DOI: https://doi.org/10.3329/medtoday.v36i1.72903

REVIEW ARTICLE OPEN ACCESS

Clinical Assessment of Early Morning Blood Pressure in Patients with Hypertension

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Abstract

A significant population experiencing hypertension, blood pressure (BP) demonstrates a significant rise during the awakening hours, it is linked to heightened cardiovascular complications during this time of the day. Many medications used to manage high BP fail to effectively control BP in the early morning, especially when administered once daily in the morning. Key factors to consider when choosing an efficient antihypertensive medication include the agent's pharmacokinetics, formulation, and timing of dosing. Examples of antihypertensive drugs with proven efficacy in regulating early morning BP include medications with extended pharmacologic half-lives, like telmisartan (an angiotensin II receptor blocker), amlodipine (a calcium antagonist), and bisoprolol (a beta-blocker). Administering chronotherapeutic preparations at bedtime has also been shown to be effective in managing early morning BP. There is a correlation between elevated early morning BP and cardiovascular risk, future clinical studies should emphasize evaluating the performance of antihypertensive drugs during this critical period of heightened risk. (Prev Cardiol. 2007;10:210–214) © 2007 Le Jacq

Keywords: *Blood Pressure, Hypertension.*

Number of Figures; 04; Number of References; 36; Number of Correspondences: 04.

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Introduction:

Blood pressure (BP) consists of a clear daily pattern, i.e.- a significant drop during sleep (known as the nocturnal dip) and a noticeable rise around the time of waking (referred to as the morning surge) (Figure 1). The incidence of acute

Received: 23 September 2023 *Accepted revised version:* 04 January 2024

cardiovascular (CV) events, such as myocardial infarction, sudden cardiac death, and stroke, also follows a circadian rhythm, with the highest frequency observed in the morning hours (Figure 2) [1,2]. A substantial body of circumstantial evidence suggests a strong association between this heightened occurrence of CV events and the increase in BP levels during the early morning. For instance, the morning BP surge is positively linked to the extent of damage to target organs, including measures like carotid intima-media thickness[3] and left ventricular hypertrophy[4]. Furthermore, the magnitude of the morning surge independently predicts cerebrovascular and cardiac events [5,6]. Although the impact of managing early morning BP on CV risk has not yet been thoroughly investigated in clinical trials, previously presented data indicate that focusing on better control of early morning BP holds promise for the treatment of hypertensive patients. In this review, we examine the factors governing the circadian variation in BP and assess the clinical significance of BP measurements taken at various times of the day using diverse measurement techniques. These approaches encompass measurements obtained in clinical or office settings, those collected during the early morning via 24-hour ambulatory BP monitoring (ABPM), and patient self-monitoring measurements. We also delve into the prognostic value of different BP measures and provide insights into the outcomes of recent trials that have incorporated 24-hour and early morning BP assessments. Finally, we evaluate antihypertensive agents that have demonstrated notable effectiveness in controlling early morning BP based on controlled clinical trials.

Physiologic and Pathologic Circadian Variations in BP:

The morning surge in blood pressure (BP) is influenced by various contributory factors. These factors possess alterations in autonomic and renin-angiotensin-aldosterone system activity, as discussed in previous studies[7]. Additionally, dietary sodium intake was also identified as a relevant factor[8]. In the early morning hours, several physiological changes occur that may potentially enhance cardiovascular (CV) risk. These changes include increased heart rate, increased vascular tone, elevated blood viscosity, and enhanced platelet aggregability[9]. Utilizing ambulatory blood pressure monitoring (ABPM) has proven instrumental in not only identifying individuals with excessive morning surges[10] but also in enabling the assessment of the efficacy of antihypertensive agents that are effective in particular groups of hypertensive populations.

The typical nighttime reduction in blood pressure (BP), usually ranging between 10% and 20%, is primarily influenced by shifts in autonomic activity [11]. Furthermore, the renin-angiotensin-aldosterone system, a crucial BP regulator, might also play a role, particularly in individuals sensitive to salt. The nocturnal BP pattern can be influenced by the intake of sodium and potassium in such cases [11]. Ambulatory blood pressure monitoring (ABPM) has enabled the identification of patients who exhibit deviations from the standard nocturnal BP pattern. These categories encompass Extreme Dippers: Individuals who manifest a significant ≥ 20% decline in nocturnal BP compared to daytime BP. Nondippers: These individuals experience a nocturnal BP decrease of less than 10% compared to their daytime BP. Inverted Dippers/Risers: This group includes patients in whom BP either remains stable or actually increases during the nighttime [Figure 1] [12]. These deviations in the nocturnal BP pattern have been linked to an elevated risk of cardiovascular disease and mortality[12,13]. Individuals classified as nondippers and risers typically do not exhibit a surge in BP upon awakening, but instead, they often experience sustained early morning hypertension (HTN). Conversely, extreme dippers frequently display an excessive morning surge[14]. It is crucial to acknowledge that physiologic and pathologic variations in BP are dynamic rather than static. Relying solely on a few BP measurements taken in a clinical setting provides isolated data points of a continuously evolving variable. Valuable clinical insights into BP behavior and its overall "burden" can be gleaned from monitoring systems that allow for the evaluation of nocturnal, early morning, and 24-hour BP patterns.

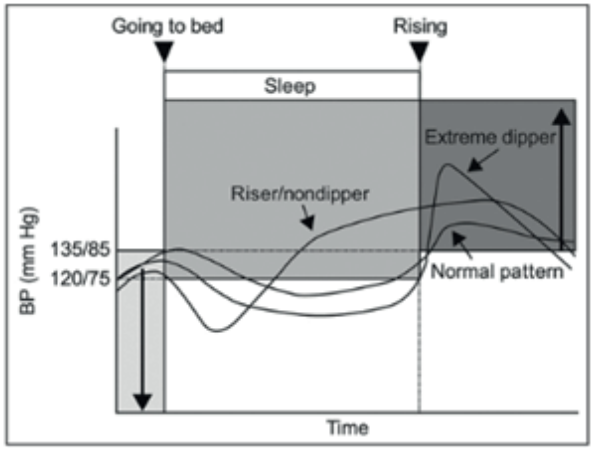

Figure 1: Normal circadian blood pressure (BP) rhythm is modified in some patients. The normal circadian BP rhythm features a nocturnal decrease in BP between 10% and 20% followed by a BP surge on awakening. Patients who exhibit this magnitude of nocturnal decrease in BP are known as dippers. Pathologic deviations from this normal pattern include extreme dipping (≥20% decline in nocturnal BP compared with daytime), nondipping (nocturnal BP decrease <10% of daytime BP), and inverted dipping/rising (no nocturnal decrease/nocturnal increase)[12]. Patients who exhibit excess dipping typically show an excessive morning BP surge[14]. Adapted with permission from Giles[7].

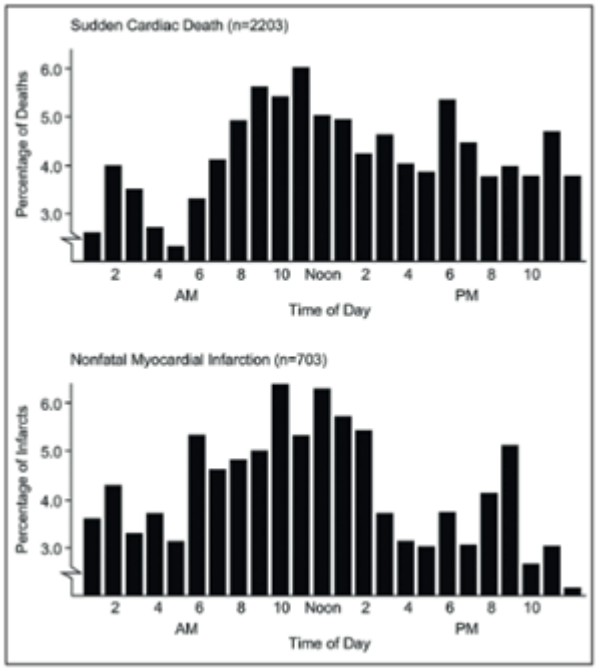

Figure 2: Occurrence of cardiovascular events peaks during the morning hours. Sudden cardiac death and nonfatal myocardial infarction both occur in a marked circadian rhythm, with a trough between midnight and 4 a.m. and a peak between 6 a.m. and noon. Reproduced with permission from Muller et al.[1]

Measurement of BP:

Blood pressure (BP) assessment can occur within clinical settings, where medical professionals, including physicians or nurses, utilize various methods such as Ambulatory Blood Pressure Monitoring (ABPM), or in the comfort of one's home through self-monitoring or home-based monitoring [15]. Despite the well-established clinical relevance of BP measurements conducted in a clinical environment, there are inherent limitations associated with this approach. These limitations encompass potential equipment calibration issues, deviations from recommended measurement protocols by healthcare practitioners, and the well-known phenomenon known as the "white coat effect." Notably, clinic-based BP measurements do not provide a comprehensive view of BP values 12 to 24 hours after medication dosing and are unable to capture BP fluctuations during sleep or the post-awakening surge. In the clinical context, an upper limit of normalcy for BP measurements is typically defined as 140/90 mm Hg for most patients[15,16]. However, individuals with hypertension (HTN) alongside diabetes mellitus or kidney disease are often assigned a lower BP target of <130/80 mm Hg[16]. In the context of ambulatory blood pressure (ABP) measurements, consensus guidelines established through a comprehensive review of existing literature have defined the reference values. These ABP assessments involve calculating averages during the daytime (while individuals are awake), nighttime (during the sleep cycle), and across a complete 24-hour cycle. According to consensus criteria endorsed by an expert group affiliated with the American Heart Association, hypertension is diagnosed when ABPM readings equal or surpass the threshold of ≥135/85 mm Hg during daytime hours and ≥120/70 mm Hg during nighttime hours, or ≥ 130/80 mm Hg when considering the entire 24-hour period [15].

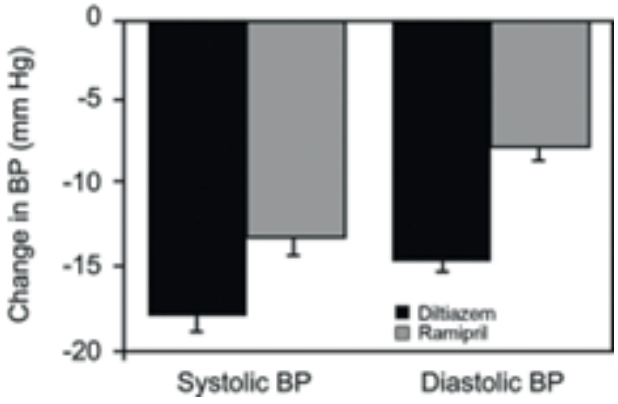

Figure 3: Bedtime administration of extended-release diltiazem (240–540 mg) is significantly more effective than bedtime administration of ramipril (5–20 mg) in reducing systolic and diastolic blood pressure (BP) in the first 4 hours after awakening (P≤.002). Adapted with permission from White et al.[27]

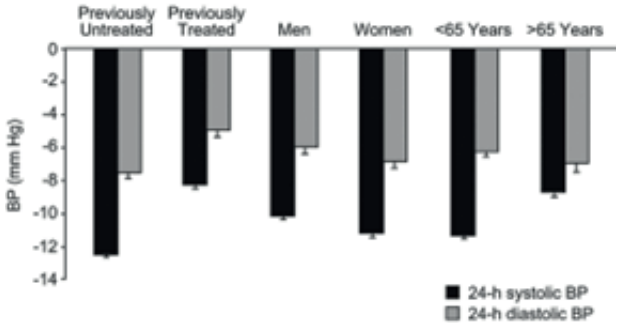

Figure 4: Reductions in 24-hour systolic and diastolic blood pressure (BP) after treatment with telmisartan alone or in combination with hydrochlorothiazide from the MICCAT-2 trial. In a 6- to 10-week community-based trial, a cohort of treated (n=675) and untreated (n=940) hypertensive patients were switched to/started with telmisartan-based antihypertensive therapy (telmisartan, 40–80 mg ± hydrochlorothiazide, 12.5 mg). Patient BP was monitored in the physician's office and using ambulatory BP monitoring. Telmisartan-based therapy was associated with significant reductions in systolic and diastolic BP in previously treated and previously untreated patients, in men and women, and in patients younger than 65 years and those aged 65 years or older (P<.0001 for all values). Adapted with permission from White et al.[33]

It's noteworthy that ABPM measurements typically yield lower values compared to BP measurements taken in clinical settings, resulting in a corresponding reduction in the threshold for defining normal daytime BP (<135/85 mm Hg versus <140/90 mm Hg). Furthermore, BP readings are generally lower when measured by patients at home compared to in-office measurements[15]. A recent examination of home-based, office-based, and ABPM readings proposed that individuals with home BP measurements below <125/76 mm Hg could be categorized as normotensive, those with home BP values ≥135/85 mm Hg should be classified as hypertensive, while individuals with intermediate home BP readings should undergo further evaluation, preferably utilizing ABPM[17]. Self-monitoring of BP presents several advantages over traditional clinic-based BP measurement, particularly when employing modern, validated electronic devices [15]. A recent meta-analysis of 18 rigorously conducted randomized controlled trials revealed that self-monitoring of BP was linked to significantly improved BP control compared to the customary office-based measurement approach[18]. Self-monitoring at home also provides patients with a heightened sense of control and engagement in their health. While it may not facilitate the assessment of the nighttime BP pattern, diligent self-monitoring can serve as a valuable tool in identifying early morning hypertension.

Prognostic Value of Different BP Measurements:

Monitoring blood pressure at home has been found in various studies to be more accurate in predicting cardiovascular events, cardiovascular-related deaths, and damage to target organs when compared to clinic-based blood pressure measurements [19–21]. However, many of these studies were conducted on general populations, making it challenging to establish normal self-monitoring values based solely on their findings.

In a particular study involving 393 untreated elderly patients, with an average age of 70, suffering from isolated systolic hypertension and enrolled in the Systolic Hypertension in Europe (Syst-Eur) trial, it was discovered that ambulatory systolic blood pressure emerged as a significant predictor of cardiovascular risk, while systolic blood pressure measured in a clinical setting did not exhibit the same predictive power [22]. Intriguingly, nighttime systolic blood pressure proved to be an even more accurate predictor of risk than daytime measurements. Similar results were reported by Clement and colleagues in a 5-year prospective cohort study, which involved 1963 middle-aged patients receiving antihypertensive treatment (with a mean baseline age of 56–57 years) [23]. In this prospective cohort study, baseline ambulatory blood pressure monitoring values remained significant independent predictors of cardiovascular events, even after accounting for major cardiovascular risk factors and clinic-based blood pressure readings [23].

Furthermore, through multivariate analyses that considered serum cholesterol levels, smoking habits, and the presence of diabetes, Björklund and associates demonstrated that ambulatory daytime systolic blood pressure and the presence of isolated ambulatory hypertension (defined as having a normal office-measured blood pressure but elevated ambulatory blood pressure, also known as masked or hidden hypertension) were both independent predictors of cardiovascular disease, while clinic-based systolic blood pressure measurements did not provide the same level of prediction [24].

Lastly, when comparing the efficacy of ambulatory blood pressure monitoring and clinic-based measurements in managing hypertensive patients, it was observed that, although both clinic and ambulatory readings were associated with similar levels of antihypertensive control and inhibition of left ventricular enlargement, patients monitored using ambulatory blood pressure monitoring required less intensive drug treatment [25].

Efficacy of Antihypertensive Agents in Controlling 24-Hour and Early Morning BP:

Achieving effective control of early morning and 24-hour mean ambulatory blood pressure [ABP] has become a highly sought-after feature of antihypertensive treatments. The extent to which antihypertensive agents can regulate blood pressure during the night and early morning hours depends on various factors, including pharmacokinetics, formulation, and timing of administration.

For instance, graded-release diltiazem is a chronotherapeutic formulation designed to counteract the circadian rhythm of blood pressure. When administered in the evening, it proves more effective than morning administration in lowering blood pressure between 6 AM and noon [26]. Furthermore, in a double-blind, titration-to-effect trial, White and colleagues demonstrated that bedtime administration of graded-release diltiazem was notably more effective at reducing early morning blood pressure than bedtime administration of ramipril (Figure 3) [27]. Similarly, administering a controlled-onset extended-release verapamil formulation at bedtime proved superior in lowering early morning blood pressure compared to the morning administration of enalapril or losartan [28].

Utilizing agents with longer half-lives has also shown promise in enhancing early morning blood pressure control. For example, a single 10-mg dose of the beta-blocker bisoprolol, taken in the morning, effectively lowered blood pressure throughout the entire 24-hour period. After four weeks of treatment in a group of 25 patients with essential hypertension, bisoprolol reduced the mean morning blood pressure from 145/97 mm Hg to 133/88 mm Hg [29]. Similarly, the calcium channel blocker amlodipine reduced morning systolic blood pressure and mitigated the magnitude of the morning systolic blood

pressure surge. In a study involving 38 hypertensive patients who received amlodipine (2.5–10 mg) immediately after breakfast for 8 to 16 weeks, the mean morning systolic blood pressure decreased from 156 mm Hg to 142 mm Hg, and the morning surge diminished by 6.1 mm Hg [30].

Recent insights into the activation of the renin-angiotensin-aldosterone system during sleep and in the early morning have prompted the investigation of angiotensin II blockade as a strategy for controlling early morning hypertension. Telmisartan, an angiotensin receptor blocker with an extended half-life, has proven effective in reducing early morning blood pressure [10,31]. In two large-scale trials comparing telmisartan with valsartan, telmisartan at doses of 40–80 mg outperformed valsartan at doses of 80–160 mg in reducing blood pressure during the last 6 hours of the inter dosing interval, aligning with the early morning period [31,32].

Moreover, the effectiveness of this therapeutic approach to ABP was evaluated in a significant, prospective, open-label trial conducted in a primary care setting [the Micardis Community Ambulatory Monitoring Trial (MICCAT-2)]. In this trial, telmisartan [with or without hydrochlorothiazide] significantly reduced 24-hour, daytime, nighttime, and early morning [post awakening] mean blood pressure in both previously treated and untreated hypertensive patients [10,33]. Specifically, post awakening blood pressure decreased by an average of 17.2/10.1 mm Hg in patients with an excessive morning blood pressure surge, surpassing the effect observed in the overall population (reduction of 11.5/7.0 mm Hg) [10].

The Prospective Randomized Investigation of the Safety and Efficacy of Micardis vs. Ramipril Using ABPM (PRISMA) studies also examined the effectiveness of telmisartan 80 mg/day compared to ramipril 10 mg/day in controlling the morning blood pressure surge in patients with mild to moderate hypertension. Pooled data from PRISMA I and II demonstrated that telmisartan reduced the overall mean morning systolic blood pressure surge, whereas patients taking ramipril experienced an increase in the morning blood pressure surge [36]. Notably, the reduction in morning systolic blood pressure surge was most pronounced in patients with the highest baseline morning systolic blood pressure surge [36]. Telmisartan also significantly reduced the magnitude of the systolic morning blood pressure surge in diapers compared to ramipril, although no significant difference was observed in nondippers [36].

Conclusions:

In individuals with good health, blood pressure exhibits a highly consistent circadian rhythm. Analyzing and understanding this pattern has been significantly enhanced by ambulatory blood pressure monitoring (ABPM), a technique proven to be more effective than clinic-based blood pressure measurements in predicting adverse events. ABPM has also enabled healthcare professionals to identify several pathological variations in this pattern, many of which are linked to an elevated risk of adverse events. These variations encompass phenomena like nocturnal nondipping and excessive morning blood pressure surges.

The early morning surge in blood pressure is of particular concern because it aligns with the peak occurrence time of cardiovascular events. Consequently, physicians and pharmaceutical researchers have directed their attention toward developing antihypertensive agents specifically tailored to address this critical morning period. Notable among these are chronotherapeutic formulations of diltiazem and verapamil, as well as medications with extended half-lives, typically spanning 20 to 30 hours. Examples include the angiotensin II receptor blocker telmisartan and the beta-blocker bisoprolol, both of which exhibit significant efficacy during the early morning hypertensive phase.

Given the well-established association between early morning blood pressure and cardiovascular risk, it is imperative that future clinical trials place a deliberate focus on evaluating the effectiveness of antihypertensive drugs during this crucial time window.

Conflict of Interest: None.

References:

1. Muller JE, Ludmer PL, Willich SN, et al. Circadian variation in the frequency of sudden cardiac death. Circulation. 1987;75:131-138. https://doi.org/10.1161/01.CIR.75.1.131 PMid:3791599

2. Cohen MC, Rohtla KM, Lavery CE, et al. Meta-analysis of the morning excess of acute myocardial infarction and sudden cardiac death. Am J Cardiol. 1997;79:1512-1516. https://doi.org/10.1016/S0002-9149(97)00181-1 PMid:9185643

3. Marfella R, Siniscalchi M, Nappo F, et al. Regression of carotid atherosclerosis by control of morning blood pressure peak in newly diagnosed hypertensive patients. Am J Hypertens. 2005;18:308-318. https://doi.org/10.1016/j.amjhyper.2004.09.013 PMid:15797646

4. Polonia J, Amado P, Barbosa L, et al. Morning rise, morning surge and daytime variability of blood pressure and cardiovascular target organ damage. A cross-sectional study in 743 subjects. Rev Port Cardiol. 2005;24:65-78.

5. Kario K, Pickering TG, Umeda Y, et al. Morning surge in blood pressure as a predictor of silent and clinical cerebrovascular disease in elderly hypertensives: a prospective study. Circulation. 2003;107:1401-1406. https://doi.org/10.1161/01.CIR.0000056521.67546.AA PMid:12642361

6. Gosse P, Lasserre R, Minifie C, et al. Blood pressure surge on rising. J Hypertens. 2004;22:1113-1118. https://doi.org/10.1097/00004872-200406000-00011 https://doi.org/10.1097/00004872-200406002-00003 PMid:15167445
7. Giles TD. Circadian rhythm of blood pressure and the relation to cardiovascular events. J Hypertens Suppl. 2006;24:S11-S16. https://doi.org/10.1097/01.hjh.0000220098.12154.88 PMid:16601555
8 Osanai T, Okuguchi T, Kamada T, et al. Salt-induced exacerbation of morning surge in blood pressure in patients with essential hypertension. J Hum Hypertens. 2000;14:57-64. https://doi.org/10.1038/sj.jhh.1000945 PMid:10673733
9. Feng DL, Tofler GH. Diurnal physiologic processes and circadian variation of acute myocardial infarction. J Cardiovasc Risk. 1995;2:494-498. https://doi.org/10.1177/174182679500200602 https://doi.org/10.1097/00043798-199512000-00002 PMid:8665366
10. White WB, Weber MA, Davidai G, et al. Ambulatory blood pressure monitoring in the primary care setting: assessment of therapy on the circadian variation of blood pressure from the MICCAT-2 Trial. Blood Press Monit. 2005;10:157-163. https://doi.org/10.1097/00126097-200506000-00008 PMid:15923818
11. Sica DA. What are the influences of salt, potassium, the sympathetic nervous system, and the renin-angiotensin system on the circadian variation in blood pressure? Blood Press Monit. 1999;4(suppl 2):S9-S16. https://doi.org/10.1097/00126097-199902001-00003
12. Ohkubo T, Imai Y, Tsuji I, et al. Relation between nocturnal decline in blood pressure and mortality. The Ohasama Study. Am J Hypertens. 1997;10:1201-1207. https://doi.org/10.1016/S0895-7061(97)00274-4 PMid:9397237
13. Kario K, Matsuo T, Kobayashi H, et al. Nocturnal fall of blood pressure and silent cerebrovascular damage in elderly hypertensive patients. Advanced silent cerebrovascular damage in extreme dippers. Hypertension. 1996;27:130-135. https://doi.org/10.1161/01.HYP.27.1.130 PMid:8591875
14. Kario K, Shimada K. Risers and extreme-dippers of nocturnal blood pressure in hypertension: antihypertensive strategy for nocturnal blood pressure. Clin Exp Hypertens. 2004;26:177-189. https://doi.org/10.1081/CEH-120028556 PMid:15038628
15. Pickering TG, Hall JE, Appel LJ, et al. Recommendations for blood pressure measurement in humans and experimental animals: Part 1: blood pressure measurement in humans: a statement for professionals from the Subcommittee of Professional and Public Education of the American Heart Association Council on High Blood Pressure Research. Hypertension. 2005;45:142-161. https://doi.org/10.1161/01.HYP.0000150859.47929.8e PMid:15611362
16. Chobanian AV, Bakris GL, Black HR, et al. The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure: the JNC 7 report. JAMA. 2003;289:2560-2572. https://doi.org/10.1001/jama.289.19.2560 PMid:12748199
17. Mansoor GA, White WB. Self-measured home blood pressure in predicting ambulatory hypertension. Am J Hypertens. 2004;17:1017-1022. https://doi.org/10.1016/j.amjhyper.2004.06.015 PMid:15533727
18. Cappuccio FP, Kerry SM, Forbes L, et al. Blood pressure control by home monitoring: meta-analysis of randomised trials. BMJ. 2004;329145-150. https://doi.org/10.1136/bmj.38121.684410.AE PMid:15194600 PMCid:PMC478224
19. Ohkubo T, Imai Y, Tsuji I, et al. Home blood pressure measurement has a stronger predictive power for mortality than does screening blood pressure measurement: a population-based observation in Ohasama, Japan. J Hypertens. 1998;16:971-975. https://doi.org/10.1097/00004872-199816070-00010 PMid:9794737
20. Tsunoda S, Kawano Y, Horio T, et al. Relationship between home blood pressure and longitudinal changes in target organ damage in treated hypertensive patients. Hypertens Res. 2002;25:167-173. https://doi.org/10.1291/hypres.25.167 PMid:12047030
21. Bobrie G, Chatellier G, Genes N, et al. Cardiovascular prognosis of "masked hypertension" detected by blood pressure self-measurement in elderly treated hypertensive patients. JAMA. 2004;291:1342-1349. https://doi.org/10.1001/jama.291.11.1342 PMid:15026401
22. Staessen JA, Thijs L, Fagard R, et al. Predicting cardiovascular risk using conventional vs ambulatory blood pressure in older patients with systolic hypertension. Systolic Hypertension in Europe Trial Investigators. JAMA. 1999;282:539-546. https://doi.org/10.1001/jama.282.6.539 PMid:10450715
23. Clement DL, De Buyzere ML, De Bacquer DA, et al. Prognostic value of ambulatory blood-pressure recordings in patients with treated hypertension. Office versus Ambulatory Pressure Study Investigators. N Engl J Med. 2003;348:2407-2415. https://doi.org/10.1056/NEJMoa022273 PMid:12802026
24. Bjorklund K, Lind L, Zethelius B, et al. Isolated

ambulatory hypertension predicts cardiovascular morbidity in elderly men. Circulation. 2003;107:1297-1302. https://doi.org/10.1161/01.-CIR.0000054622.45012.12 PMid:12628951
25. Staessen JA, Byttebier G, Buntinx F, et al. Antihypertensive treatment based on conventional or ambulatory blood pressure measurement: a randomized controlled trial. Ambulatory Blood Pressure Monitoring and Treatment of Hypertension Investigators. JAMA. 1997;278:1065-1072. https://doi.org/10.1001/jama.1997.03550130039034 https://doi.org/10.1001/jama.278.13.1065 PMid:9315764
26. Glasser SP, Neutel JM, Gana TJ, et al. Efficacy and safety of a once daily graded-release diltiazem formulation in essential hypertension. Am J Hypertens. 2003;16:51-58. https://doi.org/10.1016/S0895-7061(02)03153-9 PMid:12517683
27. White WB, Lacourciere Y, Gana T, et al. Effects of gradedrelease diltiazem versus ramipril, dosed at bedtime, on early morning blood pressure, heart rate, and the rate-pressure product. Am Heart J. 2004;148:628-634. https://doi.org/10.1016/j.ahj.2004.07.008 PMid:15459593
28. White WB, Sica DA, Calhoun D, et al. Preventing increases in early-morning blood pressure, heart rate, and the ratepressure product with controlled onset extended release verapamil at bedtime versus enalapril, losartan, and placebo on arising. Am Heart J. 2002;144:657-665. https://doi.org/10.1067/mhj.2002.124866 https://doi.org/10.1016/S0002-8703(02)00137-0 PMid:12360162
29. Mengden T, Battig B, Schubert M, et al. Comparison of casual, ambulatory and self-measured blood pressure in a study of nitrendipine vs bisoprolol. Eur J Clin Pharmacol. 1992;42:569-575. https://doi.org/10.1007/BF00265917 PMid:1352496
30. Eguchi K, Kario K, Hoshide Y, et al. Comparison of valsartan and amlodipine on ambulatory and morning blood pressure in hypertensive patients. Am J Hypertens. 2004;17:112-117. https://doi.org/10.1016/j.amjhyper.2003.09.008 PMid:14751651
31. Lacourcière Y, Krzesinski JM, White WB, et al. Sustained antihypertensive activity of telmisartan compared with valsartan. Blood Press Monit. 2004;9:203-210. https://doi.org/10.1097/00126097-200408000-00005 PMid:15311147
32. White WB, Lacourciere Y, Davidai G. Effects of the angiotensin II receptor blockers telmisartan versus valsartan on the circadian variation of blood pressure: impact on the early morning period. Am J Hypertens. 2004;17:347-353. https://doi.org/10.1016/j.amjhyper.2004.02.016 PMid:15062889
33. White WB, Giles T, Bakris GL, et al. Measuring the efficacy of antihypertensive therapy by ambulatory blood pressure monitoring in the primary care setting. Am Heart J. 2006;151:176-184. https://doi.org/10.1016/j.ahj.2005.02.014 PMid:16368314
34. Williams B, Gosse P, Lowe L, et al. The prospective, randomized investigation of the safety and efficacy of telmisartan versus ramipril using ambulatory blood pressure monitoring (PRISMA I). PRISMA 1 Study Group. J Hypertens. 2006;24:193-200. https://doi.org/10.1097/01.hjh.0000194364.11516.ab PMid:16331118
35. Lacourcière Y, Neutel JM, Davidai G, et al. A multicenter, 14-week study of telmisartan and ramipril in patients with mild-to-moderate hypertension using ambulatory blood pressure monitoring. Am J Hypertens. 2006;19:104-112. https://doi.org/10.1016/j.amjhyper.2005.10.001 PMid:16461201
36. Gosse P, Neutel JM, Schumacher H, et al. The effect of telmisartan and ramipril on early morning blood pressure surge: a pooled analysis of two randomized clinical trials. Blood.