights a common obstacle in this type of research, especially when the study includes octogenarians. A high attrition rate of participants has to be taken into account when planning future studies in this field of research.

5. Conclusion

Results of the present study demonstrated that 24-hour ABPM was higher during hospitalization than in the home environment following discharge, an environmental effect that should be considered in diagnosing and treating hypertension. The effect appeared to be linked to anxiety level. Although in-hospital ABPM proved to be a good diagnostic tool for identifying normotensive patients, apparent hypertensive patients should be reassessed at home, following discharge, to avoid unnecessary

treatment or intensification. This is particularly important in very elderly patients, who have a high prevalence of symptomatic and asymptomatic orthostatic hypotension, making them prone to hazardous effects of antihypertensive therapy.

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