

Predicting Isolated Nocturnal Hypertension Using Dawn and Dusk Home Blood Pressure Monitoring

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Abstract—Hypertension is a major global cause of morbidity and mortality. Home Blood Pressure Monitoring (HBPM) has the potential to help diagnose patients experiencing isolated nocturnal hypertension who may otherwise be missed. This paper investigates potential diagnostic thresholds for diagnosing isolated nocturnal hypertension using dawn and dusk HBPM measurements in the BP-Eth ambulatory blood pressure monitoring (ABPM) database. Depending on whether European or American diagnostic guidelines for hypertension were used, incidence of isolated nocturnal hypertension in the BP-Eth database was 17.1% or 16.8%, respectively. Using averaged dawn and dusk HBPM measurements to diagnose isolated nocturnal hypertension yielded an AUROC of 0.79 (European guidelines) or 0.84 (American guidelines). The SBP and DBP diagnostic thresholds required to detect 80% of cases of isolated nocturnal hypertension were found to be 125.4 mmHg and 75.7 mmHg, respectively (European guidelines) or 117.6 mmHg and 74.3 mmHg, respectively (American guidelines). These thresholds corresponded to a sensitivity of 80% and specificity of 63% (European guidelines) or sensitivity of 83% and specificity of 65% (American guidelines). These results demonstrate the potential for HBPM to function as an intermediate step in screening patients, determining which patients require more intensive ABPM monitoring for detection of isolated nocturnal hypertension.

Clinical relevance This study investigates the incidence of isolated nocturnal hypertension, and the possibility of using home blood pressure monitoring (HBPM) to screen for it. Isolated nocturnal hypertension is otherwise only detectable using more expensive and burdensome ambulatory blood pressure monitoring (ABPM).

I. INTRODUCTION

Hypertension (high blood pressure) is a major global cause of morbidity and mortality [1]. Early detection of hypertension is critical in managing its effects [2]. As blood pressure (BP) has a known circadian (daily) variance [3], distinct thresholds are used when diagnosing day-time and night-time hypertension [4], [5]. Detection of both day- and night-time hypertension is important: indeed, night-time BP has been shown to have a stronger association with cardiovascular disease outcomes than day-time BP [6]. However, hypertension screening typically relies upon BP readings taken at the GP clinic during the day-time [6].

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One of the tools available for diagnosing night-time hypertension is ambulatory blood pressure monitoring (ABPM). ABPM involves a patient wearing an automatically inflating BP cuff for a typically 24-hour period, providing both day- and night-time BP measurements. However, many patients find continuously wearing a BP cuff burdensome and disruptive to sleep, and ABPM devices are expensive. Indeed, ABPM is largely unavailable to primary care practitioners in the United States [6].

An alternative middle ground between clinic BP measurements and ABPM is home blood pressure monitoring (HBPM). In HBPM, a patient takes a BP cuff home and periodically measures their own blood pressure. This can provide measurements in the early morning (dawn) and late evening (dusk) outside of clinic hours, but does not provide night-time measurements (as the measurement process is manual). As the patient does not need to continuously wear a BP cuff, and an automated BP cuff is not required, this process is less burdensome and requires less specialised equipment than ABPM.

There is potential for dawn and dusk BP measurements, available using HBPM but not clinic BP monitoring, to provide an indication of night-time BP. Thus, these measurements, taken as a patient transitions between their night- and day-time BP, may allow the prediction of patients suffering from isolated nocturnal hypertension (night-time hypertension in absence of day-time hypertension). However, no existing diagnostic thresholds for hypertension exist for measurements taken during such a period.

In [7], the authors raise the possibility of evaluating morning hypertension using HBPM as an alternative to measuring nocturnal blood pressure. However, the authors note there are two subtypes of morning hypertension, one due to nocturnal hypertension and the other due to a morning blood pressure surge [8]. As it is not currently possible to distinguish between these two diurnal blood pressure changes using morning BP data, HBPM measurements at both at dusk and dawn may provide further benefit.

This paper investigates the prevalence of isolated nocturnal hypertension in a large ABPM dataset. It then investigates the potential for dawn and dusk BP measurements, as would be provided by HBPM, to predict isolated nocturnal hypertension, as well as potential diagnostic thresholds for doing so.

II. METHODOLOGY

A. Dataset - The BP-Eth Study

The BP-Eth study was an observational study conducted on primary care patients between June 2010 and December 2012 [9], [10], designed to investigate the association between the ‘white coat effect’ (a transient increase in BP in the GP clinic) and ethnicity. 770 patients aged 40 - 74 years, both with and without a previous diagnosis of hypertension, were recruited across 28 practices from the Primary Care Research Network-Central England, United Kingdom. Ethical approval for this study was granted by the Black Country Research Ethics Committee, West Midlands, United Kingdom (Ref 09/H1202/114).

The study protocol involved comparing data gathered from a 24-hour ABPM recording (Spacelabs 90217-1Q) and two sets of GP clinic BP measurements (BpTru Medical Devices BPM-100). The dataset employed in this paper is the data gathered during the ABPM sessions (of which 759 were recorded). ABPM measurements were recorded half hourly during the day (7:00 am - 10:59 pm) and hourly overnight (11:00 pm - 6:59 am).

B. Diagnosing Hypertension

Hypertension diagnostic thresholds for classifying patients undergoing ambulatory monitoring were taken from the European Society of Cardiology (ESC) [4] and American College of Cardiology (ACC) [5] guidelines. These diagnostic thresholds are presented in table I.

TABLE I
ESC/ACC THRESHOLDS FOR DIAGNOSING HYPERTENSION USING ABPM

ABPM Period	European Society [4]		American College [5]	
	Systolic	Diastolic	Systolic	Diastolic
Day	135	85	130	80
Night	120	70	110	65

In this paper, day-time was defined as 9:00 am - 5:59 pm (roughly corresponding to GP clinic hours) and night-time as 11:00 pm - 6:59 am, providing a 2 - 5 hour gap between the day and night periods. Patients were excluded from the analysis if they had fewer than 50% valid measurements during day (9 of 18) or night (4 of 8). For the remaining patients, the mean day- and night- time Systolic Blood Pressure (SBP) and Diastolic Blood Pressure (DBP) were calculated. Then, for each set of diagnostic guidelines (ESC and ACC), patients were assigned to one of three mutually exclusive cohorts:

- **Cohort A - Day Hypertension:** Any patient with mean day-time SBP or DBP in excess of diagnostic thresholds for hypertension.
- **Cohort B - Night Hypertension:** Any patient not already classified as ‘Day Hypertension’ with mean night-time SBP or DBP in excess of diagnostic thresholds for hypertension.

- **Cohort C - No Hypertension:** Any patient not already classified as ‘Day Hypertension’ or ‘Night Hypertension’.

C. Establishing HBPM Diagnostic Thresholds

In this paper, the HBPM monitoring period was defined as 7:00 am - 10:59 pm (corresponding to the period during which the BP-Eth protocol stipulated taking ABPM measurements at 30 minute intervals). As the HBPM monitoring period encompasses the ‘day-time’ monitoring period (9:00 am - 5:59 pm), the HBPM dataset inherently allows the accurate calculation of day-time BP and diagnosis of day-time hypertension. As such, day-time BP measurements, along with any patients in Cohort A, were excluded from further HBPM analysis.

The remaining HBPM measurements were those taken between 7:00 am - 8:59 am (dawn) and 6:00 pm - 10:59 pm (dusk). For each patient, the mean of these measurements was taken (a graphical breakdown of the day, night, dawn, and dusk periods is given in fig. 1). The remaining patients were labelled as ‘positive’ (Cohort B) or ‘negative’ (Cohort C) for isolated nocturnal hypertension.

HBPM diagnostic thresholds for SBP and DBP were then established using Receiver Operating Characteristic (ROC) curves. In keeping with existing hypertension diagnostic thresholds, an individual was considered ‘hypertensive’ if they met either an SBP or DBP threshold for hypertension. As establishing these thresholds involved two ROC curves (one each for SBP and DBP) that interact, the ROC curves were combined using the methodology presented in [11]. First, ROC performance was calculated for the set of possible combinations of SBP and DBP thresholds. This set of ROC performance points was then used to establish an optimum ROC curve by finding the ROC point with the maximum True Positive Rate (TPR) for each of a series of discrete bins of False Positive Rate (FPR)). This process was performed for both the ESC and ACC diagnostic thresholds. In each case, the Area Under the ROC (AUROC), the SBP and DBP diagnostic thresholds required to detect 80% of isolated nocturnal hypertension cases, and the associated true and false positive rates at these thresholds were reported.

III. RESULTS

A. Cohort Demographics

Table II provides a brief summary of patient demographics in the BP-Eth dataset. There were 759 patients with ABPM data recorded. The cohort is balanced with regards to gender, and has an average age of 58.5 years. A significant proportion of patients (51.9%) have one or more comorbidity, here defined as: High Cholesterol, Coronary Heart Disease (CHD), Coronary Artery Bypass Graft (CABG), Heart Failure, Transient Ischaemic Attack (TIA), Peripheral Vascular Disease, Atrial Fibrillation, Chronic Kidney Disease (CKD), and Diabetes.

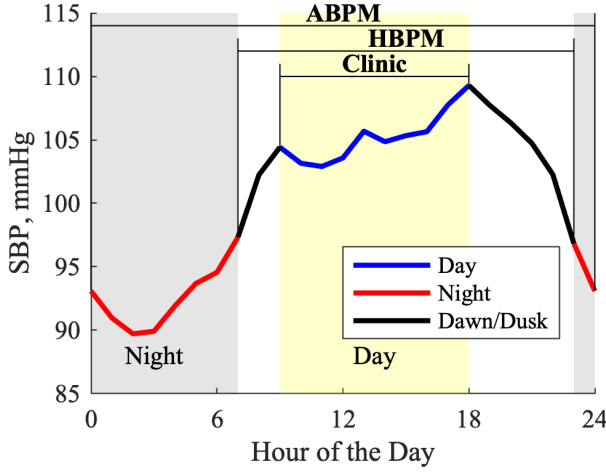


Fig. 1. Illustration of a typical SBP profile, and the relationship between day, night, dawn, and dusk periods and ABPM, HBPM, and GP clinic monitoring as defined in this paper.

TABLE II

OVERVIEW OF PATIENT COHORT DEMOGRAPHICS FOR THE BP-ETH ABPM DATASET

	Men	Women	Overall
No. of patients	378	381	759
Age	58.9 (9.7)	58.2 (9.4)	58.5 (9.5)
# measurements	24.0 (7.4)	23.8 (7.1)	23.9 (7.3)
Mean 24h SBP	130.2 (13.4)	127.8 (15.3)	129.0 (14.4)
Mean 24h DBP	78.5 (8.2)	76.5 (9.0)	77.5 (8.7)
Comorbidity, # (%)	216 (57.1)	178 (46.7)	394 (51.9)

Results presented mean (SD) unless otherwise stated.

B. Incidence of Hypertension

Of the 759 patients with ABPM data, 585 had the required 9 valid day-time and 4 valid night-time measurements. The incidence of day-time and isolated night-time hypertension among these patients in the BP-Eth dataset is shown in table III. Despite the typically 5 mmHg difference between the ESC and ACC guidelines for diagnosing hypertension, there are significant differences in the rates of hypertension diagnosed in the BP-Eth dataset when using the two sets of guidelines. ESC guidelines give significantly lesser incidence of day-time hypertension (52.5%) than ACC guidelines (69.1%), and, accordingly, a significantly greater proportion of patients are not diagnosed with hypertension when using ESC guidelines (30.4%) compared to ACC guidelines (14.2%). Importantly, when using either set of guidelines, a significant minority of hypertension cases are isolated nocturnal hypertension (17.1% of the overall cohort for ESC guidelines, and 16.8% for ACC guidelines).

TABLE III

INCIDENCE OF HYPERTENSION USING ESC AND ACC ABPM GUIDELINES

Guidelines	Day Hyp.	Night Hyp.	No Hyp.
ESC	307 (52.5%)	100 (17.1%)	178 (30.4%)
ACC	404 (69.1%)	98 (16.8%)	83 (14.2%)

C. Predicting Isolated Nocturnal Hypertension Using Dawn and Dusk HBPM

Fig. 2 presents the SBP, DBP, and combined ROC curves for diagnosing isolated nocturnal hypertension using dawn and dusk HBPM measurements, and table IV shows the AUROC for each of the curves in fig. 2. For both the ESC and ACC thresholds, the combined ROC curve yields a notable improvement in AUROC, giving an AUROC of 0.79 for ESC guidelines and 0.84 for ACC guidelines.

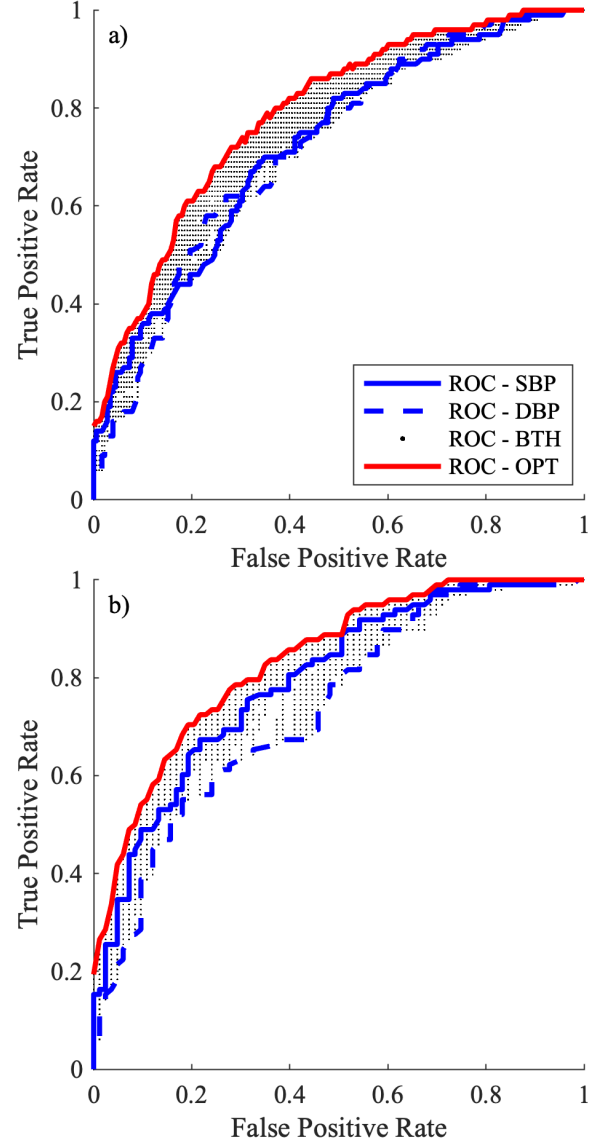


Fig. 2. ROC curves for diagnosing isolated nocturnal hypertension using HBPM data: a) Using ESC thresholds; b) using ACC thresholds. 'SBP' denotes the SBP only ROC curve, 'DBP' the DBP only ROC curve, 'BTH' the set of combined ROC points, and 'OPT' the optimal combined ROC curve.

Table V shows the SBP and DBP diagnostic thresholds required to detect 80% of isolated nocturnal hypertension cases using the combined ROC curve for the ESC and ACC guidelines. In all cases, as might be expected, these thresholds for dawn and dusk HBPM measurements lie

TABLE IV

AUROC FOR THE SBP ONLY, DBP ONLY, AND COMBINED ROC CURVES
IN FIG. 2

Guidelines	SBP	DBP	Combined
ESC	0.72	0.71	0.79
ACC	0.79	0.73	0.84

between the corresponding day- and night-time diagnostic thresholds. Using the thresholds for the ESC guidelines gives 80 of 100 cases detected, but 66 of 178 non-hypertensives as false positives. Using the thresholds for the ACC guidelines gives 81 of 98 cases detected, but 29 of 83 non-hypertensives as false positives.

IV. DISCUSSION

Table III shows that a significant proportion of the BP-Eth cohort (17.1% according to ESC guidelines, and 16.8% according to ACC guidelines) experiences isolated nocturnal hypertension. Thus, diagnosing these patients' hypertension would require BP measurements taken outside of GP clinic hours, either by ABPM or HBPM. The incidence of isolated nocturnal hypertension reported in this paper agree well with the 17 - 22% range reported in [2] for an in-hospital ward based cohort, likely due to the high incidence of cardiovascular comorbidities in the BP-Eth cohort.

Table IV and fig. 2 show that moderate AUROCs of 0.79 (ESC guidelines) and 0.84 (ACC guidelines) are achieved for diagnosing isolated nocturnal hypertension using combined SBP and DBP thresholds for dawn and dusk HBPM measurements. These AUROCs suggest that HBPM, given its greater convenience than ABPM, has potential to function as an intermediate step for screening patients to determine which of them require more intensive ABPM monitoring for isolated nocturnal hypertension.

The SBP and DBP diagnostic thresholds required to detect 80% of isolated nocturnal hypertension cases (table V) are, as expected, between the existing day- and night-time thresholds. Both sets of thresholds provide reasonable performance, with the performance for the ESC guidelines (sensitivity of 80%, specificity of 63%) slightly worse than that for the ACC guidelines (sensitivity of 83%, specificity of 65%). It is worth noting that the relative sizes of Cohorts B (isolated nocturnal hypertension) and C (no hypertension) vary significantly between the ESC and ACC guidelines, which may affect ideal threshold levels and performance.

This work explores using fixed diagnostic SBP and DBP thresholds to predict isolated nocturnal hypertension from dawn and dusk HBPM measurements. However, there are a number of other potential approaches for predicting isolated nocturnal hypertension from HBPM measurements. Time series modelling of periodic circadian blood pressure, using cosine models [12] or machine learning techniques such as gaussian processes [13], could allow direct prediction of nocturnal BP measurements from HBPM data. Such a model would, in turn, allow direct use of the existing night-time hypertension thresholds for diagnosis. Given the high

TABLE V

DIAGNOSTIC THRESHOLDS FOR HYPERTENSION USING HBPM DATA,
TRUE POSITIVE RATE (TPR), FALSE POSITIVE RATE (FPR), TRUE
POSITIVES (TP), AND FALSE POSITIVES (FP)

Guidelines	SBP	DBP	TPR	FPR	TP	FP
ESC	125.4	75.7	0.80	0.37	80/100	66/178
ACC	117.6	74.3	0.83	0.35	81/98	29/83

incidence of cardiovascular comorbidities in the population at risk of hypertension, another potential avenue for future work is the use of mixed effects models to provide insight into the impact of these comorbidities on diagnostic thresholds for hypertension [14].

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