Journal of the Postgraduate Institute of Medicine 2017; 4 (2):-E58 1- 11
http://doi.org/10.4038/jpgim.8150

Original Article

Circadian blood pressure profile and comparison with clinic blood pressure in patients with essential hypertension on treatment; experience from a Teaching Hospital in Sri Lanka

HGWAPL Bandara[1], UI Hewarathne[1], RMSP Karunarathne[1], Dr. T Kogulan[1], NW Kodithuwakku[1], A Jegavanthan[1], KP Jayawickreme[1], AWDT Ambagaspitiya[1], DMJMH Ambagammana[1], SR Jayawickreme[1], C Hathlahawatte[1], G Weerakoon[1], SNB Dolapihilla[1], A Kularatne[1], T Sirisena[1], U Ralapanawa[1]

[1]Teaching Hospital, Kandy, Sri Lanka

Keywords: ambulatory blood pressure, office blood pressure, nocturnal hypertension, nocturnal dipping pattern

Abstract

Background and Objectives

Ambulatory blood pressure monitoring (ABPM) is more reflective of an individual's blood pressure (BP) profile and its control, eliminating several confounding and contributory factors. This study looked at the circadian pattern of BP variation with respect to nocturnal BP fluctuations and compared clinic BP measurements with ambulatory readings in patients on treatment for essential hypertension

Methods

A prospective study was conducted at Teaching Hospital, Kandy from August to October 2015. The study participants were 100 patients, above 18 years of age, with stage I to III essential hypertension with normal renal functions and having no history of coronary or cerebro-vascular events. All patients underwent electrocardiography, 2D echocardiography, manual BP measurement and 24-hour ambulatory blood pressure monitoring.

Results

There was a female preponderance 72(72%) and the mean age was 61 ± 9 years. One third had uncontrolled BP, according to clinic BP readings, whereas 60% had uncontrolled BP according to ambulatory blood pressure monitoring. The agreement between the office BP and ABPM in diagnosing controlled or uncontrolled BP was low (58%, Kappa = 0.23). A significant statistical difference (p<0.001) was observed between day and night time measurements, irrespective of BP control. In the sample, 70% had abnormal dipping patterns including non-dipping (45%), reverse dipping (25%) and extreme dipping (5%).

Conclusions and Recommendations

ABPM is more reflective of an individual's naïve BP pattern. It captures the different types of diurnal variation of BP thus guiding the physician to treat the patient optimally. Moreover, its non-invasive and portable nature allows it to be used with ease. It is likely that ABPM will gather widespread recognition and acceptance as a more reliable diagnostic and prognostic tool in the future

Corresponding Author: HGWAPL Bandara, E-mail: <lakshmanbandara@gmail.com> http://orcid.org/0000-0002-8802-2014
Received: July 2017, accepted revised version October 2017, Published: December 2017
Competing Interests: Authors have declared that no competing interests exist

Introduction

Hypertension is a well-known cardiovascular disease with multi-organ involvement. It is one of the modifiable risk factors for coronary artery disease. The burden of hypertension in the world, as well as in the South Asian population, continues to rise as a result of demographic transition. In turn, hypertension based cardiovascular mortality and morbidity is increasing adding to the health burden of non-communicable disease.

The representative value of an individual's blood pressure (BP) should be critically evaluated because prognosis is dependent on achievement of BP control targets [1]. A wide variation in BP values has been observed with different techniques of BP measurement. However, diurnal BP profile is best evaluated by automated noninvasive ambulatory BP monitoring [2].

Ambulatory blood pressure monitoring (ABPM) has extended our capacity to identify the finer variations in the circadian rhythm of BP of an individual. It acts as a versatile tool for the assessment of BP in existing practice. It is particularly valuable in identifying white-coat and masked hypertension and nocturnal dipping patterns which are key determinants of cardio-vascular outcomes [3]. None of the above parameters can be derived from clinic BP measurements.

Several studies have highlighted the fact that patients with abnormal nocturnal BP dipping have a higher cardiovascular morbidity and mortality [4]. Novel evidence relating to circadian BP fluctuations has revealed that such adverse patterns correlate directly with coronary artery and cerebrovascular disease [5]. ABPM has been found to be a valuable research tool as well as a better prognostic tool in various study settings [6].

The aim of the present study was to explore the circadian pattern of BP variation, identify groups at risk for adverse cardiovascular outcomes and compare clinic BP measurements with ABPM in patients on treatment for essential hypertension.

Methods

A total of 100 patients were recruited to the study using convenient sampling. Inclusion criteria were patients who were above 18 years with stage I to III [7] hypertension with normal renal function as assessed by serum creatinine, blood urea, estimated glomerular filtration rate and having no previous history of coronary or cerebrovascular events. Patients with essential hypertension complicating pregnancy were excluded from the study.

Each patient was clinically evaluated independently by two Senior Registrars in Cardiology with a detailed history and physical examination, including pulse rate, blood pressure in both arms, cardiac auscultation and physical signs suggestive of secondary hypertension. Socio-demographic data, a history of putative vascular risk factors, past medical history and the results of recent laboratory investigations were obtained. Twenty-four-hour

Journal of the Postgraduate Institute of Medicine 2017; 4 (2):-E58 1- 11
http://doi.org/10.4038/jpgim.8150

ABPM was performed, and the patients underwent electrocardiography and two-dimensional echocardiographic assessment performed independently by two cardiology senior registrars. Manual BP measurement was performed according to a standard protocol [8]. Informed written consent was obtained from all participants. The study protocol was approved by the Research and Ethical Review Committee, General Hospital (Teaching) Kandy, Sri Lanka.

Ambulatory Blood Pressure Monitoring

Twenty-four hour ABPM measurements in the non-dominant arm were obtained using one portable oscillometric monitor (Contec ABPM 50®). This ABPM device achieves the standards of the American National Standards Institute.

The patients were allowed to engage in their regular activities of daily living and advised to abstain from vigorous physical activity during the monitoring period. Night time was defined as 2201h to 0500h and daytime was defined as between 0501h and 2200h. The pressure monitoring device was programmed to read the BP every 30 minutes from 0501h to 2200h and every 60 minutes from 2201h to 0500h.

Definition of the parameters of day and night BP variations

In the clinic, using manual BP measurement, a reading of ≥140mmg Hg and/or ≥90 mm Hg was taken as indicative of hypertension. Twenty-four-hour AMBP cut-offs were taken as ≥130 mm Hg and/or≥80 mm Hg [2]. Day time AMBP cut-offs were taken as ≥135 mm Hg and/or≥85 mm Hg whereas night time AMBP cut offs were set at ≥120 mm Hg and/or≥70 mm Hg [2]. All AMBP cut-off values are lower than those used for manual BP as AMBP calculates mean BP over a period of time rather than at a single time point as for clinic BP.

The night-to-day BP ratio was calculated using average nocturnal and daytime BP. Dipping was defined by the night-to-day BP ratio; mild dipping (0.9 <ratio <1.0); dipping (0.8 < ratio <0.9); and extreme dipping (ratio <0.8) [2]. Night time rise of BP (i.e. reverse dipping) was defined as a ratio >1.0 [8].

Morning surge was defined as a difference of the morning blood pressure during the first 2 hours after awakening and the average of the lowest nighttime BP [9]. Heart rate non-dippers were defined as those who showed a reduction in heart rate less than 10% between day and night [10].

Statistical tests

SPSS version 17.0 was used for data entry and analysis. The statistical significance of continuous variables between the subgroups was evaluated using the student t-test and variation between categorical variables was evaluated by the x^2 square test. A p value of <0.05 or confidence limit of 95 % was considered as significant.

Journal of the Postgraduate Institute of Medicine 2017; 4 (2):-E58 1- 11
http://doi.org/10.4038/jpgim.8150

Results

Demographic data and blood pressure profile

There were 100 subjects in the study sample with 28% (n=28) males and 72% (n=72) females. The mean age of the sample was 61±9 years. Baseline characteristics, co-morbidities and pharmacotherapy are described in Table 01. The ABPM profile of the sample is illustrated in Table 02.

Table 1: Characteristics of the study group

Characteristic	**Result N(%)**
Age in years (mean ± SD)	60.9±8.7
Gender	
Male	28(28)
Female	72 (72)
Co-morbidities N (%)	
Diabetes Mellitus	25 (25)
Dyslipidemia	62 (62)
Pharmacotherapy N (%)	
ACEIs/ARBS	81 (81)
CCBs	27 (27)
Diuretics	39 (39)
β Blockers	21 (21)
Statins	64 (64)

SD = Standard deviation, ACEIs=Angiotensin Converting Enzyme Inhibitors, ARBs=Angiotensin Receptor Blockers, CCBs=Calcium channel blockers

Table 2: Outcome parameters of ABPM profile

Parameter	**Mean ± SD**
Blood Pressure (mmHg)	
24hour average SBP	135.4±16.3
24hour average DBP	78.7±10.8
Daytime average SBP	137.0±16.5
Daytime average DBP	79.9±11.1
Nocturnal average SBP	127.9±18.4
Nocturnal average DBP	73.4±11.7
Pulse (beats/minute)	
24hour average pulse pressure	56.7±12.2
Average morning surge	30±16
Heart rate (Beats/min*)*	
24hour average HR	71.9±10.4
Daytime average HR	73.75±10.8
Nocturnal average HR	65.8±10.6

BP=blood pressure, SBP= systolic blood pressure, DBP= diastolic blood pressure, HR= heart rate, ABPM=ambulatory blood pressure monitoring

Journal of the Postgraduate Institute of Medicine 2017; 4 (2):-E58 1- 11
http://doi.org/10.4038/jpgim.8150

Comparison of clinic BP measurement versus ABPM

The mean systolic BP (SBP) by manual office BP measurement was 135±9mm Hg whereas it was 135±16mmHg by AMBP (Figure 01). The mean diastolic BP (DBP) by manual office BP measurement was 81±5mmHg while by AMBP it was 79±11 mmHg (Figures 1 and 2).

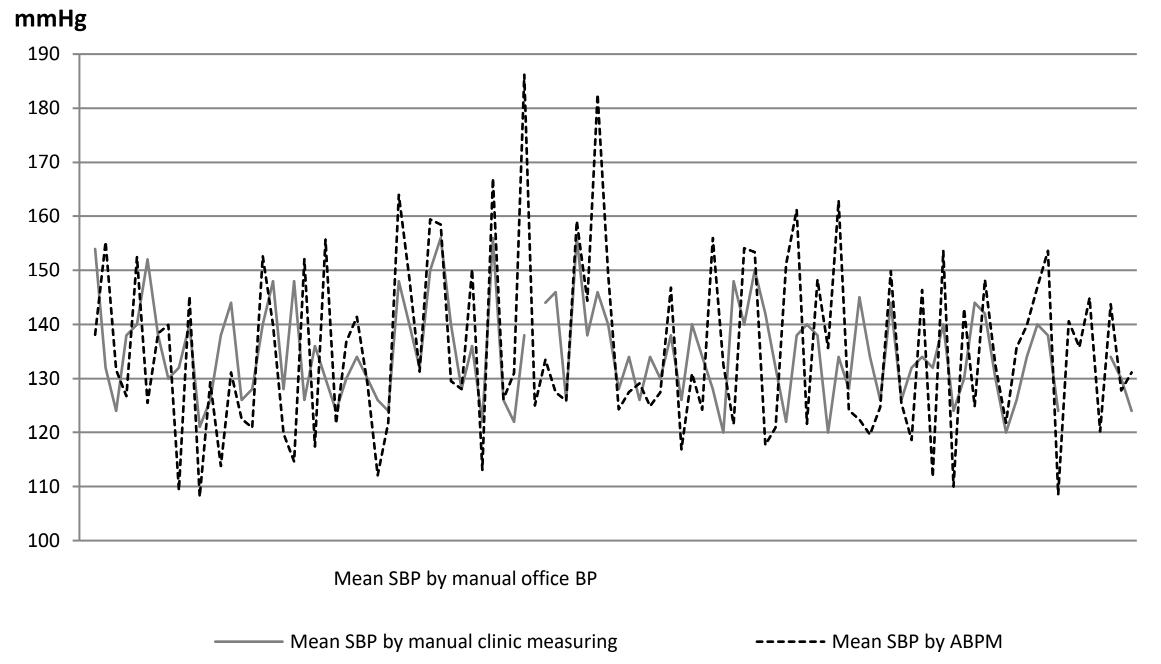

Figure 1: Mean SBP by manual office BP versus Mean SBP by ABPM

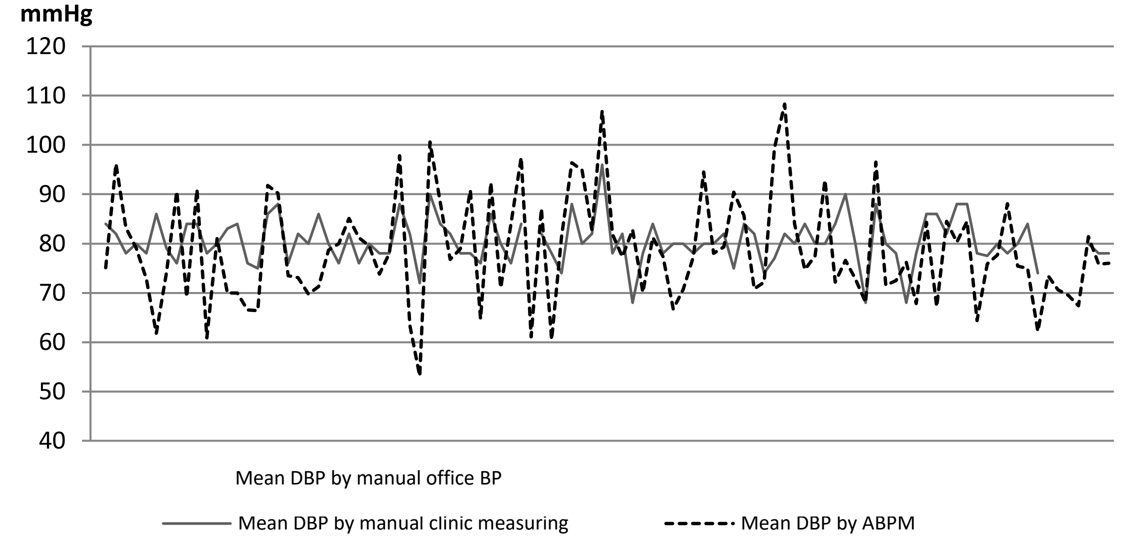

Figure 2 : *Variation of mean DBP by manual office BP versus mean DBP by ABPM*

Journal of the Postgraduate Institute of Medicine 2017; 4 (2):-E58 1- 11
http://doi.org/10.4038/jpgim.8150

There were 33 (33%) patients with uncontrolled BP according to manual clinic BP measurements (≥140/90mmHg) whereas 60 (60%) had uncontrolled BP according to ABPM (≥130/80 mmHg) (Figure 3*)*.

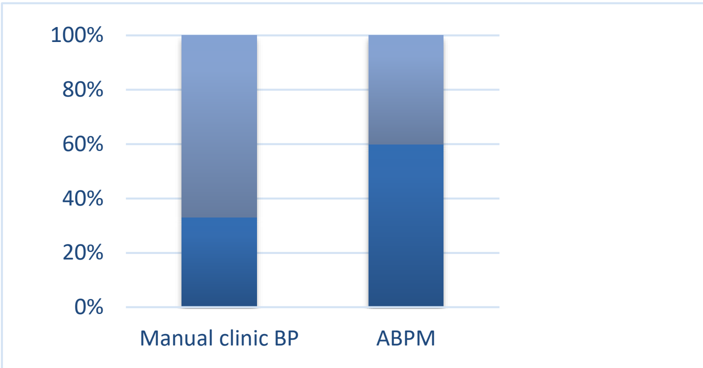

Figure 3*: State of hypertension control by ABPM versus manual office BP monitoring*

The agreement between the clinic BP and ABPM for diagnosing controlled or uncontrolled BP was low (58%, Kappa = 0.23).

Distribution of dipping pattern

There was a statistically significant difference ($p<0.001$) between the day-time systolic BP (137±16.5 mmHg) versus night-time systolic BP (127.93±18.4 mmHg) measurements according to ambulatory blood pressure. Similarly, there was a statistically significant difference ($p<0.001$) between the day-time diastolic BP (79.87±11.7 mmHg) and nocturnal diastolic BP (73.4±11.7 mmHg) (Table 02). In the study sample 30% (n=30) had a normal dipping pattern. The 70% (n=70) who had abnormal dipping patterns included non-dipping in 45% (n=45), reverse dipping in 20% (n=20) and extreme dipping in 5% (n=5) (Figure 04).

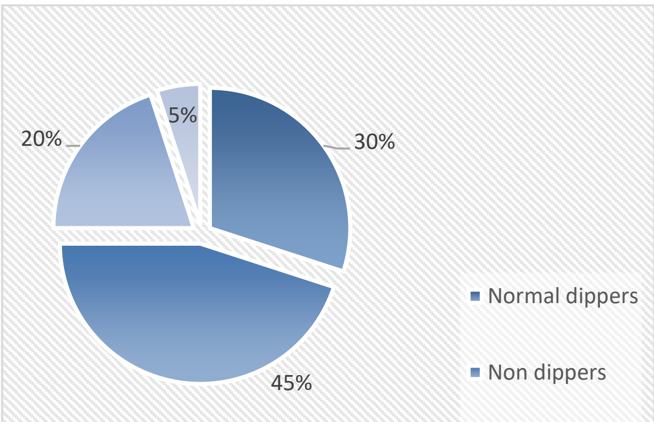

Figure 4*: Distribution of dipping pattern*

Journal of the Postgraduate Institute of Medicine 2017; 4 (2):-E58 1- 11
http://doi.org/10.4038/jpgim.8150

There were 64% (n=64) who had well controlled BP according to clinic BP cutoffs (<140/90 mmHg). Out of them, only 20% (n=13) had a normal dipping pattern whereas 80% (n=51) had abnormal dipping pattern.

BP in dippers and non-dippers

Day and night BP and HR variation of dippers versus non-dippers is shown in Table 3. There was no statistically significant difference observed in relation to 24 hour ABPM mean SBP, day time SBP and night time SBP, 24 hour ambulatory DBP variables and heart rate between dippers and non-dippers.

Table 3: Mean SBP, mean DBP and HR among dippers and non-dippers

Parameters	Dippers	Non-dippers
Blood Pressure	mmHg±SD	mmHg±SD
24 hour average SBP (p=0.9)	137.5±17.8	134.2±15.4
24 hour average DBP (p=0.3)	79.2±11.7	78.4±10.4
Daytime average SBP (p=0.184)	141.4±18.2	134.0±15.2
Daytime average DBP (p=0.414)	81.5±11.8	78.9±10.7
Nocturnal average SBP (p=0.623)	120.2±16.9	132.1±17.9
Nocturnal average DBP (p=0.269)	68.7±12.3	75.9±10.7
Heart Rate	bpm±SD	bpm±SD
24 hour average HR(p=0.324)	72.9±9.3	71.3±10.9
Daytime average HR(p=0.323)	74.1±9.5	72.7±11.1
Nocturnal average HR (p=0.866)	67.4±10.4	64.9±10.8
SBP= Systolic blood pressure, DBP= Diastolic blood pressure, HR=Heart rate, bpm =beats per minute		

BP behavior in reverse dippers (risers)

There were 20 (20%) patients who had a reverse dipping pattern. They were found to have an average day time SBP of 137.3±16.3mmHg and a night time SBP 145.4±17.4mmHg (p=0.939). Their average day and night time DBP was 77.9±10.1 and 78.9±10.6 mmHg respectively (p=0.905). But this difference was not statistically significant.

Heart rate variation in the study sample

The 24-hour average HR of the study sample was 71.8/min. Nocturnal and day time HR of the study were 65.3/min and 73.2/min respectively. There was no statistically significant difference (p=0.866) noted in the average nocturnal HR in non-dippers (64.9/min) compared to dippers (67.4/min). HR non dippers, defined as those who showed a nocturnal dip in HR of less than 10% of the day time value [8], accounted for 65% (n=65) of the subjects.

Discussion

The use of ABPM devices is increasingly encountered in the management of hypertensive patients. The advantage of this technique is the provision of a better understanding of the diurnal variation in BP compared to static clinic BP measurements. Often, abnormalities in the biological rhythm of BP in an individual are not given importance or consideration when managing hypertension in a busy clinic. The present study was aimed at studying the behavior of diurnal BP in essential hypertensives as well as to compare the diagnostic strength of office BP with ABPM in our local health setting.

Variation of day time and nocturnal blood pressure

The study highlights that there is a statistically significant difference between nocturnal BP compared to daytime BP suggesting that decision making dependent on daytime office BP in the outpatient setting may give an inaccurate verdict on the actual BP control of an individual. This element has been highlighted in several other studies as well [8]. In this study, the patients were advised to abstain from vigorous physical activity since that can give rise to high blood pressure values which may markedly affect the diurnal variation. This instruction helped to eliminate the confounding effect of exercise induced high day time blood pressure in the study sample.

Nocturnal dipping

Evidence is mounting that nocturnal high BP, blunting of nocturnal dipping and increased morning surge of BP contribute to adverse cardiovascular outcomes and end organ damage [11]. Multiple sources of evidence propose an association between adverse cardiovascular outcomes such as acute MI and cerebrovascular events and altered circadian BP pattern [5]. Additionally, many studies suggest that suboptimal nocturnal BP dipping can result in a variety of complications associated with elevated cardiac morbidity and mortality [12, 13, 4]. The present study revealed that a majority of patients with hypertension have abnormal dipping. It is likely that these patients have an elevated risk of vascular complications such as myocardial infarction and stroke. Therefore, this special group needs more attention and close control of vascular risk factors to prevent future adverse cardiovascular outcomes.

The difference between the behavior of dippers and non-dippers and its association to prognosis is an emerging field in the dynamic BP era. In our study, the dippers were not different to non-dippers in their 24-hour average SBP or DBP. Also, there was no difference in their daytime average SBP or DBP. However, they differed by their nocturnal average SBP and DBP. Similar nocturnal variation had been reported in a study done by Seo W.S et al. [8]. This observation strengthens the importance of the contribution of nocturnal hypertension in hypertensive patients. According to our study, the majority had nocturnal hypertension which would not be discovered by office BP.

There was no difference in the 24-hour average HR, daytime average HR or nocturnal average HR among dippers and non-dippers, in our study. It has been observed in one study that the daytime heart rate is lower in non-dippers than dippers [8]. This suggests that dippers and non-dippers should be identified as different subgroups having their own clinical characteristics, and different prognostic pathways. This reinforces the importance of ABPM in hypertensive patients to identify their prognostic category.

Reverse dipping and early morning fluctuation of BP

Cuspidi et al. [14] have revealed that a persistent non-dipper pattern is linked with an increased left ventricular mass index, a thicker interventricular septum and enlarged left atrium and the aortic root in previously untreated hypertensive patients. It will be interesting to determine the changes that occur in reverse dippers.

There is mounting evidence connecting early morning rise in BP and augmented cardiovascular risk [15]. Though the mechanisms underlying this observation are not identified, many neurohumoral mechanisms may be responsible. Reverse dippers have been shown to display a broader range of pulse pressure at night than any other groups signifying the probable role of arterial stiffness as a contributing mechanism for their elevated adverse cardiovascular risk [1]. ABPM may assist the physician to identify such specific high risk groups for more intensive control. Our study was able to identify that one quarter of the sample had a reverse dipping pattern suggesting it is not uncommon in our health practice.

Antihypertensive therapy and individualized decision making

There is some evidence that non-dippers may have a different response to antihypertensive pharmacotherapy than normal dippers suggesting that they are difficult to treat by conventional therapy [16].

There is also some evidence that antihypertensive pharmacotherapy may blunt the nocturnal rise in non-dippers and reverse dippers [17]. This may vary according to the type of antihypertensive drug as well as the timing of drug dose [18].

Conclusion and Recommendations

Our study highlights the importance of individualized therapy for hypertension based on the diurnal BP profile of an individual rather than merely achieving a therapeutic target. The study shows that this is applicable even to patients in a resource poor setting.

We recommend that physicians practice ABPM more frequently since it produces a better picture of an individual’s overall blood pressure status. If cost is a limiting factor, the test should be performed in selected cases such as in patients where it is difficult to achieve BP targets. Further studies to explore the blood pressure variation and response among our hypertensive patients is encouraged.

Limitations

A limitation of our study is the convenient sampling method. Since we excluded patients with coronary artery disease, females were over represented. Subgroup analysis i.e. patients with diabetes mellitus, obesity, antihypertensive class etc. was not possible due to a relatively small sample size.

Acknowledgements

We thank our patients at the Cardiology Unit, Kandy and the staff of the Cardiology Unit, for their contribution towards the success of this study.

References

1. Jerrard-Dunne P, Mahmud A, Feely J. Circadian blood pressure variation: relationship between dipper status and measures of arterial stiffness. J Hypertens 2007; 25: 1233–1239. https://doi.org/10.1097/HJH.0b013e3280eec79f PMid:17563536
2. Kaplan NM & Victor RG 2014, Kaplan's Clinical Hypertension, 11th edition, Wolters Kluwer Publishers.
3. Head GA, et al. 'Ambulatory blood pressure monitoring in Australia: 2011 consensus position statement' Journal of Hypertension 2012 Feb;30(2):253-66. https://doi.org/10.1097/HJH.0b013e32834de621 PMid:22179076
4. Higashi Y, Nakagawa K, Kimura M, Noma K, Hara K, Sasaki S, Goto C, Oshima T, Chayama K, Yoshizumi M. 'Circadian variation of blood pressure and endothelial function in patients with essential hypertension: a comparison of dippers and non-dippers' Journal of the American College of Cardiology 2002; 40: 2039–2043. https://doi.org/10.1016/S0735-1097(02)02535-4
5. Giles T, 'Relevance of blood pressure variation in the circadian onset of cardiovascular events' Journal of Hypertension 2005; 23(Suppl 1): S35–S39. https://doi.org/10.1097/01.hjh.0000165626.57063.b1
6. Chughtai IS, Peixoto AJ, 'Ambulatory blood pressure monitoring: a review of its clinical and prognostic relevance' Hospital Physician, march 2003, 47-62.
7. Giuseppe M, Robert F, Krzysztof N, Josep R, Alberto Z, et al. ESH/ESC Guidelines for the management of arterial hypertension: The Task Force for the management of arterial hypertension of the European Society of Hypertension (ESH) and of the European Society of Cardiology (ESC), Journal of Hypertension 2013, 31:1281–1357. https://doi.org/10.1097/01.hjh.0000431740.32696.cc PMid:23817082
8. Seo WS, Oh HS, 'The circadian rhythms of blood pressure and heart rate in the hypertensive subjects: dippers and non-dippers' Yonsei Medical Journal. 2002 Jun;43(3):320-328. https://doi.org/10.3349/ymj.2002.43.3.320 PMid:12089739
9. Hoshide Y, Morinari M, Murata M, Kuroda T. Morning Surge in Blood Pressure as a Predictor of Silent and Clinical Cerebrovascular Disease in Elderly Hypertensives A Prospective Study. 2003; https://doi.org/10.1161/01.CIR.0000056521.67546.AA

10. Siti Suhaila MY, Juwita S, Harmy MY, Tengku Alina TL. 'Circadian Blood Pressure Profile and Associated Cardiovascular Risk Factors in Non-Dippers' The international medical journal Malaysia, Dec 2013,Volume 12 Number 2,23-31.
11. Hassler C, Burnier M. Circadian variations in blood pressure: implications for chronotherapeutics. Am J Cardiovasc Drugs 2005; 5: 7–15 https://doi.org/10.2165/00129784-200505010-00002 PMid:15631533
12. Cuspidi C, Meani S, Valerio C, Fusi V, Zanchetti A. Nocturnal non-dipping pattern in untreated hypertensive at different cardiovascular risk according to the 2003 ESH/ESH guidelines. Blood Press 2006; 15: 37–44 https://doi.org/10.1080/08037050500496018 PMid:16492614
13. Della Mea P, Lupia M, Bandolin V, Guzzon S, Sonino N, Vettor R, Fallo F. Adiponectin, insulin resistance, and left ventricular structure in dipper and nondipper essential hypertensive patients. Am J Hypertens 2005; 18: 30–35. https://doi.org/10.1016/j.amjhyper.2004.08.029 PMid:15691614
14. Cuspidi C, Meani S, Salerno M, Valerio C, Fusi V, Severgnini B, Lonati L, Magrini F, Zanchetti A. Cardiovascular target organ damage in essential hypertensives with or without reproducible nocturnal fall in blood pressure. J Hypertens 2004; 22: 273–280. https://doi.org/10.1097/00004872-200402000-00010 PMid:15076184
15. Weber MA. The 24-h blood pressure pattern: does it have implications for morbidity and mortality? Am J Cardiol 2002; 89(Suppl 2A): 27A–33A. https://doi.org/10.1016/S0002-9149(01)02324-4
16. Kario K, Shimada K. Differential effects of amlodipine on ambulatory blood pressure in elderly hypertensive patients with different nocturnal reductions in blood pressure. Am J Hypertens. 1997; 10: 261-268. https://doi.org/10.1016/S0895-7061(96)00409-8
17. Nelson CP, Gracey J, Tobin M, Tomaszewski M, Samani NJ. Determinants of day – night difference in blood pressure, a comparison with determinants of daytime and night-time blood pressure. Journal of Human Hypertension (2017) 31, 43–48; https://doi:10.1038/jhh.2016.14
18. De la Sierra A, Banegas JR, Redon J, de la Cruz JJ, Segura J, Gorostidi M, Ruilope LM. Response to timing of antihypertensive therapy and circadian blood pressure patterns. Hypertension 2009; 53: e42. https://doi.org/10.1161/hypertensionaha.109.132704