Long-Term Reproducibility of Ambulatory Blood Pressure is Superior to Office Blood Pressure in the Very Elderly

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Abstract

While it is known that reproducibility of ambulatory blood pressure (BP) is superior to office BP in middle-aged subjects, little is known older age groups. Hence, we compared the long-term reproducibility of ambulatory and office BP readings in subjects over the age of 75 years. A cohort of 72 subjects 75-90 years of age (mean, 82 years at baseline) had repeat office and ambulatory blood pressures 2 years apart under similar conditions. On the same day, patients underwent office BP measurements by a semi-automated device and then by ambulatory BP monitoring. Awake and sleep periods were divided according to a diary kept by each patient. The agreement between studies was assessed using the standard deviation of the differences (SDD) and Bland-Altman plots. There were minimal mean changes in office, 24-hour, awake and sleep mean BP values between baseline and 2 years later. The SDDs between visits were lower for 24-hour BP compared to the office BP (11.7/5.9 mmHg versus 17.8/9.0 mmHg, $p < 0.01$). The SDD for 24-hour BP was also lower than the SDDs for the awake and sleep BP ($p < 0.05$). Nocturnal BPs defined by absolute values were more reproducible than categories of dippers and non-dippers. These data demonstrate that long-term reproducibility of 24-hour BP is superior to office measurements for very elderly subjects. In a clinical trial involving this age group, far fewer subjects would be required if 24-hour BP was the primary efficacy endpoint rather than the office BP.

Keywords

blood pressure reproducibility; ambulatory blood pressure; very elderly

Introduction

Repeated ambulatory blood pressure (BP) measurements have been shown to have better reproducibility than repeated clinic (or office) BP measurements in short- and long-term studies in which there were no interventions[1-3]. This characteristic of reduced BP variability

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observed with ambulatory monitoring yields a reduction in sample size for clinical trials compared to requirements when clinic BP is the endpoint[1, 3-5]. These findings have led to an increased utility of ambulatory BP as an endpoint in clinical trials as both the sample size can be reduced and an intervention can be assessed more objectively. [4,5]

Prior assessments of clinic and ambulatory BP variability have focused on middle-aged subjects who typically participate in antihypertensive trials of new therapies[5] although one short-term study[6] evaluated the reproducibility of the morning BP surge in individuals who were over 70 years old. Since the Hypertension in the Very Elderly Trial (HYVET) demonstrated that antihypertensive treatment in patients > 80 years old is of significant benefit after a mean of only 1.8 years [7] and there is evidence that ambulatory BP has prognostic relevance in elderly patients [8-11], data on the reproducibility of BP measurements in a very elderly group would be of interest for future clinical trial development. Thus, we studied the reproducibility of clinic and ambulatory BP in a very elderly population who underwent measurements at intervals of 2 years as part of a long-term study on the relations among BP, mobility, cognitive function, and the development of white matter lesions of the brain[12].

Methods

Subjects and Design

The study was initiated in late 2005 with 99 subjects aged 75-89 stratified according to age and mobility function. Of those, 95 subjects had complete testing including 24-hour BP monitoring. The cohort returned for a second evaluation period in 2007-2008 coinciding with the 24th month from their initial studies. The study was approved by the Institutional Review Board at the University of Connecticut Health Center, Farmington and all subjects signed consent prior to any study-related procedures taking place. Subjects were excluded if they had: a systemic or neurological disease that limited mobility, impaired mental status, unstable cardiovascular disease (myocardial infarction in past 6 months or unstable angina, congestive heart failure or stroke), oxygen-dependence, weight > 114 kg (due to difficulty with magnetic resonance imaging (MRI) and/or successful application of the ambulatory BP recorder cuffs), metallic foreign body precluding use of MRI, or a short expected lifespan (< 4 years). Subjects underwent a history and physical exam to determine eligibility and during a screening and evaluation period had determinations of duplicate clinical BP readings made on 3 separate office visits. The clinic BP determinations obtained on visits coinciding with the 24-hour ambulatory BP monitoring were utilized in the analyses. The ambulatory BP recordings were performed using an validated device (Oscar 2 recorder, Suntech Medical Instruments, Morrisville, NC)[13]. Ambulatory BP monitors were placed on weekdays and obtained automated BP values every 15 minutes while patients were awake and every 30 minutes during sleep. We strongly advocated that subjects remain physically active during the day and avoid naps. Sleep times, any symptoms and medication dosing were recorded by the subjects on patient-kept diaries.

Analytical methods

Data obtained for the ambulatory BP measurements included 24-hour mean, awake and sleep systolic and diastolic BP values. Only physiologically impossible values are deleted from individual records (e.g. diastolic > systolic BP, pulse pressures < 10 mmHg). In addition, BP surge measurements during the early morning period were calculated as the mean of first 2 hours post-awakening – the mean of last 2 hours pre-awakening.

Descriptive statistics were used to calculate the mean, standard deviation of the two time periods. Paired t-tests were used to test for differences between Time 2 and Time 1 (T2 – T1). Standard deviation of the differences (SDD) and repeatability coefficient (RC) were calculated for all BP measurements. These values were then used to construct Bland-Altman plots[14] to determine the limits of agreement between the types of measurement differences. Pitman's test for correlated variances was used to compare the variances of the different BP measurements[15]. All analyses were performed using SAS 9.2 (Cary, N.C.).

The changes in the declines in BP during sleep compared to the awake period (the 'dipping' status) were calculated for each subject at study periods 1 and 2. Dipping and non-dipping status were defined as 10% reduction in nocturnal systolic BP relative to awake systolic and 0 to < 10 % reduction in nocturnal systolic BP, respectively. Change in dipping status was calculated as one of the following potential scenarios: a) Dipper remaining a dipper; b) Dipper changing to a non-dipper, c) non-dipper remaining a non-dipper, d) non-dipper changing to a dipper. Changes in absolute values of nocturnal hypertension using values of nocturnal systolic BP 120 and 125 mmHg to define hypertension and a nocturnal systolic BP < 120 and 125 mmHg to define normotension as previously described[16].

Evaluation of the impact of the BP variability on sample size requirements for a clinical trial in the very elderly using power of 80% and $p = 0.05$ in a two-tailed test was calculated, varying the effect size of systolic BP between 3 and 9 mmHg.

Results

Subjects

There were initially 99 subjects enrolled in the study with a mean age of 82 ± 3.8 years. Of this group, 95 completed an ambulatory BP recording (Table 1). Two years later, a total of 23 subjects had died, moved into a convalescent home, had a pacemaker implant or declined participation in the 24-hour BP monitoring portion of the study leaving 72 subjects in the final analysis. Of the subjects who enrolled into the study, 70% had hypertension, 13% had coronary artery disease, 6% had diabetes, and 48% had dyslipidemia (LDL cholesterol > 130 mg/dl). Of the 72 subjects who had BP monitors at baseline and following 2 years, there were no major changes in body weight (mean BMI: 26.8 vs. 26.3 kg/m^2) and only 3 patients had major interval medical problems: development of stroke, heart failure or valvular disease. There were 3 patients who stopped antihypertensive therapy and 4 patients who were initiated on antihypertensive therapy. Clinical decisions related to drug therapies were made by the patient's primary care physician without input from the study staff.

Mean clinic and ambulatory BP measurements

There were no differences between repeated measurements for the majority of the clinic, 24-hour, awake and sleep BPs over the 2 year period; exceptions were the clinic diastolic BP, pre-awakening systolic BP, sleep pulse pressure, and post-awakening pulse pressure (Table 1). For both baseline and repeat measurements the ambulatory BP readings were slightly lower than the clinic measurements (Table 1) reflecting the usual impact of sleep on the 24-hour BP values.

Repeated 24-hour systolic and diastolic BP had significantly less variability and hence, greater reproducibility compared to clinic blood pressure (systolic SDD: 11.6 vs. 17.8 mmHg and diastolic SDD, 9.0 vs 6.0 mmHg, for 24-hour versus clinic, respectively, p < 0.01 for both, Table 1). The SDD of the 24-hour mean BP was also lower than awake and sleep blood pressures (Table 1). In contrast, early morning BPs (both pre- and post-awake systolic BP) had SDDs similar to that of the clinic BPs. As expected, the reproducibility for the pulse pressure (systolic – diastolic BP) was between the reproducibility of systolic and diastolic pressure (Table 1). Results for the 65 subjects who had no changes in antihypertensive medications over the same 2 year period were unchanged from the data shown in Table 1 (data not shown).

Analyses of the Bland-Altman plot for clinic and 24-hour ambulatory systolic pressures are shown in Figure 1. The limits of agreement for the clinic systolic BP are substantially larger than for the 24-hour ambulatory systolic BP. The upper and lower limits of agreement across a wide range in systolic BPs were 35.5 and -35.5 mmHg for the clinic pressure and 24.5 mmHg and - 22.3 mmHg for the 24-hour BPs, respectively.

Analysis of nocturnal blood pressure classifications

The changes in categories of circadian BP profiles according to nocturnal declines in BP during sleep over 2 years are shown in Table 2. Of the subjects who were initially classified as dippers (>10% reduction in nocturnal systolic BP relative to awake systolic BP), 30% remained dippers at the second evaluation and 70% converted to another category. Similarly, of the 24 patients who were initially classified as non-dippers (0 to < 10 % reduction in nocturnal systolic BP), 42% remained non-dippers at the second evaluation and 58% converted to another category. In total 60% patients changed their dipping status over the 2-year period of assessment. Changes in hypertensive status based on absolute nocturnal systolic BP demonstrated improved reproducibility compared to categorical changes (Table 2). For those patients originally classified as having nocturnal hypertension (based on a systolic BP   120 or   125 mmHg), 83% and 70%, respectively remained in the hypertensive category 2 years later; for those originally classified as normotensive (based on systolic BP < 120 and < 125 mmHg), 66% and 75%, respectively remained normotensive 2 years later.

Impact of reproducibility on sample size requirements for a clinical trial

Sample size calculations for a very elderly population being evaluated in a clinical interventional trial is shown in Table 3 across a variety of estimated mean effects. As shown in the Table, a much smaller study population could be used to detect an effect of an

intervention on systolic BP or pulse pressure using 24-hour BP versus clinic BP (e.g. for mean changes in systolic BP of 5 mmHg, 85 vs. 198 subjects per treatment arm). The required sample size would also be less if awake or sleep BP was the endpoint of interest; in contrast, assessment of changes in the early morning BP would require a large sample, similar to that of the clinic BP (Table 3).

Discussion

Principal Findings

Our study demonstrated that in a very elderly patient group, unselected with regard to hypertensive status, 24-hour ambulatory BP measurements were substantially more reproducible than standardized measurements performed in the clinic (or office) environment. Both the systolic and diastolic BP, as well as the pulse pressure, showed this pattern. As the ambulatory BP components were broken into smaller segments of time (e.g., the awake, sleep or early morning period), the reproducibility lessened but the awake and sleep BP variability was still less than that observed in the clinic. These findings show that in this older population, interventional studies with non-drug or drug therapies could use much smaller sample sizes if the ambulatory BP was used as the primary efficacy endpoint relative to the sample size required than if the clinic BP was used as the primary endpoint.

Comparisons with prior studies on clinic and ambulatory BP reproducibility

Our data show relatively similar results to the findings in younger subjects that demonstrate that the reproducibility of the 24-hour BP is superior to that of the clinic BP in both short-term[17,18] and longer-term assessments [5,6]. However, since our patient group is in a much older population, we focused on systolic and pulse pressure, which are of greater prognostic importance than diastolic BP and would be a more likely target for intervention[7,10,11]. As in other studies, the systolic BP variability for clinic BP is nearly twice that of the 24-hour systolic BP (Table 1). The findings of Mansoor et al[5] are similar to the present results – in that study, long-term evaluation of 24-hour ambulatory BP revealed superior reproducibility over office BP with a SDD for 24-hour BP of 9.8 mmHg versus 17 mmHg for the office pressure.

Classification of Nocturnal BP Decline

The classification of patients according to the decline in nocturnal BP has been highly controversial. Indeed, in our study of a very elderly cohort, approximately 60-70% of patients changed their dipping versus non-dipping status over the 2 years based on repeat 24-hour BP measurements. Our data confirm results of other studies that have reported a poor reproducibility of dipping-status[17-21]. We advocated in the past that the absolute nocturnal BP values were a more sensible means to assess the effects of antihypertensive therapy[16] as it is more reproducible than dipping status. The finding that 34% fewer patients had a change in their nocturnal blood pressure classification when using absolute nocturnal BP values confirms the improved reproducibility (Table 2). Our findings have been corroborated by Burr and colleagues[6] who demonstrated that night-time blood pressure is the strongest predictor of cardiovascular outcome in an older population in Ireland. Although the PAMELA study[22] reported high cardiovascular mortality associated with a

blunted nocturnal dipping pattern, it is unclear how one can practically use that information in individual patients when the reproducibility of an individual patients' dipping-status is so poor (Table 2).

Impact of our findings on clinical trials in very old hypertensive subjects

Previous studies two decades ago showed that a significant reduction in study size could be attained if ambulatory BP was used rather than clinic BP in a short-term trial4. In fact, it was determined that a 50% reduction in the standard deviation of the difference (SDD) as an indicator of BP variability would translate to a 75% reduction in sample size needed in a clinical trial 1,4. We have determined fairly similar results in a much older population and one in which the follow-up period is much longer and similar to that of HYVET 7. In fact, if one was trying to plan a study to determine if an active agent could lower systolic BP by at least 4 mmHg better than a placebo in a patient population > 80 years of age, using 24-hour BP as the primary endpoint would lower the sample size by 67% (Table 4). Until HYVET, lack of experience in the very elderly population with regards to outcomes, kept this important patient group out of clinical trials. That should no longer be the case and our data support using 24-hour systolic BP as the primary endpoint in clinical trials of antihypertensive therapies.

Study limitations

The proportion of subjects from the cohort available for assessment at year 2 declined substantially due to death and disability. Of the 23 subjects unavailable, only 5 were due to unwillingness to wear the ABP recorder. Of the 72 patients who wore the monitor twice, 71 of these patients had complete data (nocturnal BP was missing in 1 subject (Table 3). The results of our study suggest that in performing a clinical trial of the very elderly using ambulatory BP recordings, expectations for a 20-25% loss of data in a long-term study would be appropriate and the sample size calculations should take this into consideration.

Conclusions

The results of this study demonstrate that the reproducibility of 24-hour systolic and pulse pressure are superior to the office BP in very elderly subjects. This translates into major impact on the sample size of a clinical trial if 24-hour ambulatory BP was used as an end-points rather than office BP; in fact, a reduction in the required sample by 67%. Similar to findings in a middle-aged population, we also found that defining nocturnal hypertension using absolute values is more reproducible than using categories of nocturnal hypertension related to changes from day to night.

Acknowledgments

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References

1. Trazzi S, Mutti E, Frattola A, Imholz B, Parati G, Mancia G. Reproducibility of non-invasive and intra-arterial blood pressure monitoring: implications for studies on antihypertensive treatment. J Hypertens. 1991; 9:115–119. [PubMed: 1849525]

2. Des Combes BJ, Porchet M, Waeber B, Brunner HR. Ambulatory blood pressure recordings reproducibility and unpredictability. Hypertension. 1984; 6:110–114. [PubMed: 6693140]

3. James GD, Pickering TG, Yee LS, Harshfield GA, Riva S, Laragh JH. The reproducibility of average ambulatory, home and clinic pressures. Hypertension. 1988; 11:545–549. [PubMed: 3384470]

4. Conway J, Johnston J, Coats A, Somers V, Sleight P. The use of ambulatory blood pressure monitoring to improve the accuracy and reduce the numbers of subjects in clinical trials of antihypertensive agents. J Hypertens. 1988; 6:111–116. [PubMed: 3280674]

5. Mansoor GA, McCabe EJ, White WB. Long-term reproducibility of ambulatory blood pressure. J Hypertens. 1994; 12:703–708. [PubMed: 7963496]

6. Wizner B, Dechering DG, Thijs L, Atkins N, Fagard R, O'Brien E, de Leeuw PW, Parati G, Palatini P, Clement D, Grodzicki T, Kario K, Staessen JA. Short-term and long-term repeatability of the morning blood pressure in older patients with isolated systolic hypertension. J Hypertens. 2008; 26:1328–1335. [PubMed: 18551007]

7. Beckett NS, Peters R, Fletcher AE, Staessen JA, Liu L, Dumitrascu D, Stoyanovsky V, Antikainen RL, Nikitin Y, Anderson C, Belhani A, Forette F, Rajkumar C, Thijs L, Banya W, Bulpitt CJ. Treatment of hypertension in patients 80 years of age or older. N Engl J Med. 2008; 358:1887–1898. [PubMed: 18378519]

8. Burr ML, Dolan E, O'Brien EW, O'Brien ET, McCormack P. The value of ambulatory blood pressure in older adults: the Dublin outcome study. Age Ageing. 2008; 37:201–206. [PubMed: 18349014]

9. Staessen JA, Thijs L, Fagard R, O'Brien ET, Clement D, de Leeuw PW, Mancia G, Nachev C, Palatini P, Parati G, Tuomilehto J, Webster J. Predicting cardiovascular risk using conventional vs ambulatory blood pressure in older patients with systolic hypertension. JAMA. 1999; 282:539–546. [PubMed: 10450715]

10. Bjorklund K, Lind L, Zethelius B, Berglund L, Lithell H. Prognostic significance of 24-h ambulatory blood pressure characteristics for cardiovascular morbidity in a population of elderly men. J Hypertens. 2004; 22:1691–1697. [PubMed: 15311096]

11. Khattar RS, Swales JD, Dore C, Senior R, Lahiri A. Effect of aging on the prognostic significance of ambulatory systolic, diastolic and pulse pressure in essential hypertension. Circulation. 2001; 104:783–789. [PubMed: 11502703]

12. Moscufo N, Guttmann CR, Meier D, Csapo I, Hildenbrand PG, Healy BC, Schmidt JA, Wolfson L. Brain regional lesion burden and impaired mobility in the elderly. Neurobiol Aging. 2009 May 8. Epub ahead of print.

13. Goodwin J, Bilous M, Winship S, Finn P, Jones SC. Validation of the Oscar 2 oscillometric 24-h ambulatory blood pressure monitor according to the British Hypertension Society protocol. Blood Pressure Monit. 2007; 12:113–117.

14. Bland JM, Altman DG. Statistical methods for assessing agreement between two methods of clinical measurement. Lancet. 1986; 1:307–311. [PubMed: 2868172]

15. Pitman EJG. A note on normal correlation. Biometrika. 1939; 31:9–12.

16. White WB, Larocca G. Improving the utility of the nocturnal hypertension definition by using absolute sleep blood pressure rather than the 'Dipping' proportion. Am J Cardiol. 2003; 92:1439–1441. [PubMed: 14675581]

17. Palatini P, Mormino P, Canali C, Santonastaso M, De Venuto G, Zanata G, Pessina AC. Factors affecting ambulatory blood pressure reproducibility: Results of the HARVEST Trial. Hypertension. 1994; 23:211–216. [PubMed: 8307631]

18. Kario K, Ishikawa J, Pickering TG, Hoshide S, Eguchi K, Morinari M, Hoshide Y, Kuroda T, Shimada K. Morning hypertension: the strongest independent risk factor for stroke in elderly hypertensive patients. Hypertens Res. 2006; 29:581–587. [PubMed: 17137213]

19. Metoki H, Ohkubo T, Kikuya M, Asayama K, Obara T, Hara A, Hirose T, Hashimoto J, Totsune K, Hoshi H, Satoh H, Imai Y. Prognostic significance of night-time, early morning and daytime blood pressures on the risk of cerebrovascular mortality: the Ohasama Study. J Hypertens. 2006; 24:1841–1848. [PubMed: 16915034]

20. Omboni S, Parati G, Palatini P, Vanasia A, Muiesan ML, Cuspidi C, Mancia G. Reproducibility and clinical value of nocturnal hypotension: prospective evidence from the SAMPLE study. J Hypertens. 1998; 16:733–738. [PubMed: 9663912]

21. Cuspidi C, Meani S, Valerio C, Sala C, Fusi V, Masaidi M, Zanchetti A, Mancia G. Reproducibility of dipping/non-dipping pattern in untreated essential hypertensive patients: impact of sex and age. Blood Press Monit. 2007; 12:101–106. [PubMed: 17353653]

22. Mancia G, Bombelli M, Facchetti R, Madotto F, Corrao G, Quarti Trevano F, Grassi G, Sega R. Long-term prognostic value of blood pressure variability in the general population: Results of the Pressioni Arteriose Monitirate e Loro Associazioni Study. Hypertension. 2007; 49:1265–1270. [PubMed: 17452502]

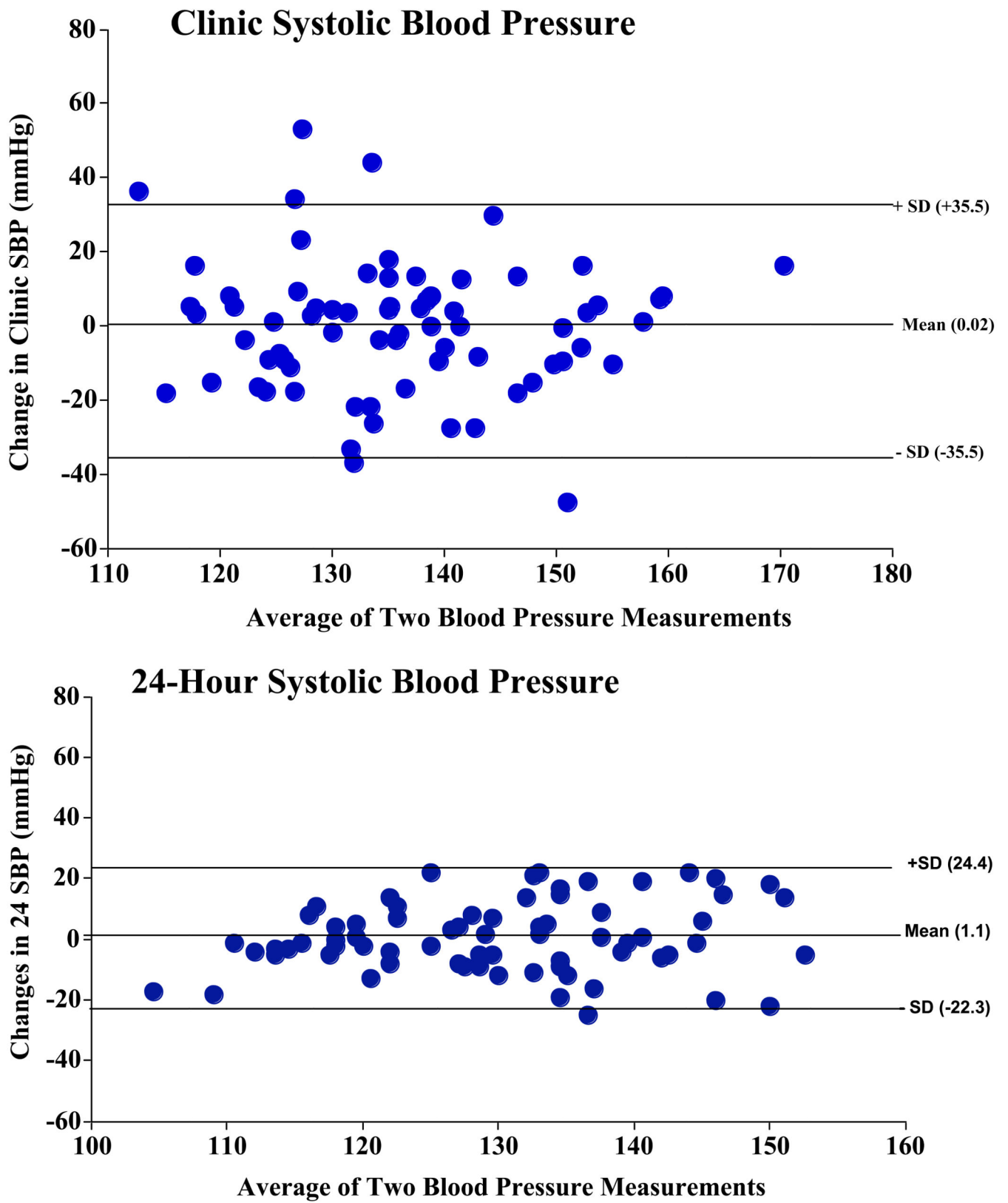**Figure 1.**

Limits of agreement for the office systolic BP in a very elderly cohort taken 2 years apart (panel A) and for systolic BP taken by 24 hour BP monitoring (panel B) using the methods of Bland and Altman.14

Table 1

Clinic and Ambulatory Blood Pressures at the 2 Study Periods (n = 72)

BP Parameter (mmHg)	Initial Study (Mean BP)	2-Year Study (Mean BP)	Changes Between Study Periods	P-value Between Study Periods	Standard Deviation of the Differences	Repeatability Coefficient (RC)
Clinic systolic	136	136	0.02	0.990	17.8*	35.5*
Clinic diastolic	71	68	-2.9	**0.008**	9.0*	18.0*
Clinic PP	65	68	2.9	0.080	14	28
24 hour systolic	130	131	1.1	0.433	11.7	23.3
24 hour diastolic	66	67	0.2	0.814	6.0	12.0
24 hour PP	63	64	0.92	0.270	7.1	14.2
Awake systolic	132	132	0.5	0.754	12.7**	25.5**
Awake diastolic	68	68	0.04	0.956	6.4**	12.8**
Awake PP	63	64	0.50	0.599	8.0	16.0
Sleep systolic	122	125	3.2	0.052	13.7**	27.5**
Sleep diastolic	60	60	0.72	0.441	7.8	15.6
Sleep PP	62	64	2.5	**0.016**	8.7	17.4
Pre-awake systolic	126	129	4.3	**0.036**	16.7	33.4
Pre-awake diastolic	62	63	1.6	0.191	9.9	19.9
Pre-awake PP	64	66	2.7	0.065	12.0	24
Post-awake systolic	134	138	4.3	0.066	19.4	38.9
Post-awake diastolic	72	71	-0.44	0.726	10.4	20.9
Post-awake PP	62	67	4.7	**0.011**	15.4	30.8

PP – pulse pressure; bolded typeface are significant p-values

*
p < 0.01 compared to clinic BP;

**
p < 0.05 compared to 24-hour BP

Table 2

**Changes from Baseline in Nocturnal Blood Pressure Categories at Two Years
(Categorical and Absolute values)**

Categorical[*]	Status at Second Study (year 2) N (% of subgroup)			
Baseline Status N (%)	**Dipper**	**Non-Dipper**	**Extreme Dipper**	**Riser**
Dipper N= 20 (28)	6 (30)	11 (55)	3 (15)	0 (0)
Non-Dipper N= 24 (33)	3 (12.5)	10 (42)	2 (8.3)	9 (37.5)
Extreme Dipper N= 10 (14)	5 (50)	1 (10)	3 (30)	1 (10)
Riser N= 18 (25)	1 (5.5)	7 (39)	0 (0)	10 (55)
Absolute Values	**Status at Second Study (year 2) N (% of subgroup)**			
Baseline Nocturnal Blood Pressure Status N (%)	**Nocturnal Hypertension**	**Nocturnal Normotension**		
Nocturnal Hypertension SBP ≥ 125mm Hg N = 27 (38%)	19 (70)	8 (30)		
Nocturnal Normotension SBP < 125mm Hg N = 44 (62%)	11 (25)	33 (75)		
Nocturnal Hypertension SBP ≥ 120 mmHg N = 36 (51%)	30 (83)	6 (17)		
Nocturnal Normotension SBP < 120 mmHg N = 35 (49%)	12 (34)	23 (66)		

[*] Definitions of Categorical Groups:

Dipper - > 10% reduction in nocturnal systolic BP relative to awake systolic BP

Non-Dippers - 0 to <10% reduction in nocturnal systolic BP relative to awake systolic BP

Extreme Dipper - > 20% reduction in nocturnal systolic BP relative to awake systolic BP

Riser – Nocturnal systolic BP > awake systolic BP

Table 3

Sample Size estimation Based on utility of Clinic and Ambulatory BP components in a Clinical Trial of very elderly subjects

	Number of subjects required per group for systolic BP (SBP) change from baseline				
Effect Size for SBP (mmHg)	**Clinic BP**	**24hr SBP**	**Awake SBP**	**Sleep SBP**	**Early Morning SBP**
3	553	239	281	327	656
4	311	135	158	184	370
5	199	86	101	118	236
7	102	44	52	60	121
9	62	27	31	36	73
	Number of subjects required per group for pulse pressure change from baseline				
Effect Size for pulse pressure (mmHg)	**Clinic Pulse Pressure**	**24hr Pulse Pressure**	**Awake Pulse Pressure**	**Sleep Pulse Pressure**	**Early Morning Pulse Pressure**
3	342	88	112	132	414
4	192	50	63	74	233
5	123	32	40	48	149
7	63	16	20	24	76
9	38	10	12	15	46

Table 4

What is known about this topic

- Short and long-term ambulatory blood pressure (BP) is more reproducible than office BP in young and middle-aged patients with hypertension.

- The HYVET trial proved that antihypertensive therapy is effective at reducing cardiovascular events in < 2 years in the very elderly.

What this study adds

- This 2-year study provides data that demonstrate that long-term reproducibility of ambulatory BP is more reproducible in patients > 80 years old.

- In clinical intervention trials, 24-h ambulatory BP will allow for significant reduction in sample size compared to the office BP.

- Categories of nocturnal BP decline (e.g. dipper and nondipper) are poorly reproducible in very old people; absolute values for nocturnal hypertension (e.g. > 120 or 125 mmHg vs < 120 or 125 mmHg) showed improved reproducibility over 2 years.