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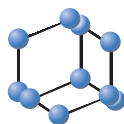
Ambulatory Blood Pressure Monitoring in Type 2 Diabetes Mellitus: A Cross-sectional Study

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Abstract: *Background*: Ambulatory blood pressure (ABP) monitoring in type 2 diabetes (T2DM) is not yet routine in clinical practice.

Objectives: To quantify abnormal ABP patterns and their associations with diabetic complications, and to assess the reliability of office blood pressure (OBP) for assessing BP in T2DM.

Methods: In a cross-sectional study, eligible patients with T2DM underwent OBP and 24- hour ABP measurements under standardized conditions and screening for diabetic complications.

Results: 56 patients (mean age 67 $\pm$ 10 years, males 50%) completed assessment. 43(73%) had a known history of hypertension. Non-dipping and nocturnal systolic hypertension (SHT) were prevalent in 31(55%) and 32(57%) patients, respectively. 16(29%) demonstrated masked phenomenon, but only three (7%) demonstrated white coat effect. Nocturnal SHT had a significant association with composite microvascular complications independent of daytime systolic BP control (adjusted odds ratio (OR) 1.72(CI 1.41-4.25). There was no association between other abnormal ABP patterns and diabetic complications. The sensitivity and specificity of OBP for diagnosing HT or assessing BP control was 59% and 68% respectively. The positive and negative predictive values were 74% and 52% respectively.

Conclusion: Non-dipping, reverse dipping, nocturnal SHT and masked phenomenon are highly prevalent in patients with T2DM with or without a known history of hypertension. Compared with non-dipping, nocturnal SHT may be a stronger predictor of end organ damage. The reliability of OBP for assessing BP in T2DM is only modest. Patients with T2DM are likely to benefit from routine ABP monitoring.

Keywords: Ambulatory blood pressure, type 2 diabetes mellitus, non dipping, nocturnal hypertension, masked hypertension.

1. INTRODUCTION

Hypertension (HT) is a common comorbidity in DM. In addition to blood glucose control, blood pressure (BP) control remains the cornerstone of the management of micro and macrovascular complications of diabetes [1-3]. Given the pitfalls of office blood pressure, ambulatory blood pressure monitoring (ABPM) has been recommended for the assessment of HT [4, 5]. Besides being able to detect white coat and masked HT, ABPM also gives information on nocturnal blood pressure and circadian blood pressure rhythm, which have been shown to have prognostic significance independent of BP control [5-8]. However, ambulatory BP monitoring has not yet become routine in type 2 diabetes, or diabetes in general. This is evidenced by the paucity of recommendations on the use of ABP monitoring in the current diabetic guidelines [9]. This study was therefore designed to determine the prevalence of abnormal ambulatory blood pressure patterns and their associations with complications with the view to validate the clinical utility of routine ABP monitoring in type 2 diabetes mellitus in a real world clinical setting. In addition, the study also investigated the reliability of office BP for diagnosing HT or assessing BP control.

2. METHODS

2.1. Participants and Measurements

The sample was derived from all consecutive patients with type 2 diabetes who attended the diabetes clinic at East-

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ern Health, Melbourne, Australia, over a 6-month period from 2nd of March 2015 until 4th of September 2015. Patients aged 40 years or older with a formal diagnosis of type 2 diabetes and were receiving pharmacologic treatment (either oral hypoglycaemic agent/s, insulin or both) were eligible to participate in the study. Patients with atrial fibrillation and sleep disordered breathing and those who were night shift workers and were not able to follow instructions in English were excluded. Patients were also excluded if they were not able to attend the clinic for two consecutive days for completing ambulatory blood pressure monitoring. All clinic attendees were initially screened by the research assistant and those who were willing and able to consent were further assessed by one the investigators for inclusion in the study. After obtaining consent the following information was gathered by interviewing patients and review of medical and laboratory records: demographic data, measurement of height and weight (which were used to estimate Body Mass Index (BMI), details of the history of diabetes, such as duration and complications, HT and other comorbidities, usual medications, alcohol intake (2 ≥ standard drinks/day) and smoking history. Laboratory investigations included most recent HbA1c, urine albumin/ creatinine ratio and estimated eGFR within six months of assessment. Microvascular complications were defined by the presence of either microalbuminuria, retinopathy or neuropathy, and were determined by the most recent record of examination in the medical history within six months of undertaking ambulatory BP measurements. As part of the routine practice all patients attending the diabetes clinic underwent periodical assessment for retinopathy, peripheral neuropathy and microalbuminuria. Macrovascular complications were deemed present if there was a history of coronary artery, cerebrovascular or peripheral vascular disease. Patients did not undergo specific investigations, such as CT or MRI scan of the brain, arterial doppler study, or coronary angiogram, *etc*., to confirm macrovascular complications for the purpose of the study. However, if the relevant investigations were available they were reviewed to confirm macrovascular complications. The study was approved by the Eastern Health Research Ethics Committee.

2.2. Blood Pressure Measurements

Office blood pressure: Prior to commencing 24-hour ABPM, office blood pressure (OBP) was obtained under standardized conditions by one of the investigators using patients' non-dominant arm. Blood pressure was measured using a calibrated oscillometric automated digital blood pressure apparatus and an appropriate size cuff after a minimum rest of five minutes in a seated position. The mean of three BP measurements measured at least two minutes apart was taken for analysis as the final OBP reading.

24-hour ABPM: A TM2430 ambulatory blood pressure monitor (A&D Medical Australia) was used to perform 24-hour ambulatory BP measurements using patients' non-dominant arm. Automated measurements were recorded every 30 minutes for 24 hours. Readings were evaluated if the percentage of successful readings was more than 80%**.** The following ABP parameters were evaluated: mean 24-hour, daytime and night time BP, and circadian BP patterns. The prevalence of white coat and masked phenomena was also determined. The awake and sleep periods were defined using the sleep and awakening times reported by patients. Standard ABP diagnostic criteria were used to define blood pressure control and abnormal ABP patterns (Table **1**) [10]. However, we defined nocturnal HT only on the basis of systolic BP (*i.e.* nocturnal systolic HT), as only nocturnal systolic HT has been consistently shown to be associated with diabetic complications and adverse vascular outcomes [11, 12]. For the purpose of analysis, the non and reverse dippers

Table 1. Diagnostic criteria for ambulatory blood pressure parameters.

Blood pressure thresholds for diagnosing hypertension	
Office BP	≥140/90mmHg
Ambulatory BP (mean)	
24-hour	≥130/80mmHg
Night time	≥120/70mmHg
Daytime	≥135/85mmHg
Circadian BP patterns	
Normal dipping	A night-time BP fall ≥10% but <20% relative to daytime mean (night to day BP ratio 0.8 < ratio ≤0.9)
Extreme dipping	A night-time BP fall ≥20% in relative to daytime BP (night to day BP ratio ≤0.8)
Non-dipping	No night-time BP fall or a night-time BP fall <10% (night to day BP ratio 0.9 < ratio ≤1)
Reverse dipping	BP rise at night time (night to day BP ratio >1.0)
Hypertensive syndromes	
White coat hypertension/effect[†]	Office BP ≥140/90 AND awake ABP <135/85 and 24- hour ABP <130/80 and sleep ABP <120/70
Masked hypertension/masked uncontrolled hypertension[‡]	Normal office BP <140/90 AND 24-hour mean ABP ≥130/80 and/or awake mean ABP ≥135/85 and/or sleep mean ABP ≥120/70

[†]White coat effect: in treated patient. [‡]Masked uncontrolled hypertension: in treated patient.

and the normal and extreme dippers were grouped together due to the relatively small sample size.

2.3. Outcome Measures

2.3.1. Primary

1. The prevalence of non-dipping, nocturnal systolic HT, and white coat (white coat HT or white coat effect) and masked phenomena (*i.e.* masked HT or masked uncontrolled HT).

2.3.2. Secondary

1. The association between abnormal ABP patterns and microvascular and macrovascular complications.

2. The reliability of office BP for diagnosing HT (by determining the sensitivity and specificity as well as the positive and negative predictive values of office BP for either diagnosing HT or assessing BP control using 24-hour ABP mean as the gold standard).

3. STATISTICAL ANALYSIS

Descriptive information on sample characteristics was presented as absolute number of cases and percentage of total group data or with mean $\pm$ standard deviation. Continuous variables were compared using Student's t-test, and Chi-square or Fisher's exact test was used for categorical variables, as appropriate. A logistic regression analysis was undertaken for those ambulatory blood pressure parameters that had a significant univariate association with either micro or macro vascular complications in order to determine the association between them after controlling for the relevant covariates. A two tailed $P < 0.05$ indicated statistical significance. All analyses were conducted using IBM SPSS Statistics for Windows, Version 21.0(released 2012, IBM Corp, Armonk, NY, USA).

Table 2. **Characteristics of non dippers.**

-	Non Dippers (Patients with Non/reverse Dipping (n=31))	Normal Dippers (Patients with Normal/extreme Dipping (n=25))	P values
Mean age (years)	69 $\pm$ 11	65 $\pm$ 8	0.144
Sex (male)	11 (35%)	17 (68%)	0.015*
Mean BMI	27.8 $\pm$ 7.0	30.1 $\pm$ 6.0	0.217
Mean duration of DM (years)	17 $\pm$ 8	16 $\pm$ 12	0.775
Known history of HTN	24 (77%)	19 (76%)	0.900
Microvascular complications			
- Microalbuminuria	15 (48%)	9 (36%)	0.352
- Neuropathy	9 (29%)	5 (20%)	0.542
- Retinopathy	6 (19%)	3 (12%)	0.716
- Composite microvascular complications	19 (61%)	11 (44%)	0.197
Macrovascular complications			
- Cardiovascular	11 (35%)	7 (28%)	0.355
- Stroke	3 (10%)	5 (20%)	0.444
- PVD	5 (16%)	2 (8%)	0.443
- Composite macrovascular complications	14 (45%)	10 (40%)	0.698
HbA1c > 7%	16 (52%)	12 (48%)	0.788
eGFR (ml/min/1.73m2)			
- <60	5 (16%)	5 (20%)	0.738
- <45	2 (7%)	1 (4%)	0.999
24-hour mean ABP <130/80mmHg	7 (23%)	13 (52%)	0.022*
Daytime mean ABP <135/85mmHg	12 (39%)	11 (44%)	0.689
Nocturnal mean ABP <120/70mmHg	4 (13%)	20 (80%)	<0.001*
Anti-hypertensive medications, mean(SD)	1.7 $\pm$ 1.5	1.0 $\pm$ 0.8	0.029*
$\geq$ 3 anti-hypertensive medications	9 (29%)	1 (4%)	0.031*

*Statistically significant. Abbreviations: BMI: body mass index. DM: diabetes mellitus. PVD: peripheral vascular disease. ABP: ambulatory blood pressure. eGFR: estimated glomerular filtration rate.

4. RESULTS

Of the 173 patients with type 2 diabetes mellitus who attended the clinic during the study period, 70 patients were deemed suitable to participate in the study during the initial assessment. The predominant reason for exclusion was the inability of patients to attend hospital for ABP monitoring on week days. Further assessment resulted in the exclusion of 12 more patients: seven declined to participate, one was a night shift worker and four had obstructive sleep apnoea (OSA). Of the 58 patients who underwent ABP monitoring two were excluded due to incomplete ABP data. 56 were included in the final analysis (mean age 67±10 years, males 50%). 21% were non Caucasians. The mean duration of diabetes was 16±10 years. The mean HbA1c and eGFR were 7.4 ± 1.2% and 76 ± 19ml/min/1.73m2, respectively. The

majority of patients 41 (73%) were non-smokers and only 2 (4%) consumed significant alcohol (> 2 standard drinks/ day) on a regular basis. The mean BMI was 28.8 ± 6.7. 43 (77%) had a known history of HT and received 2.0±1.1 antihypertensive medications. The mean office BP in patients with and without a known history of HT was 143/76±18/11mmHg and 130/79±9/7mmHg, respectively. The corresponding mean 24-hour ABP was 135/75±14/8mmHg and 135/80±11/7mmHg, respectively.

4.1. Circadian BP

31 patients (55%, 95% CI, 41%- 68%) were found to have abnormal circadian BP rhythm with non or reverse dipping patterns, and this included seven (23%) without a known history of HT. Of these, 26 (84%) were non dippers

Table 3. Characteristics of patients with nocturnal hypertension.

-	Patients with Nocturnal Hypertension (n=32)	Patients without Nocturnal Hypertension (n=24)	P values
Mean age (years)	69.7 ± 10	63.3 ± 8.1	0.017*
Sex (male)	14 (44%)	14 (58%)	0.280
Mean BMI	28.4 ± 7.1	29.6 ± 6.0	0.501
Mean duration of DM (years)	17 ± 7.9	15 ± 12.1	0.499
Known history of HTN	25 (78%)	18 (75%)	0.784
Microvascular complications			
- Microalbuminuria	17 (53%)	7 (29%)	0.073
- Neuropathy	8 (25%)	6 (25%)	0.999
- Retinopathy	7 (22%)	2 (8%)	0.274
- Composite of microvascular complications	21 (66%)	9 (38%)	0.037*
Macrovascular complications			
- Cardiovascular	11 (34%)	7 (29%)	0.680
- Stroke	4 (13%)	4 (17%)	0.713
- PVD	5 (16%)	2 (8%)	0.686
- Composite macrovascular complications	15 (47%)	9 (38%)	0.483
HbA1c > 7%	21 (65%)	12 (50%)	0.239
eGFR (ml/min/1.73m2)			
- < 60	6 (19%)	4 (17%)	0.999
- < 45	1 (3%)	2 (8%)	0.570
24-hour mean ABP <130/80mmHg	4 (13%)	18 (75%)	<0.001*
Daytime mean ABP <135/85mmHg	9 (28%)	14 (58%)	0.023*
Non/reverse dipping	27 (84%)	4 (17%)	<0.001*
Normal/extreme dipping	5 (16%)	20 (83%)	<0.001*
Anti-hypertensive medications, mean (SD)	1.6 ± 1.5	1.1 ± 0.8	0.148
≥ 3 anti-hypertensive medications	9 (28%)	1 (4%)	0.032*

*Statistically significant. Abbreviations: BMI: body mass index. DM: diabetes mellitus. PVD: peripheral vascular disease. ABP: ambulatory blood pressure. eGFR: estimated glomerular filtration rate.

Table 4.　**Characteristics of patients with masked phenomenon.**

-	Patients with Normal Office BP and Normal ABPδ (n=13)	Patients with Masked Phenomenon (MH/MUCH) (n= 16)	P values
Mean age (years)	63 $\pm$ 7.4	65 $\pm$ 9.2	0.574
Sex (male)	8 (62%)	6 (38%)	0.280
Mean BMI	27.2 $\pm$ 4.8	26.8 $\pm$ 4.8	0.943
Mean duration of DM (years)	11 $\pm$ 5.7	12 $\pm$ 6.3	0.659
Known history of HTN	7 (54%)	9 (56%)	0.897
Microvascular complications			
- Microalbuminuria	3 (23%)	6 (38%)	0.454
- Neuropathy	2 (15%)	2 (13%)	0.999
- Retinopathy	0 (0%)	2 (13%)	0.487
- Composite of microvascular complications	4 (31%)	7 (44%)	0.702
Macrovascular complications			
- Cardiovascular	3 (23%)	6 (38%)	0.454
- Stroke	3 (23%)	3 (19%)	0.999
- PVD	1 (8%)	2 (13%)	0.999
- Composite of microvascular complications	5 (38%)	6 (38%)	0.999
HbA1c > 7%	5 (38%)	9 (56%)	0.340
eGFR (ml/min/1.73m2)			
- < 60	1 (8%)	2 (13%)	0.999
- < 45	1 (8%)	0 (0%)	0.448
Anti-hypertensive medications, mean (SD)	0.6 $\pm$ 0.6	1.0 $\pm$ 1.2	0.250
$\geq$ 3 anti-hypertensive medications	0 (0%)	2 (13%)	0.487

δ Normal ABP refers to normal mean 24-hour, daytime, and nocturnal blood pressure. Abbreviations: BMI: body mass index. DM: diabetes mellitus. PVD: peripheral vascular disease. ABP: ambulatory blood pressure. MH: masked hypertension. MUCH: masked uncontrolled hypertension. eGFR: estimated glomerular filtration rate.

and five (16%) were reverse dippers. Of the 26 non-dippers, 16 (62%) had non-dipping for both systole and diastole and 10 (38%) had non-dipping only for systole. All five (100%) reverse dippers had reverse dipping for both systole and diastole. 25 (45%) patients had normal or extreme dipping patterns; 20 (80%) normal dippers and 5 (20%) extreme dippers. Of the five extreme dippers, two (40%) had extreme dipping for both systole and diastole, two (40%) had extreme dipping for only systole with normal dipping for diastole, and one (20%) had extreme dipping for only diastole with normal dipping for systole. All (100%) normal dippers had normal dipping for both systole and diastole.

Compared with normal or extreme dippers, non or reverse dippers had a significantly fewer patients with controlled 24-hour and nocturnal BP, although there was no difference between groups for daytime BP control (Table **2**). There was no difference in age between groups, although non or reverse dippers had a greater number of females. The total number of anti-hypertensive medications used and the use of ≥3 anti-hypertensive medications were also significantly greater among non or reverse dippers. However, non

or reverse dipping was not associated with impaired renal function or other diabetic complications, either microvascular or macrovascular (Table **2**). It was also not associated with the duration of diabetes or diabetes control.

4.2. Nocturnal Hypertension

Nocturnal systolic HT was prevalent in 32 (57%, 95% CI 43%- 70%) patients and this included 7 (22%) without a known history of HT. Compared to those without nocturnal systolic HT, patients with nocturnal HT were significantly older, more likely to have non or reverse dipping and poor 24-hour and daytime BP control and more likely to take ≥ 3 anti-hypertensive medications (Table **3**). Nocturnal systolic HT also had a significant univariate association with composite microvascular complications (*i.e.* either microalbuminuria, retinopathy or neuropathy). This association remained significant after adjustment for daytime systolic BP control, age, gender and dipping status (adjusted OR 1.72 (CI 1.41- 4.25). There were no differences between groups for individual microvascular complications, although there was a trend toward significance for microalbuminuria (Table **3**).

The achieved power of the study, however, with the sample sizes and the results observed to detect a significant difference in the composite microvascular complication between groups was only 55%. The prevalence of macrovascular complications was similar between groups.

4.3. Masked and white Coat Phenomena

A total of 16 (29%, 95%CI 17%-42%) patients were found to have masked phenomenon which included nine of the 43 (21%) with a known history of HT (masked uncontrolled HT) and seven of the 13 (54%) without a known history HT (masked HT). The mean office and 24-hour ambulatory blood pressures in patients with masked uncontrolled and masked HT were 128/75 ± 10/9mmHg vs.135/77 ± 7/8mmHg and 129/79 ± 12/9mmHg vs. 136/80 ± 9/6mmHg, respectively. Of the nine patients with masked uncontrolled HT, in five (56%) ambulatory BP was found to be elevated in all three parameters, *i.e.* daytime, night time and 24-hour mean; in three (33%) ambulatory BP was elevated in two parameters (elevated 24-hour and daytime mean BP in two and elevated 24-hour and nocturnal mean BP in one); and in one (11%) ABP was elevated in only daytime mean BP. Of the seven patients with masked HT, four (57%) had elevated ambulatory BP in all three parameters, two (29%) had elevated ABP in two parameters (one with elevated 24-hour and daytime mean and the other with elevated 24-hour and nocturnal mean BP), and one (14%) had elevated ABP only in nocturnal mean BP. Masked phenomenon was not associated with diabetic complications, either micro or macro vascular, or any other clinical or demographic variables (Table **4**).

The white coat effect was seen in three (7%, 95% CI 5%-24%) of the 43 patients with a known history of HT (mean office and 24-hour ambulatory blood pressures were 145/84 ± 5/4mmHg and 126/73 ± 3/2mmHg respectively). However, none of the 13 patients without a known history of HT had white coat HT.

4.4. Alignment of BP Control between Office and Ambulatory BP

Concordance for BP control between office BP and ABP was seen in 15 (27%) patients for optimal BP control (*i.e.* office BP < 140/90 and 24-hour mean ABP <130/80) and in 20 (36%) for poor BP control (*i.e.* office BP ≥ 140/90 and 24-hour mean ABP ≥130/80). The sensitivity and specificity of office BP for confirming the diagnosis of HT or assessing blood pressure control using 24-hour mean ABP as the gold standard were 59% and 68%, respectively. The positive and negative predictive values of the office BP were 74% and 52 %, respectively. The sensitivity and specificity of office BP for confirming the diagnosis of HT or assessing BP control using mean daytime ABP as the gold standard were 61% and 70 % respectively, and the positive and negative predictive values were 74% and 55%, respectively.

5. DISCUSSION

The study confirms a high prevalence of non or reverse dipping, nocturnal systolic HT and masked phenomenon in patients with type 2 diabetes with or without a known history of HT. The findings also suggest that office BP is only moderately sensitive and specific for assessing blood pressure in patients with type 2 diabetes. The findings further demonstrate a significant association between nocturnal (systolic) HT and microvascular complications independent of daytime systolic BP control.

5.1. Prevalence of Non-dipping and Nocturnal Hypertension (Reversal of Circadian Pattern)

In agreement with the present study, most previous studies have reported a high prevalence of abnormal circadian BP patterns in type 2 diabetes, and 55% non -dipping noted in the present study is consistent with the current literature [11-13]. De la Sierra *et al.* demonstrated that type 2 diabetes mellitus was independently associated with non–dipping in a cohort of 34,563 treated and 8384 untreated hypertensive patients in a registry based study [14]. Ukkola *et al.* demonstrated this association in patients with impaired glucose tolerance [15] and Lyhne *et al.* in newly diagnosed type 2 diabetics [16]. The prevalence of non-dipping in the latter study was 40.2%. Fogari *et al.* in a case control study that included 47 normotensive and 49 hypertensive type 2 diabetics demonstrated that the association between type 2 diabetes and non or reverse dipping, particularly for systolic BP, was independent of the history of HT [17]. Ayala *et al.* confirmed that this association was independent of chronic kidney disease, obstructive sleep apnoea and treatment of HT in a sample of 2954 type 2 diabetic and 9811 non-diabetic hypertensive patients. The prevalence of non dipping and reverse dipping for systolic BP in this study was 62.1 % and 19.1%, respectively [13]. Kalaycioglu *et al.* in a cohort of 86 hypertensive diabetics described non-dipping in 59.3% [18] and Draman *et al.* found 47.4% to have non-dipping for systolic BP in a cohort of 859 type 2 diabetics [11].

As with non or reverse dipping, an increased prevalence of nocturnal systolic HT or higher nocturnal systolic BP in relation to daytime BP has been described in type 2 diabetics [11-13], and this was confirmed by the present study as well. Ayala *et al.* reported a prevalence of 89.2% nocturnal HT in type 2 diabetics with poor BP control [13]. Draman *et al.* demonstrated a higher nocturnal systolic BP in relation to daytime BP in 859 type 2 diabetics in a case control study [11]. Interestingly, diabetics were found to have a lower day and night diastolic BP compared to controls in this study. The prevalence of nocturnal HT observed in the present study is somewhat lower than other studies. The reason for this is unclear but may due to the varying characteristics of the sample. As observed in the present study, nocturnal HT and non-dipping, particularly reverse dipping, would be expected to be present together, as one would be the natural consequence of the other [12, 13]. Furthermore, as a consequence of nocturnal HT, as shown in the present study, one would expect poor 24-hour BP control to be highly prevalent among patients with nocturnal HT and non or reverse dipping. This has been observed in previous studies as well [12, 13]. The significant association of nocturnal hypertension and non-dipping with the use of three or more antihypertensive medications was also probably the reflection of poor blood pressure control in these patients.

5.2. The Association between Non-dipping, Nocturnal Hypertension and Adverse Outcomes

Studies have demonstrated that non or reverse dipping [18-23] and nocturnal HT [11, 12] are associated with diabetic complications and adverse cardiovascular outcomes. Fogari *et al.* demonstrated that non-dipping was independently associated with microalbuminuria [24]. This was also confirmed by Knudsen *et al.* in a prospective cohort study in a sample of 112 type 2 diabetics [25]. De la Sierra *et al.* found that non-dipping had a significant association with impaired renal function and cardiovascular disease [20]. The association between elevated nocturnal systolic BP and microalbuminuria has also been demonstrated in both cross sectional [26] and longitudinal studies [27]. For example, Draman *et al.* in a prospective cohort study demonstrated that nocturnal BP predicted cardiovascular mortality independent of mean daytime and 24-hour BP [11].

Although both non-dipping and nocturnal HT, particularly systolic HT, have been associated with adverse outcomes, the overall evidence appears to suggest that, compared with non-dipping, nocturnal systolic HT is a stronger and more sensitive predictor of organ damage and adverse cardiovascular outcomes [11, 12, 28]. This is further underpinned by those studies that failed to demonstrate any association between non-dipping and adverse outcomes [16]. The findings of the present study also appear to support this concept, as only nocturnal systolic HT, and not non-dipping, was found to be associated with microvascular complications. However, this needs to be interpreted in the context of the small sample size.

5.3. Masked and White Coat Phenomena

The prevalence of masked HT and white coat HT in type 2 diabetes has been variably reported. Overall, however, compared with white coat HT, masked HT or masked uncontrolled HT appears more prevalent in type 2 diabetes and has been associated with end organ damage and adverse cardiovascular outcomes [29]. The prevalence of masked hypertension in patients with diabetes has been quoted between 25 and 47% [29] and the overall prevalence of 29% found in this study is largely consistent with the literature [30, 31]. However, in the sub group of patients without a known history of hypertension the observed prevalence of 54% MH would be considered high and is out keeping with the current literature. But this is probably explained by the small sample size of 13 patients and by the fact that we used all three ABP measurement periods, i.e. ambulatory day, night, and 24-hour periods, to define masked phenomenon in this study, unlike most previous studies that used only the daytime ABP period [30, 31]. In fact, if had used only the daytime ABP to define MH the prevalence would have been 38%. As one would expect, the studies that used all three ambulatory blood pressure measurement periods to define MH have generally reported higher prevalence rates of masked phenomenon. This was eloquently demonstrated in the Jackson Heart Study by Booth *et al.* [32], who reported a prevalence of 44.1% when all three ambulatory BP periods were used to define MH as compared with 22.1% when only the daytime ABP period was used.

As with the ABP periods, the office BP threshold used for defining masked phenomenon is also likely to influence the prevalence of masked phenomenon. For example, had we used the office BP threshold of 130/80, the office BP cut point that is commonly used in clinical practice for patients with diabetic nephropathy, the study would have estimated a lower prevalence of masked phenomenon, but at the same time would have estimated a higher prevalence of white coat hypertension/white coat effect (results not shown). Unlike other studies we did not find any significant association between masked phenomenon and diabetic complications, but this could be due to the limited statistical power of the study.

5.4. Alignment of BP Control between Office and Ambulatory BP

The findings suggest that the sensitivity and specificity and positive and negative predictive values of the office BP for either diagnosing HT or assessing blood pressure control were only modest regardless of the mean ABP measurement period, *i.e.* mean 24-hr or mean daytime, used as the gold standard. While this is consistent with the findings of Masding *et al.* [33] and Hodgkinson *et al.* [34], it contradicts the results of Strachan *et al.*, who reported a good correlation between office BP and ABPM [35]. The reasons for this discrepancy are not entirely clear but may be in part due to the varying prevalence of masked and white coat phenomena in these studies.

The study observed that the mean 24-hour systolic ABP measurements between those with and without a known history of HT were very similar. While this may be explained by the high prevalence of masked phenomenon and nocturnal hypertension seen in this sample, this could be a chance finding in view of the small sample size.

6. LIMITATION

The results of this study should be interpreted within the context of some potential weaknesses. The study has limited statistical power in view of the small sample size. There was no control group; therefore, the prevalence of abnormal ABP patterns in diabetes in relation to the normal population or patients with essential HT could not be determined. Although microvascular complications were formally assessed, this was not the case with macrovascular complications; therefore, cases could have been potentially misclassified. Patients were also not screened for secondary causes of HT. However, the study was conducted under real world clinical setting and the assessment of macrovascular complications and causes of HT was consistent with routine clinical practice. Given the cross-sectional design, it is also not possible to establish a cause and effect association between nocturnal HT and microvascular complications. The study also did not formally assess the practicalities of providing ABPM as part of the routine care for patients with type 2 diabetes or whether the findings resulted in management changes.

CONCLUSION

Despite these limitations, the study provides confirmatory information on the prevalence of abnormal ABP patterns and the limitations of the office BP for either diagnos-

ing HT or assessing BP control in patients with type 2 diabetes. Although the results of this study are not novel, the overall findings suggest that 24-hour ABP monitoring in patients with type 2 diabetes may be a useful diagnostic procedure regardless of the BP control assessed on the basis of office BP and provide further evidence for the clinical utility of ABPM in type 2 diabetes.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

The study was approved by the Eastern Health Research Ethics Committee, Australia.

HUMAN AND ANIMAL RIGHTS

No animal were used in this research. All humans research procedures followed were in accordance with the standards set forth in the Declaration of Helsinki <https://www.wma.net/policiespost/wma-declaration-of-helsinki-ethicalprinciples-for-medical-research-involving-human-subjects/>principles of 1975, as revised in 2008 (http://www.wma.net/en/20activities/10ethics/10helsinki/).

CONSENT FOR PUBLICATION

All participants gave an Informed consent for the study.

FUNDING

CONFLICT OF INTEREST

The authors declare no conflict of interest, financial or otherwise.

ACKNOWLEDGEMENTS

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