Discrepancy Between Tonometric Ambulatory and Cuff-Based Office Blood Pressure Measurements in Patients With Type 1 Diabetes

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The aim of the current study was to compare ambulatory blood pressure (ABP) with office blood pressure (OBP) in diagnosing hypertension (HTN) in type 1 diabetes. The cross-sectional study included 569 type 1 diabetes patients, with a mean±standard deviation (SD) age of 55±13 years and diabetes duration of 33±16 years, and 315 (55%) men. Blood pressure ≥130/80 mm Hg defined HTN. ABP was measured by tonometry and OBP by sphygmomanometry. Elevated ABP with normal OBP defined masked uncontrolled HTN, and normal ABP with elevated OBP defined isolated uncontrolled clinic HTN. Mean±SD 24-hour ABP, daytime ABP, and OBP was 128±16/75±10 mm Hg, 133±16/77±11 mm Hg, and 136±14/76±8 mm Hg, respectively ($P<.001$). With 24-hour and daytime ABP, HTN was present in 256 (45%) and 304 (53%) patients; normal BP in 102 (18%) and 88 (15%) patients; isolated uncontrolled clinic HTN in 154 (27%) and 104 (%) patients; and masked uncontrolled HTN in 57 (10%) and 73 (13%) patients. Twenty-four–hour ABP and OBP showed disagreement in diagnosing HTN in 211 (37%) patients. Daytime ABP and OBP disagreed in 177 (31%) patients. HTN by 24-hour and daytime ABP was present in 313 (55%) and 377 (66%) patients. ABP measurements were well-tolerated and successful in 98%. A total of 92% would volunteer for repeat measurements and 83% preferred the tonometry to conventional cuff-based devices. In patients with type 1 diabetes, tonometric ABP measurements are feasible. ABP and OBP disagree in diagnosing HTN in 31% to 37% of patients. Furthermore, 55% to 66% of patients do not reach target BP of <130/80 mm Hg despite regular follow-up. *J Clin Hypertens (Greenwich)*. 2012;00:00–00. ©2012 Wiley Periodicals, Inc.

In diabetes, hypertension (HTN) significantly increases the risk of developing microvascular and macrovascular complications.[1–4] In contrast, blood pressure (BP) control significantly prevents or delays complications.[4,5] An office BP (OBP) ≥130/80 mm Hg defines HTN in diabetes,[6] while a specific cut-off BP for diagnosing HTN based on ambulatory BP (ABP) measurements is less clear and is therefore yet to be determined.

Thus, HTN is often solely diagnosed by OBP rather than ABP, despite ABP being superior to OBP in predicting risk of adverse outcome.[7,8] Part of the reason for refraining from using ABP more frequently in HTN diagnostics most likely has to do with ABP being more cumbersome and costly. Routine ABP measurements are required to diagnose isolated uncontrolled clinic HTN or masked HTN. Isolated uncontrolled clinic HTN is present in patients with elevated OBP and normal ABP, whereas masked HTN is present in patients with normal OBP and elevated ABP. Both isolated uncontrolled clinic HTN and masked HTN are frequently seen in diabetes.[9,10] Little is known about long-term risk of isolated uncontrolled clinic HTN, but it probably does not carry an increased risk of adverse outcome.[11,12] However, masked HTN is associated with increased end organ damage and adverse cardiovascular disease (CVD) outcome.[8,13–15] Usually BP is measured with a sphygmomanometric device consisting of an inflatable cuff intended to occlude blood flow and a manometer for measuring pressure.[16] During the past 3 decades, arterial tonometry has emerged as an alternative method of BP measuring.[17] Pulse wave configurations at the site of a peripheral artery are recorded by a small sensor and converted into BP readings based on specific transfer functions,[18] without requiring a cuff. Tonometry has proved valuable in risk prediction in various populations, as it provides information on various parameters of arterial stiffness along with specific BP measurements.[19]

In this study, we compare tonometric ABP with clinic OBP based on repeated measurements in the outpatient clinic in patients with type 1 diabetes in order to clarify the association between the two methods of BP measurement. We evaluate the concordance in diagnosing hypertension in patients with type 1 diabetes overall and according to kidney function. Furthermore, we investigate patient satisfaction with tonometric ABP and whether it offers a feasible and patient-oriented alternative to cuff-based ABP measurement.

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METHODS

Patients

From September 2009 until June 2011, Caucasian patients with type 1 diabetes who attended the

outpatient clinic at the Steno Diabetes Center were invited to enter a cross-sectional study (the Profil study) investigating the association between BP and diabetic complications. A total of 1285 patients were invited to participate in the study, of which 676 gave informed consent. In addition, a control group of 51 nondiabetic patients were included in the Profil study.

Mean 24-hour and daytime ABP was compared with mean OBP, as OBP serves as a clinical relevant measure on which regulation of antihypertensive treatment (AHT) is often based.

The ABP data were adequate if $\geq$14 BP recordings were obtained during the day and $\geq$7 BP recordings were obtained during nighttime, according to present guidelines.[20] Mean OBP was calculated as the average of three measurements from separate visits within 1 year prior to ABP.

Of the 676 patients, 660 patients had adequate ABP readings, while 16 patients had insufficient ABP recordings according to guidelines.[20] A total of 581 patients had a minimum of three separate OBP measurements within 1 year prior to ABP measurement, while 95 patients had insufficient measurements available as a result of either infrequent follow-up visits or because they were newly referred for treatment at the Steno Diabetes Center and therefore did not have a past medical record of 1 year. Thus, in total, 569 patients had both sufficient ABP and OBP measurements available for comparison.

Baseline Clinical and Laboratory Methods

All 569 patients were followed at the Steno Diabetes Center in Denmark. ABP was recorded with a tonometric watch-like device, 24-hour BPro HealthStats (BPro; Healthstats, Singapore), which captures the radial pulse wave reflection and thereby calculates ambulatory brachial BP. The BPro has been previously validated and meets European Society of Hypertension and Advancing Safety in Medical Technology standards.[21,22] The BPro device records BP every 15 minutes during a 24-hour period. Daytime ABP was defined as the time interval from 7 AM to 11 PM, while nighttime ABP was from 11 PM to 7 AM. In the current study, the BPro device was calibrated with an oscillometric device (A&D Medical; UA 787)[23] prior to BP measurement.

OBP was measured twice in sitting position after 10 minutes rest during regular clinical visits with an oscillometric device (A&D Medical; UA787 or UA852, Tokyo, Japan)[24] or a mercury sphygmomanometer (Riester Empire, Jungingen, Germany).

Masked uncontrolled HTN was defined as normal OBP and elevated ABP, whereas isolated uncontrolled clinic HTN was defined as elevated OBP and normal ABP. The definitions "masked uncontrolled" and "isolated uncontrolled" clinic HTN were used, as some but not all patients received AHT. HTN by OBP, 24-hour ABP, and daytime ABP was defined by values $\geq$130/80 mm Hg.[6]

All patients had blood samples and demographic data collected. Hemoglobin A_{1c} (HbA_{1c}) was measured by high-performance liquid chromatography (normal range, 4.1%–6.4%; 21–46 mmol/mol [Tosoh G7; Tosoh Bioscience, Grove City, OH]), urinary albumin excretion rate (UAER) was measured in two 24-hour urine samples by enzyme immunoassay, and serum creatinine was measured by an enzymatic method (Hitachi 912; Roche Diagnostics, Penzberg, Germany).

Patients were stratified as normoalbuminuric if they had persistent normoalbuminuria with UAER $<$30 mg/24-hour or microalbuminuric or macroalbuminuric if UAER was between 30 and 300 mg/24 hours or $>$300 mg/24 hours, respectively, in 2 of 3 consecutive measurements in the absence of other kidney or urinary disease. Glomerular filtration rate (GFR) was measured annually in patients with macroalbuminuria as plasma clearance after a single injection of ^{51}Cr-EDTA[25] with a mean day-to-day coefficient of variation of 4% in our laboratory. Estimated GFR (eGFR) was calculated by the 4-variable Modification of Diet in Renal Disease formula.[26] Patients with end-stage renal disease, defined as dialysis or renal transplantation, or a GFR/eGFR $<$15 mL/min/1.73 m^2 were excluded from entering the study.

Of the 676 patients, 659 patients had sinus rhythm, 13 patients had atrial fibrillation or atrial flutter, 1 patient had second-degree atrioventricular block Mobitz 1 (2AV1), and 3 patients had pacemaker rhythm. In only 1 of 17 patients without sinus rhythm did ABP measuring fail. Because ABP measurements in patients with atrial fibrillation and in patients with pacemaker rhythm are reliable,[27,28] and BP measuring in patients with 2AV1 is likely to be reliable as well, no patients were excluded from the analysis based on cardiac rhythm.

Based on standardized questionnaires, patients who smoked $\geq$1 cigarettes/cigars/pipes per day were classified as smokers and all others as nonsmokers. Previous CVD events were myocardial infarction, coronary revascularization, stroke, or peripheral vascular disease.

The Profil study conformed to the Declaration of Helsinki, was approved by the Danish National Committee on Biomedical Research Ethics (2009-056), and all patients gave written informed consent.

Statistical Analysis

Normally distributed variables are given as mean$\pm$standard deviations (SDs), whereas non-normally distributed variables are given as median (range) and $\log_{10}$ transformed before analysis. We compared 24-hour ABP and daytime ABP with mean OBP and mean OBP with last-obtained OBP in patients entering the study. Comparisons between BPs were performed by an unpaired Student *t*-test, analysis of variance, or linear regression correlation. Subsequently, we compared 24-hour ABP and daytime ABP with OBP in

diagnosing HTN, using a cut-off BP of ≥130/80 mm Hg. Chi-square test was used to compare noncontinuous variables. A two-tailed *P*-value ≤.05 was considered statistically significant. All calculations were performed using commercially available SPSS 15.0 for Windows (SPSS Inc, Chicago, IL).

RESULTS

Baseline

Of the 676 patients included, 569 (84%) had adequate ABP and OBP available, while 105 patients had inadequate ABP and/or OBP measurements available (16 patients had incomplete ABP, 95 patients had incomplete OBP, and 4 patients had neither ABP nor OBP available). In the 95 patients without an available OBP, the systolic 24-hour ABP was similar and the diastolic 24-hour ABP was higher compared with patients with available OBP (130±16/79±12 mm Hg vs 128±16/75±10 mm Hg; *P*=.22 and *P*<.001, respectively). Daytime systolic ABP was similar, while diastolic daytime ABP was lower in patients with available OBP vs without 133±16/77±11 mm Hg vs 135±17/82±13 mm Hg (*P*=.09 and *P*<.001, respectively).

Mean OBP in the 569 participating patients was similar to mean OBP in the 609 nonparticipating patients, suggestive of similar BP control in the two groups (data not shown).

Baseline characteristics of the 569 patients are shown in Table I. The patients included were 55±13 years of age, with 33±16 years' duration of diabetes, and 315 (55%) were men. Overall, 254 (45%), 152 (27%), and 163 (29%) had normoalbuminuria, microalbuminuria, and macroalbuminuria, respectively. Renal function was generally well preserved, as mean GFR in patients with macroalbuminuria was 69±13 mL/min/1.73 m^2 and a mean eGFR in all patients was 82±28 mL/min/1.73 m^2. AHT was prescribed to 418 (74%) patients, and 389 (68%) received medications that block the renin angiotensin aldosterone system.

Blood Pressure

24-Hour ABP. Of the 676 patients included in the study, 660 (98%) had adequate 24-hour ABP measurements. Mean 24-hour ABP, daytime ABP, and nighttime ABP was 128±16/75±10 mm Hg; 133±16/77±11 mm Hg, and 120±16/70±11 mm Hg, respectively.

Increasing albuminuria was associated with increasing BP; however, the 3 albuminuria groups had an overall mean ABP within 5 mm Hg of each other. This was partly achieved by AHT, as 48%, 90%, and 98% of patients received AHT in the normoalbuminuric, microalbuminuric, and macroalbuminuric groups, respectively (Table I).

Regarding the prevalence of different levels of BP, systolic 24-hour and daytime ABP was <130 mm Hg in 354 (54%) and 235 (43%); 130 mm Hg to 139 mm Hg in 159 (24%) and 160 (28%); 140 mm Hg to 149 mm Hg in 85 (13%) and 95 (17%); 150 mm Hg to 159 mm Hg in 48 (7%) and 52 (9%); and ≥160 mm Hg in 14 (2%) and 27 (5%) patients. Diastolic 24-hour and daytime ABP was <80 mm Hg in 437 (66%) and 330 (58%); 80 mm Hg to 89 mm Hg in 170 (26%) and 172 (30%); 90 mm Hg to 99 mm Hg in 42 (6%) and 54 (10%); and 100 mm Hg to 109 mm Hg in 11 (2%) and 12 (2%), while none and 1 patients had a diastolic BP >110 mm Hg (Figure 1a-d). Thus, only 14 (2%) patients had a 24-hour systolic ABP ≥160 mm Hg, all but one of these had systolic daytime ABP >150 mm Hg, and of these only one did not receive AHT. The mean number of different AHTs prescribed in maximal recommended dose was 2.4±1.7 among the 14 patients. Thirteen of the patients did attend regular follow-up, and 12 had sustained HTN based on both OBP and ABP.

Office BP. Mean OBP in the 569 patients was 136±14/76±8 mm Hg. Dividing patients according to albuminuria revealed SBP to be significantly higher among macroalbuminuric patients compared with normoalbuminuric patients, who had the lowest systolic BP (SBP) (*P*=.006). Diastolic BP (DBP) was highest in normoalbuminuric patients (*P*=.007) and similar in microalbuminuric and macroalbuminuric patients (*P*>.05) (Table I). An elevated OBP was present in 72% of patients, independent of albuminuria status (*P*>.05) (Table II).

Mean OBP was used as a frame of reference despite knowing OBP to be dynamic and dependent on alterations in lifestyle, health, and medication, all of which we did not adjust for in our study. In order to visualize whether mean OBP was a stable measure of OBP, we compared mean OBP with the last OBP prior to ABP. Mean OBP was similar to last OBP 136±14/76±8 mm Hg vs 136±17/75±10 mm Hg (*P*=.739 and .059) and was therefore regarded to be suited for comparison with ABP.

24-Hour ABP vs OBP. Among the 569 patients with both 24-hour ABP and OBP measurements available, ABP was lower than mean OBP, 128±16/75±10 mm Hg vs 136±14/76±8 mm Hg (*P*<.001 for both SBP and DBP) (Table I), with a mean difference in SBP and DBP of 7.8±16.0 mm Hg and 0.9±9.0 mm Hg, respectively. Correlations for SBP and DBP were *r*=0.42 and *r*=0.53 (*P*<.001 for both). Comparing 24-hour ABP with last OBP of 136±17/75±10 mm Hg revealed correlations of *r*=0.40 and *r*=0.45 for SBP and DBP, respectively (*P*<.001 for both).

When dividing the patients according to either normal OBP or elevated OBP ≥130/80 mm Hg, similar correlations for SBP and DBP (*r*=0.32 and *r*=0.26 vs *r*=0.55 and *r*=0.38; *P*<.005 for all) were found.

TABLE I. Baseline Characteristics for 569 Patients With Valid ABP and OBP Included in the Study

	Normoalbuminuria	Microalbuminuria	Macroalbuminuria	All Patients	*P* Value
Sex, %	51/49	61/39	58/42	55/45	.126
Age, y	53±14	58±12	55±11	55±13	<.001
Hemoglobin A_{1c}, %	7.8±1.1	8.1±1.0	8.4±1.3	8.0±1.1	<.001
Hemoglobin A_{1c}, mmol/mol	62±12	65±11	68±14	64±12	<.001
Total cholesterol, mmol/L	4.8±0.8	4.7±0.9	4.6±1.0	4.7±0.9	.263
Duration of diabetes, y	27±18	36±15	39±12	33±16	<.001
AHT, %	48	90	98	74	<.001
AHT, No.	0 (0–3.8)	1.8 (0–5.2)	2 (0–4.8)	1.2 (0–5.2)	<.001
RAAS inhibition, %	44	83	93	68	<.001
Smoking, %	16	16	21	17	.515
Previous CVD, %[a]	11	30	29	21	<.001
BMI, kg/m^2	24.8±3.5	25.9±4.2	25.8±4.7	25.4±4.1	.009
Creatinine, μmol/L	74±15	87±43	120±60	91±45	<.001
UAER, mg/24-hour[b]	8 (2–39)	33 (4–4512)	129 (4–8271)	18 (2–8271)	<.001
eGFR, mL/min/1.73 m^2	93±21	83±26	65±30	82±28	<.001
Mean OBP SBP, mm Hg	134±14	139±15	137±15	136±14	.007
Mean OBP DBP, mm Hg	77±8	75±8	75±9	76±8	.006
Last OBP SBP, mm Hg	134±16	139±18	137±18	136±17	.047
Last OBP DBP, mm Hg	76±9	75±10	74±10	75±10	.026
Calibration SBP, mm Hg	129±16	134±18	134±18	132±17	.003
Calibration DBP, mm Hg	75±9	73±9	74±10	74±9	.078
24-Hour ABP SBP, mm Hg	128±15	128±18	130±15	128±16	.122
24-Hour ABP DBP, mm Hg	76±10	73±10	75±15	75±10	.001
Day ABP SBP, mm Hg	132±15	131±19	134±14	133±16	.185
Day ABP DBP, mm Hg	79±10	75±10	77±10	77±11	.001
Night ABP SBP, mm Hg	119±15	119±18	124±16	120±16	.007
Night ABP DBP, mm Hg	71±12	68±10	71±12	70±11	.041

Abbreviations: ABP, ambulatory blood pressure; BMI, body mass index; DBP, diastolic blood pressure; GFR, glomerular filtration rate; OBP, office blood pressure; RAAS, renin-angiotensin-aldosterone system; SBP, systolic blood pressure; UAER, urinary albumin excretion. Data are number (percentage), mean±standard deviation, or median (range). [a]Previous cardiovascular disease (CVD) events were myocardial infarction, coronary revascularization, stroke, or peripheral vascular disease. [b]Some patients with previously persistent microalbuminuria or macroalbuminuria receiving antihypertensive treatment (AHT) had values <30 mg/24-hour at the time of investigation.

Hypertension Diagnosis by 24-Hour ABP vs OBP. Office HTN (≥130/80 mm Hg) was present in 409 (72%) patients, of which 256 (45%) also had ABP HTN and 153 (27%) had isolated uncontrolled clinic HTN. Normal BP by ABP and OBP was present in 103 (18%) patients, while 57 (10%) had masked uncontrolled HTN.

We divided the patients according to sex and albuminuria. Neither sex nor albuminuria status influenced agreement between devices (*P*=.473 and *P*=.085) (Table II and Figure 2).

Since a BP ≥140/90 mm Hg is the limit for HTN in nondiabetic patients, and until recently also has been the limit of HTN in patients with diabetes, we investigated how many patients reached a BP <140/90 mm Hg. Overall, 432 (76%) had a 24-hour ABP <140/90 mm Hg. When analyzing both ABP and OBP, 79 (14%) had sustained HTN, 137 (24%) had isolated uncontrolled clinic HTN, 56 (10%) had masked uncontrolled HTN, and 297 (52%) had normal levels of both ABP and OBP.

Daytime ABP vs OBP. In the 569 patients with available ABP and OBP, daytime ABP and OBP were 133±16/77±11 mm Hg and 136±14/76±8 mm Hg (*P*<.001 for both) (Table I), with mean differences in SBP and DBP of 3.5±16.0 and −1.8±9.2, respectively. Correlations between OBP and daytime ABP SBP and DBP were *r*=0.44 and *r*=0.55, respectively (*P*<.001 for both).

Comparison of daytime ABP with last OBP revealed correlations of *r*=0.39 and *r*=0.46 for SBP and DBP, respectively (*P*<.001 for both).

Hypertension Diagnosis by Daytime ABP vs OBP. Of the 409 (72%) patients with office HTN (≥130/80 mm Hg), 304 (53%) also had daytime ABP HTN, 104 (18%) had isolated uncontrolled clinic HTN, 88 (15%) had normal BP, and 73 (13%) had masked uncontrolled HTN (Table II and Figure 2).

If defining HTN by a BP ≥140/90 mm Hg for both daytime ABP and OBP, then 191 (34%) patients had a daytime ABP HTN, 107 (19%) had sustained HTN, 109 (19%) had isolated uncontrolled clinic HTN, 84 (15%) had masked uncontrolled HTN, and 269 (47%) had normal levels of both daytime ABP and OBP.

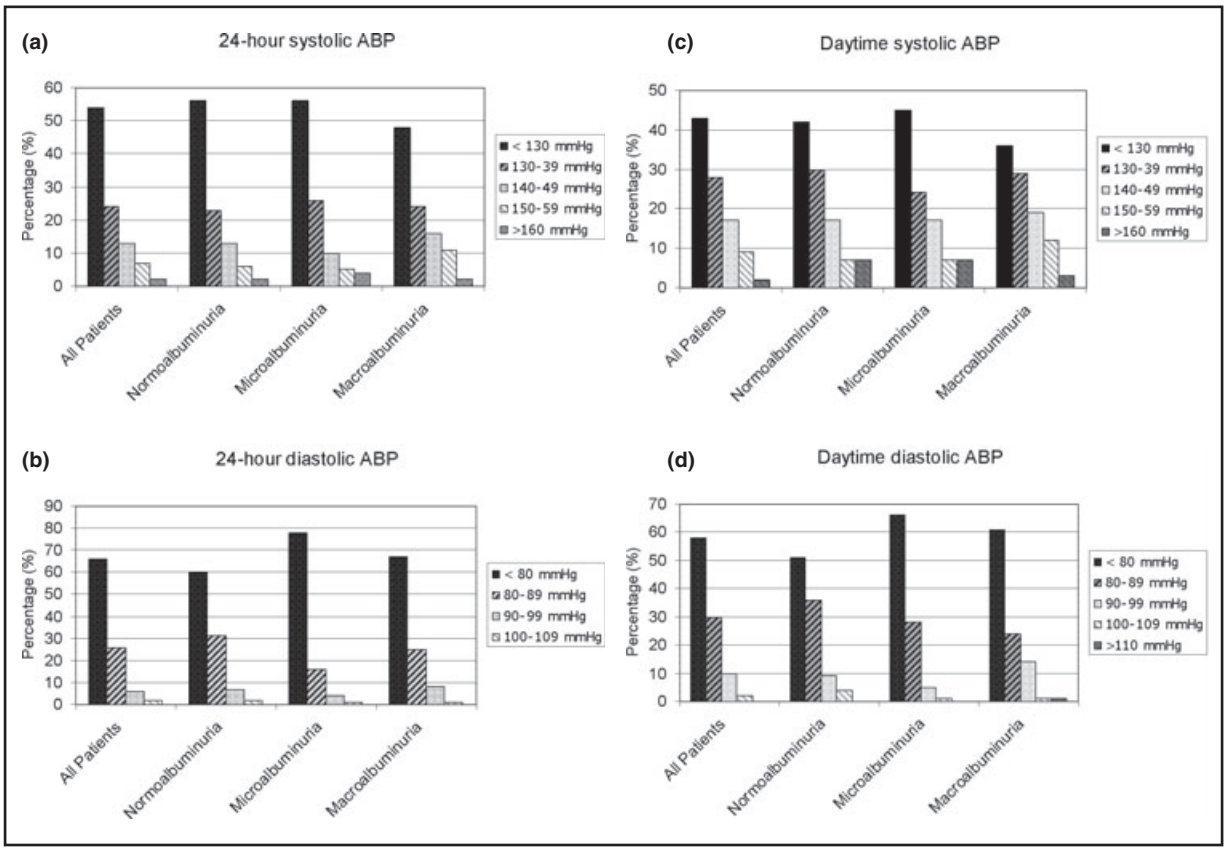

FIGURE 1. (a–d) Barplots showing the distribution of 24-hour and daytime ambulatory blood pressure (AMBP) levels in all patients and according to albuminuria status.

Patient Satisfaction. Of the 727 participants (patients and controls) entering the study, 711 (98%) had a valid 24-hour ABP measurement performed. Patients and controls were asked to enter a satisfaction survey, and 644 (89%) answered all or some of the queries in the survey. Of 617 responders, 568 (92%) agreed to repeat the ABP with the BPro device if necessary. Only 261 patients had undergone ABP measuring with a cuff-based device in the past. Among these, 217 (83%) preferred the BPro to a cuff-based device. Among 49 patients who did not want to repeat ABP with the tonometric device, 36 (73%) had never tried a cuff-based device. Patients and controls were asked to grade their discomfort with the BPro device. Of the 638 patients who graded their discomfort, 378 (59%) experienced little discomfort, 176 (28%) experienced some discomfort, and 84 (13%) complained of significant discomfort.

DISCUSSION

In this observational study that included a representative cohort of 569 patients with type 1 diabetes, we investigated the association between ABP measured with a wristwatch-like tonometer and OBP measured with sphygmomanometry. We found a relatively poor association between 1 year average of both clinic-measured OBP vs 24-hour ABP and clinic-measured OBP vs daytime ABP. The level of OBP was not influential on the correlations between ABP and OBP. Mean 24-hour and daytime ABP was significantly lower than mean OBP. Overall, 31% to 37% of patients were misdiagnosed by OBP as compared with daytime and 24-hour ABP, respectively.

Our results, in accordance with others, show that OBP is inadequate in diagnosing HTN in a substantial number of patients.[9,10,29] The degree of disagreement between ABP and OBP was independent of sex and albuminuria status.

ABP is still only performed infrequently. This may to some extent be due to ABP being more cumbersome to perform as well as more expensive. More patient-friendly ways to measure ABP, such as the tonometric technique tested in this study, should therefore be evaluated. Leitão and colleagues recently suggested that patients with diabetes and an OBP $>120/70$ mm Hg should undergo ABP measurement.[33] Based on our results, more or maybe even all patients with diabetes should undergo ABP as part of BP determination, as

TABLE II. Agreement in Hypertension Diagnosis Between Mean 24-Hour ABP and Mean OBP and Between Mean Daytime ABP and Mean OBP for 569 Patients

	All Patients (N=569)	Normoalbuminuria (n=254)	Microalbuminuria (n=152)	Macroalbuminuria (n=163)
24-Hour ABP				
Sustained hypertension, No. (%)	256 (45)	116 (46)	63 (41)	77 (47)
Isolated clinic hypertension, No. (%)	154 (27)	58 (23)	55 (36)	40 (25)
Masked hypertension, No. (%)	57 (10)	28 (11)	10 (7)	19 (12)
Normal blood pressure, No. (%)	102 (18)	52 (21)	24 (16)	27 (17)
Concordance between ABP and OBP, No. (%)	358 (63)	168 (66)	87 (57)	104 (64)
Daytime ABP				
Sustained hypertension, No. (%)	304 (53)	136 (53)	79 (52)	89 (55)
Isolated clinic hypertension, No. (%)	104 (18)	38 (15)	39 (26)	27 (17)
Masked hypertension, No. (%)	73 (13)	36 (14)	14 (9)	23 (14)
Normal blood pressure, No. (%)	88 (15)	45 (18)	20 (13)	23 (14)
Concordance between ABP and OBP, No. (%)	392 (69)	181 (71)	99 (65)	112 (69)

Abbreviation: OBP, office blood pressure. The agreement in diagnosis of hypertension was similar between albuminuria groups for 24-hour ambulatory blood pressure (ABP) or daytime ABP (*P*=.085 and .122).

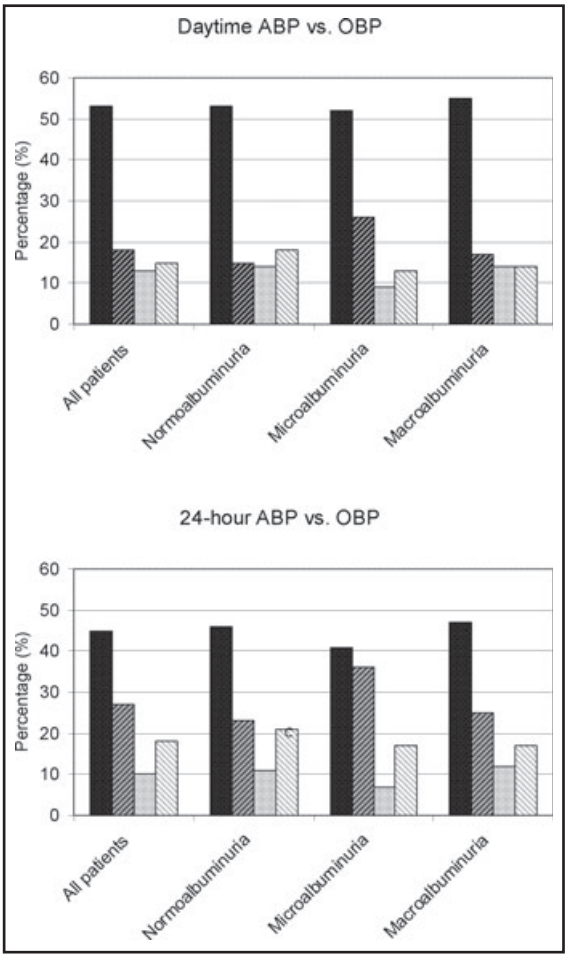

FIGURE 2. Barplot showing the distribution of sustained, isolated uncontrolled clinic and masked uncontrolled hypertension and normal blood pressure in 569 patients. Distribution of blood pressures is similar between albuminuria groups (*P*=.122 for daytime ambulatory blood pressure [AMBP] and *P*=.085 for 24-hour ABP). OBP indicates office blood pressure.

we found marked disagreement between ABP and OBP regardless of the BP level. This is in accordance with the latest National Institute for Health and Clinical Excellence (NICE) guidelines, in which ABP is recommended for patients suspected of HTN based on repeated OBP measurements.[34] This may even be economically substantiated, as a recent paper by Lovibond and colleagues[35] showed ABP to be more cost-effective in HTN diagnostics in the general population compared with OBP.

Furthermore, ABP provides information on circadian BP including nocturnal BP, which has been shown to predict development of microalbuminuria in patients with type 1 diabetes[30,31] and mortality in type 2 diabetes.[32] Treatment of nocturnal hypertension may be important and has been shown to reduce CVD mortality and morbidity in patients with type 2 diabetes.[36]

In our study, ABP recordings with radial artery tonometry were successful in 98% of cases and overall well tolerated by patients, wherein 92% of patients found the discomfort associated with tonometric ABP measurements as acceptable and 83% found tonometric ABP preferable to cuff-based measurements.

Tonometry based on pulse wave features enables not only measurements of various BPs including brachial BP and central aortic BP (CASP) but also enables measures of arterial stiffness such as pulse wave velocity and aortic stiffness index. Measures of arterial stiffness are useful as indices of vascular health and as risk predictors for outcome.[37] The efficacy of AHT may not solely be evaluated based on brachial BP but also on measures of arterial stiffness, particularly because brachial arterial BP is an inferior risk marker of CVD outcome as compared with markers of arterial stiffness.[37] Since patients with diabetes have increased arterial stiffness,[38] measuring indices of arterial stiffness such as pulse wave velocity, augmentation index, and CASP rather than brachial BP may prove to be

not only a better risk marker, but also a better target for monitoring BP control.

Clearly, the target BP of <130/80 mm Hg was not reached in half of the patients, despite regular follow-up and the fact that 74% of the patients received AHT. On the other hand, 66% to 76% of patients had a BP <140/90 mm Hg and only 2% to 5% of patients had an SBP ≥160 mm Hg. In hypertensive type 2 diabetic patients, the UK Prospective Diabetes Study (UKPDS) study showed that a BP reduction from 154/87 mm Hg to 144/82 mm Hg was associated with a significant risk reduction of diabetic complications.[4] Also, for type 2 diabetic patients, the Action in Diabetes and Vascular Disease: Preterax and Diamicron Modified Release Controlled Evaluation (ADVANCE) study showed a reduction in OBP to 135/75 mm Hg, which is similar to the level in our patients, to significantly reduce CVD mortality and renal events.[39] Furthermore, in the Action to Control Cardiovascular Risk in Diabetes (ACCORD) trial, hypertensive type 2 diabetic patients were randomized to either intensive or standard BP treatment, reaching a mean SBP of 119 mm Hg and 134 mm Hg, respectively, after 1 year of treatment. Despite significant differences in SBP, there was no difference in combined CVD end points after a median follow-up of 4.7 years.[40] There was, however, a significant reduction in stroke and progression of albuminuria. It is possible that BP reduction to <130/80 mm Hg is beneficial in patients with diabetes but without CVD complications, whereas it may be harmful in patients with CVD. This is supported by findings from Mancia and colleagues, where it was concluded that data advocating a lower treatment target (<130/80 mm Hg) for patients with diabetes is lacking.

The studies conducted so far on BP control in patients with diabetes have predominantly included patients with type 2 diabetes. No larger studies on target BP in type 1 diabetic patients with or without complications have been carried out. It is therefore possible that existing data from clinical trials regarding treatment targets for BP control in patients with type 1 diabetes are insufficient.

Another important issue further elucidated by our study is the discrepancy between ABP and OBP.[7,8] Since most of the major studies on BP control in diabetes have utilized OBP rather than ABP, these BP measures may be inaccurate. Thus, future studies on ABP in patients with diabetes are needed and indices of arterial stiffness need investigation for the purpose of improving risk prediction and treatment targeting. BP measurements with tonometry proved feasible in our cohort and could serve as the way of obtaining ABP in future studies.

STUDY STRENGTHS AND LIMITATIONS

Patients enrolled in the study were recruited from a pool of approximately 3500 patients with type 1 diabetes attending the outpatient clinic at the Steno Diabetes Center. Thus, almost 20% of patients followed at the Steno Diabetes Center were investigated, representing a broad segment of the Steno population. However, in order to ensure a broad spectrum of albuminuria, we sought to include a substantial number of patients with impaired kidney function. Thus, patients with kidney impairment (microalbuminuria and macroalbuminuria) were overrepresented. ABP was done with tonometry while OBP was performed with automatic oscillometric or auscultatoric devices. We have previously shown that tonometry measurements by BPro correlates well with the sphygmomanometric devices used at the Steno Diabetes Center in diabetic patients.[22]

ABP was compared with the mean value of 3 OBPs, as the OBP serves as a clinically relevant measure on which regulation of AHT is often based. It has not been possible to include changes in medication over time or changes in lifestyle in our analysis. However, comparing mean OBP with last OBP prior to the ABP measurement showed similar values, suggesting that changes in medication and lifestyle did not explain the differences between ABP and OBP. OBP measurements were obtained retrospectively from medical records, rather than prospectively in connection with the study. We did not repeat ABP measurements, but we have previously demonstrated that ABP measurements with tonometry are reproducible.[22]

CONCLUSIONS

In this cohort of patients with type 1 diabetes, tonometric ABP measurement was well tolerated and successful in the majority of patients. The measurements revealed a low correlation between ABP and OBP. In total, 55% to 66% of patients did not reach target BP of <130/80 mm Hg despite regular follow-up, and in 31% to 37% of patients, OBP and ABP disagreed in the diagnosis of HTN. Thus, routine ABP measurements should be considered in the management of BP in patients with diabetes.

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References

1. Parving HH, Andersen AR, Smidt UM, et al. Diabetic nephropathy and arterial hypertension. *Diabetologia*. 1983;24:10–12.
2. Nielsen S, Schmitz A, Poulsen PL, et al. Albuminuria and 24-h ambulatory blood pressure in normoalbuminuric and microalbuminuric NIDDM patients. A longitudinal study. *Diabetes Care*. 1995;18:1434–1441.
3. Chen G, McAlister FA, Walker RL, et al. Cardiovascular outcomes in framingham participants with diabetes: the importance of blood pressure. *Hypertension*. 2011;57:891–897.
4. Tight blood pressure control and risk of macrovascular and microvascular complications in type 2 diabetes: UKPDS 38. UK Prospective Diabetes Study Group. *BMJ*. 1998;317:703–713.

5. Adler AI, Stratton IM, Neil HA, et al. Association of systolic blood pressure with macrovascular and microvascular complications of type 2 diabetes (UKPDS 36): prospective observational study. *BMJ*. 2000;321:412–419.
6. American Diabetes Association. Standards of medical care in diabetes–2012. *Diabetes Care*. 2012;35(suppl 1):S11–S63.
7. Dolan E, Stanton A, Thijs L, et al. Superiority of ambulatory over clinic blood pressure measurement in predicting mortality: the Dublin outcome study. *Hypertension*. 2005;46:156–161.
8. Ohkubo T, Kikuya M, Metoki H, et al. Prognosis of "masked" hypertension and "white-coat" hypertension detected by 24-h ambulatory blood pressure monitoring 10-year follow-up from the Ohasama study. *J Am Coll Cardiol*. 2005;46:508–515.
9. Rodrigues TC, Canani LH, Viatroski RS, et al. Masked hypertension, nocturnal blood pressure and retinopathy in normotensive patients with type 1 diabetes. *Diabetes Res Clin Pract*. 2010;87:240–245.
10. Ng CM, Yiu SF, Choi KL, et al. Prevalence and significance of white-coat hypertension and masked hypertension in type 2 diabetics. *Hong Kong Med J*. 2008;14:437–443.
11. Pierdomenico SD, Lapenna D, Di MR, Cuccurullo F. Short- and long-term risk of cardiovascular events in white-coat hypertension. *J Hum Hypertens*. 2008;22:408–414.
12. Bursztyn M, Ben-Dov IZ. White-coat hypertension should not be treated in subjects with diabetes. *Diabetes Care*. 2009;32(suppl 2):S310–S313.
13. Kotsis V, Stabouli S, Toumanidis S, et al. Target organ damage in "white coat hypertension" and "masked hypertension." *Am J Hypertens*. 2008;21:393–399.
14. Sega R, Trocino G, Lanzarotti A, et al. Alterations of cardiac structure in patients with isolated office, ambulatory, or home hypertension: data from the general population (Pressione Arteriose Monitorate E Loro Associazioni [PAMELA] Study). *Circulation*. 2001;104:1385–1392.
15. Ben-Dov IZ, Ben-Ishay D, Mekler J, et al. Increased prevalence of masked blood pressure elevations in treated diabetic subjects. *Arch Intern Med*. 2007;167:2139–2142.
16. Perloff D, Grim C, Flack J, et al. Human blood pressure determination by sphygmomanometry. *Circulation*. 1993;88(Pt 5):2460–2470.
17. Kelly R, Hayward C, Avolio A, O'Rourke M. Noninvasive determination of age-related changes in the human arterial pulse. *Circulation*. 1989;80:1652–1659.
18. Chen CH, Nevo E, Fetics B, et al. Estimation of central aortic pressure waveform by mathematical transformation of radial tonometry pressure. Validation of generalized transfer function. *Circulation*. 1997;95:1827–1836.
19. Wang KL, Cheng HM, Sung SH, et al. Wave reflection and arterial stiffness in the prediction of 15-year all-cause and cardiovascular mortalities: a community-based study. *Hypertension*. 2010;55:799–805.
20. O'Brien E, Asmar R, Beilin L, et al. European Society of Hypertension recommendations for conventional, ambulatory and home blood pressure measurement. *J Hypertens*. 2003;21:821–848.
21. Nair D, Tan SY, Gan HW, et al. The use of ambulatory tonometric radial arterial wave capture to measure ambulatory blood pressure: the validation of a novel wrist-bound device in adults. *J Hum Hypertens*. 2008;22:220–222.
22. Theilade S, Joergensen C, Persson F, et al. Ambulatory tonometric blood pressure measurements in patients with diabetes. *Diabetes Technol Ther*. 2012;14(6):453–456.
23. Longo D, Toffanin G, Garbelotto R, et al. Performance of the UA-787 oscillometric blood pressure monitor according to the European Society of Hypertension protocol. *Blood Press Monit*. 2003;8:91–95.
24. Bonso E, Ragazzo F, Palatini P. Validation of A&D UA-85X device for blood pressure measurement. *Blood Press Monit*. 2008;13:339–341.
25. Brochner-Mortensen J, Rodbro P. Selection of routine method for determination of glomerular filtration rate in adult patients. *Scand J Clin Lab Invest*. 1976;36:35–43.
26. Levey AS, Coresh J, Greene T, et al. Using standardized serum creatinine values in the modification of diet in renal disease study equation for estimating glomerular filtration rate. *Ann Intern Med*. 2006;145:247–254.
27. Almeida L, Amado P, Vasconcelos N, et al. [Is ambulatory blood pressure monitoring reliable in hypertensive patients with atrial fibrillation?]. *Rev Port Cardiol*. 2001;20:647–650.
28. Quaglione R, Calcagnini G, Censi F, et al. Effect of pacemaker rate-adaptation on 24 h beat-to-beat heart rate and blood pressure profiles. *Europace*. 2005;7:366–373.
29. Hodgkinson J, Mant J, Martin U, et al. Relative effectiveness of clinic and home blood pressure monitoring compared with ambulatory blood pressure monitoring in diagnosis of hypertension: systematic review. *BMJ*. 2011;342:d3621.
30. Lurbe E, Redon J, Kesani A, et al. Increase in nocturnal blood pressure and progression to microalbuminuria in type 1 diabetes. *N Engl J Med*. 2002;347:797–805.
31. Hansen KW, Poulsen PL, Mogensen CE. Ambulatory blood pressure and abnormal albuminuria in type 1 diabetic patients. *Kidney Int Suppl*. 1994;45:S134–S140.
32. Astrup AS, Nielsen FS, Rossing P, et al. Predictors of mortality in patients with type 2 diabetes with or without diabetic nephropathy: a follow-up study. *J Hypertens*. 2007;25:2479–2485.
33. Leitao CB, Rodrigues TC, Kramer CK, et al. Which patients with diabetes should undergo ambulatory blood pressure monitoring? *J Hypertens*. 2011;29:236–241.
34. Ritchie LD, Campbell NC, Murchie P. New NICE guidelines for hypertension. *BMJ*. 2011;343:d5644.
35. Lovibond K, Jowett S, Barton P, et al. Cost-effectiveness of options for the diagnosis of high blood pressure in primary care: a modelling study. *Lancet*. 2011;378:1219–1230.
36. Hermida RC, Ayala DE, Mojon A, Fernandez JR. Influence of time of day of blood pressure-lowering treatment on cardiovascular risk in hypertensive patients with type 2 diabetes. *Diabetes Care*. 2011;34:1270–1276.
37. Boutouyrie P, Tropeano AI, Asmar R, et al. Aortic stiffness is an independent predictor of primary coronary events in hypertensive patients: a longitudinal study. *Hypertension*. 2002;39:10–15.
38. Wilkinson IB, MacCallum H, Rooijmans DF, et al. Increased augmentation index and systolic stress in type 1 diabetes mellitus. *QJM*. 2000;93:441–448.
39. Patel A, MacMahon S, Chalmers J, et al. Effects of a fixed combination of perindopril and indapamide on macrovascular and microvascular outcomes in patients with type 2 diabetes mellitus (the ADVANCE trial): a randomised controlled trial. *Lancet*. 2007;370:829–840.
40. Cushman WC, Evans GW, Byington RP, et al. Effects of intensive blood-pressure control in type 2 diabetes mellitus. *N Engl J Med*. 2010;362:1575–1585.