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Torffvit, Ole

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PO Box 117
221 00 Lund
+46 46-222 00 00

The effect of achieving a systolic blood pressure of 140 mmHg.

A prospective study of ambulatory measurements in type 2 diabetic patients

with nephropathy.

Ole Torffvit, MD, PhD. Department of nephrology, Institution of Clinical Sciences,
University hospital of Lund, S-221 85 Lund.

Running headline: ambulatory blood pressure

Correspondence:

Ole Torffvit, Associate Professor

Primary Care Unit (Vårdcentralen)

Bryggaregatan 15, S-284 32 Perstorp, Sweden

Tel +46 435 666330; E-mail Ole.Torffvit@med.lu.se

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Abstract

Objectives. What is the prognostic significance of achieving a systolic blood pressure of <140 mmHg?

Setting. Diabetic renal polyclinic, university hospital of Lund, Sweden

Subjects. 118 type 2 diabetic patients with micro-macroalbuminuria were followed for four years (range 1-8 years).

Method and main outcome measures. The prognostic significance of office, day- and nighttime measurements of blood pressure (BP) for development of cardiovascular complications was studied.

Results. Forty-two percent (n=49) developed one or more of the following cardiovascular endpoints: 23% (n=27) death, 9% (n=10) stroke, 9% (n=11) myocardial infarction, 9% (n=11) heart failure, 31% (n=36) uremia and 17% (n=20) need for dialysis. Reaching the goal for day- and nighttime systolic BP (SBP) at baseline of <140 mmHg was associated with lower risk for developing uremia. Reaching the goal for nighttime SBP was associated with a decreased risk for developing myocardial infarction and need for dialysis treatment. None of these associations was found for office SBP.

Patients not achieving the goal for nighttime systolic blood pressure of <140 mmHg had a 12.9 times higher risk of developing myocardial infarction and 3.9 times increased risk of uremia and 2.7 times increased risk for death than patients achieving the goal.

Conclusion. Nighttime blood pressure had better prognostic significance for developing cardiovascular and renal complications than office and daytime blood pressure.

Abbreviations. ABPM = ambulatory blood pressure measurements. BP = blood pressure. SBP = systolic blood pressure. DBP = diastolic blood pressure. GFR = glomerular filtration rate.

Keywords: Ambulatory blood pressure, diabetic nephropathy, hypertension, macroalbuminuria, microalbuminuria, uremia.

Introduction

Treating hypertension in patients with diabetic nephropathy offers a special challenge as these patients have a high mortality and high risk of developing need for dialysis/transplantation treatment within a short time period. Furthermore, the patients are sensitive to overtreatment because of autonomic neuropathy. In our previous ten year observation study of type 2 diabetic patients we found a cut-off blood pressure (BP) level of 140/75 for development of uremia but not for myocardial infarction, stroke or death (Torffvit and Agardh, 2002).

Ambulatory blood pressure measuring (ABPM) showed increased nighttime systolic BP to be associated with increased albuminuria (Mitchell, Nolan, Henry, Cronin, Baker, Greely and Orelund, 1997), decreased glomerular filtration rate (Torffvit, Tapia, Rippe, Alm, Willner and Tencer, 2004), development of endstage renal failure (Nakano, Ogihara, Tamura, Kitazawa, Nishizawa, Kigoshi and Uchida, 1999) and death (Palmas, Pickering, Teresi, Schwartz, Moran, Weinstock and Shea, 2009).

Patients with normal daytime BP may have a masked nocturnal hypertension (Wijkman, Länne, Engvall, Lindström, Östgren and Nystrom, 2009). Increased ambulatory BP is a better predictor for cardiovascular disease than office BP (Bauduceau, Genès, Chamontin, Vaur, Renault, Etienne and Marre, 1998b; Eguchi, Ishikawa, Hishide, Pickering, Schwartz, Shimada and Kario, 2009) and an independent predictor of nephropathy in type 2 diabetic patients (Knudsen, Laugesen, Hansen, Bek, Mogensen and Poulsen, 2009). Especially, the nighttime BP is associated with development of cerebral infarction (Kukla, Sander, Schwarze, Wittich and Klingelkhöfer, 1998). Recently it has been stressed that not only treatment of BP but a multifactorial treatment of diabetic patients is of importance (Gæde, Vedel, Larsen, Jensen, Parving and Pedersen, 2003).

We have previously shown that 24 h blood pressure (BP) is related to structural changes in renal biopsy (Torffvit, Tapia, Rippe, Alm, Willner and Tencer, 2004). We now show the long term results on the prognostic value of 24 h BP measurements. The aim was to examine whether the nocturnal BP was of higher prognostic significance than the daytime BP and the office BP. We also intended to evaluate our aim for BP treatment, systolic BP <140 mmHg.

Methods

118 type 2 diabetic patients, with micro- (n=36) and macroalbuminuria (n=82) were studied prospectively in a renal biopsy study for median 4 years (0-8 years) at the diabetic renal policlinic, University Hospital in Lund. All patients with the indication for renal biopsy, which was micro-macroalbuminuria, were followed. In total 52 (44%) of the patients had had a renal biopsy, which showed diabetic nephropathy and some degree of nephrosclerosis, two had glomerulonephritis and one minimal changes and two normal tissue. The results of the biopsy findings are presented elsewhere (østerby, Tapia, Nyberg, Tencer, Willner, Rippe and Torffvit, 2001; Torffvit, Tapia, Rippe, Alm, Willner and Tencer, 2004). The study was approved by the Ethical Committee of University of Lund and the patients gave their informed consent.

Office BP was measured with a sphygmomanometer in the supine position after five minutes at rest. A mean of three measurements at one minute intervals were used. ABPM was investigated with a 24-h, automated, portable BP device (Model 90207, SpaceLab analysis system, Wokingham, UK). The monitor was programmed for cuff insufflations every 20 min between 07:00 and 22:00 h and every 30 min from 22:00 to 07:00 h. The first period, 08:00 to 22:00 was defined as daytime. We selected the period 01:00 to 05:00 to define night-time as this was “night” for all patients according to their protocols.

Aim for routine treatment: The diabetic-renal polyclinic had well-defined aims: Systolic blood pressure during day- and nighttime measurements < 140 mmHg, $\text{HbA}_{1c} \leq 7.4\%$ and total s-cholesterol ≤ 5.0 mmol/l. The investigation of retinopathy was performed at the department of ophthalmology after pupillary dilatation. The classification of retinopathy was based on routine examinations based on findings from fundus photographs using a 45j Topcon camera. Three fields per eye were obtained through dilated pupils: one nasal, one central with stereo pairs, and one temporal field. In cases in which photographs were not available, the evaluation was based on the detailed description of retinopathy performed by an experienced ophthalmologist using biomicroscopy after dilation of the pupils. Retinopathy in the present study was defined as normal, background or severe diabetic retinopathy, including proliferative changes or macular edema.

Definition

Achieved goal was defined as mean of all measurements of SBP < 140 mmHg. This was taken from our previous study showing a cut-off level for uremia of 140/75 mmHg (Torffvit and Agardh, 2002). Uremia was defined as a $\text{GFR} \leq 30$ ml/min/1.73m². The diagnosis myocardial infarction was used when two of the following criteria were fulfilled: 1) chest pain, 2) changes in serum activity of troponin T and 3) ECG changes typical for myocardial infarction. The diagnosis of stroke was based on a persistent neurologic deficit and computerized tomography. Microalbuminuria was defined as 3-20 mg/mmol or a urinary albumin excretion of 20–200 $\mu\text{g}/\text{min}$, and macroalbuminuria as levels above these levels.

Laboratory measurements

We used routine methods for analysis. Glycosylated hemoglobin (HbA_{1c}) was analyzed by HPLC. The normal value was 4.0–5.3%. Serum and urinary creatinine concentrations were

analyzed by an enzymatic method (creatinine amidinohydrolase; Kodak Ektachem analyser, Instrument Kodak, NY). Urinary albumin concentration (UAC) for inclusion criteria was measured by turbidimetry (Cobras Mira, Roche, Stockholm, Sweden) (detection limit, 5 mg/l). Urinary albumin excretion was then determined in three timed overnight samples by an ELISA technique (Torffvit and Wieslander, 1986). Glomerular filtration rate (GFR) was evaluated by using iohexol clearance in the no fasting state. Five ml of iohexol (Omnipaque 300 mg I/ml) was given intravenously. The blood sample was taken after 245 min. The clearance was corrected to 1.73 m^2 body surface area.

Yearly measurements were performed of 24 h blood pressure, timed overnight urine collections and GFR, analyzed by clearance of Iohexol. In some patients (n=24) GFR was estimated from weight, age, gender and plasma creatinine (Cockcroft and Gault, 1976).

Statistics

The chi-square or, if small numbers, Fisher's exact test was used for differences between groups. Odds ratios were calculated from the crosstables with Mantel-Haenszels common odds ratio estimate. Associations were tested by Spearman's rho. Non-parametric methods for non-paired analysis were used for comparison between groups and paired analysis for differences between blood pressure levels at baseline and during observation time. Cox regression analysis with observation time as time variable and the backward conditional method was used for prognostic difference between variables. Level for the statistical significance was $P < .05$ (two-way). We used the SPSS program 17.0 (Chicago, IL).

Results

The patients were followed for median four years (range 1-8 years). Baseline data are presented in table 1. The patients were predominantly males. The office systolic and diastolic

BP levels were clearly higher than the daytime levels from the 24 hour readings. Thirty-one had no retinopathy, 17 had background and 60 had severe retinopathy, while data were missing in 10 patients. Patients who reached the goal had shorter diabetes duration, lower office systolic BP, lower day- and nighttime ABPM, higher GFR, and lower u-albumin than patients who did not reach the goal (Table 1). A clear majority (95%) were treated with insulin and antihypertensive drugs, predominantly diuretics (Table 2). Fewer patients with the goal reached had β blockers and insulin than the patients who did not reached the goal. Twenty-eight (24%) had had heart disease and 21 (18%) a stroke before the study.

At baseline, the SBP was less than 140 mmHg in 17 patients (14%) in the office and in 33 (28%) during daytime measurements. A few more patients, 36 (31%), reached the goal for treatment during the observation period. Similarly, the night SBP was less than 140 mmHg in 61 (52%) at baseline and a few more, 65 (55%) had reached the goal during the observation time. Sixty-eight patients had their 24 h BP measured several times, but there were no statistical difference between baseline and during the observation period of the daytime or nighttime SBP.

Forty-two percent (n=49) developed one or more of the following cardiovascular endpoints: 31% (n=36) uremia, 17% (n=20) need for dialysis, 23% (n=27) death, 9% (n=10) stroke, 9% (n=11) myocardial infarction, 9% (n=11) heart failure while none had renal transplantation. Having reached the goal for day- and nighttime SBP at baseline was associated with fewer patients developing uremia and need for dialysis treatment (nighttime SBP only) (Table 3). In contrast, development of heart failure was associated with a lower daytime SBP at baseline. Reaching the goal for nighttime SBP was associated with a decreased risk for developing myocardial infarction (Table 3). None of these associations was found for office SBP (data not shown).

Twenty-three patients had a systolic blood pressure during daytime < 135 mmHg. Not achieving this goal was associated with increased risk for developing uremia (odds ratio 5.9 (1.3-26.5), $p=0.023$). No association was found with death, development of stroke, myocardial infarction, heart failure or need for dialysis. 19 patients had a systolic night blood pressure <120 mmHg. Not achieving this goal was not associated with development of uremia (odds ratio 4.4 (1.0-20.4), $p=0.07$) or need for dialysis (odds ratio 2.2 (0.7-43.4), $p=0.07$) or risk for death, stroke, myocardial infarction or heart failure.

With Cox regression analysis we found that patients who had had a stroke had a 2.4 times (1.1-5.2, 95% CI, $p = 0.025$) increased risk for developing uremia, 3.3 times (1.5-7.4, $p = 0.004$) higher risk of death, but no increased risk for myocardial infarction, heart failure, or stroke. Having a history of heart disease increased the risk for developing heart failure by 3.5 times (1.1-11.5, $p = 0.04$) but not the risk for stroke, myocardial infarction or uremia.

Systolic blood pressure daytime, nighttime and office were included in Cox regression analysis and only nighttime was of prognostic significant value (Table 4). With the goal reached, the number with uremia and dialysis decreased to fewer than half of the patients (Table 4+fig 1).

There was a very poor correlation between office and daytime/nighttime SBP (Fig 2+3).

Twenty-eight patients were non-dippers and 90 dippers. Non-dipping was not associated with a combination of the endpoints studied and thus not with development of stroke, death, heart failure, uremia (COX reg. analysis). However, it was associated with development of myocardial infarction ($n=11$, $p=0.043$) and angina pectoris ($n=19$, $p=0.006$).

Pulse pressure (PP = difference between systolic and diastolic BP), MAP, and dippers and non-dippers (decrease or no decrease in SBP, by the difference between day- and nighttime analysis) together with daytime and nighttime and office SBP were analyzed with the Cox

regression analysis. PP daytime ($P = 0.003$) and MAP nighttime ($P = 0.006$) were independently associated with development of uremia. PP in the office ($P = 0.029$), daytime ($P = 0.028$) and nighttime SBP ($P = 0.046$) were associated with having a new stroke. While only nighttime MAP was associated with having a new myocardial infarction ($P = 0.007$). PP in the office was associated with death ($P = 0.009$).

We compared the magnitude of day-night SBP difference with the absolute level of night SBP in the Cox regression analysis and found that only the latter was associated with development of uremia ($p=0.000$), stroke ($p=0.028$) and myocardial infarction ($p=0.017$).

Discussion

The key message in the present study was office BP had no prognostic significance, while night BP was the most important parameter. In the study population many needed dialysis. Thus, the economic gain of prophylactic treatment will be high. Similarly, the population had a high incidence of cardiovascular disease, 42% had an endpoint, and thus in few years the effect of an intervention will pay off. One may speculate why we found no significant value of office BP. Perhaps this observation may explain why studies and guidelines aim for lower and lower BP? The present study showed that if you reach the goal for night SBP you also gain the benefit of the efforts, a 12 times' risk reduction of uremia. Having had stroke before the study started was associated with high risk of uremia and death. Although we were eager and decisive we "only" reached the goal of <140 mmHg in nighttime SBP in 55% of the patients. In the VALUE trial reaching an office SBP less than 140 mmHg was associated with significant benefits (Weber, Julius, Kjeldsen, Brunner, Ekman, Hansson, Hua, Laragh, McInnes, Mitchell, Plat, Schork, Smith and Zancheti, 2004).

There are no established goals for ambulatory blood pressure in high risk group: Chronic kidney disease and diabetes. Most of the prior studies in chronic kidney disease populations have used the goals recommended by JNC Report 7 and European Society of HTN with daytime SBP goal of <135 mmHg and nighttime SBP <120 (Journal of HTN. May 2003)

There was no difference in the endpoints for those who achieved daytime SBP < 135 Vs 140 and Nighttime SBP < 120 Vs 140 mmHg except for not achieving the former goals being of poorer significance for the prediction of risks than the latter. In the reappraisal of European guidelines 2009 the authors concluded on the basis of current data: The BP goal traditionally recommended in diabetes, that is, less than 130/80 is not supported by outcome evidence from trials, and has been difficult to achieve in the majority of the patients. Thus, it may be prudent to recommend lowering SBP/DBP to values within the range 130-139/80-85 mmHg in all hypertensive patients including diabetic patients. Furthermore: "It appears realistic to only recommend to pursue a sizeable BP reduction without indicating a goal which is unproven." Furthermore, in the recent ROADMAP study an aim of SBP of less than 130 mmHg resulted in significant higher mortality (Haller, Ito, Izzo, Januszewicz, Katayarna, Menne, Mimran, Rabelink, Ritz, Ruilope, Rump and Viberti, 2011). Thus, recommendations and studies and guidelines should be focused on addressing this issue.

There was a very poor correlation between office and daytime/nighttime BP as shown previously (Waeber, Weidmann, Wohler and Le Bloch, 1996). The consequence, if 24h measurements represent the real BP, will be that a systolic BP of 140 mmHg may equal 120-200 mmHg in the office. And as such may be untreated or overtreated.

Our aim for treatment was clinically predefined based on our previous ten year observation study of type 2 diabetic patients (Torffvit and Agardh, 2002). In the present study, we confirmed nighttime SBP predicted endstage renal failure (Nakano, Ogihara, Tamura, Kitazawa, Nishizawa, Kigoshi and Uchida, 1999). As nighttime SBP is associated with degree of albuminuria (Mitchell et al., 1997; Leittao, Molon, Canani, Pinotti, Polson and

Gross, 2005) and inversely with glomerular filtration rate (Torffvit, Tapia, Rippe, Alm, Willner and Tencer, 2004) it may be possible to directly measure the effect of treatment on nighttime SBP by evaluating the effect on albuminuria/GFR. In contrast, office BP levels are not associated with albuminuria (Bauduceau, Genes, Chamontin, Vaur, Renault, Etienne and Marre, 1998a). Furthermore, a decrease in office BP on ACE inhibitor was not associated with decrease in albuminuria in contrast to a decrease in ABPM SBP (Bauduceau, Genes, Chamontin, Vaur, Renault, Etienne and Marre, 1998a). Others have found an association between ABPM and death during follow-up (Palmas et al., 2009).

A high office SBP and normal ABPM have been suggested in a cross-sectional study to represent white coat hypertension and to be treated (Kramer, Canani, Leitão and Gross, 2009). However, we were unable in our prospective study to confirm this. Progression in microalbuminuria has even been related to increments in 24 h AMBP (Nielsen, Hansen, Schmitz, Mogensen and Poulsen, 1995). Recently, it has been stressed that not only treatment of BP but multifactorial treatment is of importance (Gæde et al., 2003). Thus, we must bear in mind that even the present study had several aims for the treatment and represents a multifactorial approach.

In this study, the ABPM data has been divided into daytime (8 am to 10 pm) and nighttime (1 am-6 am) omitting the BP readings between 10 pm and 1 am and early morning surge between 6-8 am. Therefore, we are not able to discuss the importance of the early morning surge. It is well known that non-dippers are associated with an increased risk of cerebral infarction and high early morning surge is associated with high risk of cerebral hemorrhage (Kario, Pickering, Umeda, Hoshide, Hoshide, Morinari, Murata, Kuroda, Schwartz and Shimida, 2003; Metoki, Ohkubo, Kikuya, Asayama, Obara, Hashimoto, Totsune, Hoshi, Satoh and Imai, 2006). Non dippers can independently increase the risk of stroke,

cardiovascular disease, left ventricular hypertrophy in people with hypertension (Verdecchia, Schillaci, Guerrieri, Gatteschi, Benemio, Boldrini and Porcellati, 1990). This has also been shown in patients on hemodialysis (Liu, Takahashi, Morita, Maruyama, Mizuno, Yuzawa, Watanabe, Toriyama, Kawahara and Matsuo, 2003; Tripepi, Fagugli, Dattolo, Parlongo, Mallamaci, Buoncristiani and Zoccali, 2005). But no one has studied this in non dialysis chronic kidney disease patients with diabetes mellitus like this report. We found in the present study non-dipping was not associated with development of stroke, death, heart failure or uremia. However, it was associated with development of myocardial infarction and angina pectoris.

Pulse pressure has been suggested to be an independent determinant of decline in renal function in patients with essential hypertension, pointing to the possibility of barotraumas of the glomeruli from increased arterial stiffness (Gosse, Coulon, Papaioannou, Litalien and Lemetayer, 2009). Pulse pressure may be associated with development of cardiovascular but not cerebrovascular events during eight years of observation (Nakano, Nishizawa, Konishi, Nakagawa, Furuya, Kigoshi, Uehara and Uchida, 2005). High PP was associated with development of uremia in our study and high PP in the office was actually associated with development of stroke. However, pulse pressure is a measure very difficult to treat as no one has a clear reference for normal value. In this study, we found that keeping the SBP below 140 mmHg was associated with lesser risk for cardiovascular complications and it is easy to have as a reference in daily clinical practice. However, even with special interest in the treatment it is still difficult to achieve.

Overall patients who did not reach the goal had more treatment in the effort reaching the goal. Why did they not? We have recently published our substudy on patients who had a renal biopsy done and found that patients who did not reach the goal had more serious changes in the kidneys caused by diabetes (Torffvit, Tencer and Rippe, 2010). Furthermore, the non

achievers had significantly longer duration of diabetes mellitus 15 years with higher proteinuria and lower GFR (all $p < 0.05$) and thus may have more serious structural changes which can be one of the major reasons behind failure to achieve the goal BP and hence, increased risk of cardiovascular and renal complications. A recent study in non diabetics chronic kidney disease patients has shown nighttime BP to be a better prognostic indicator of endstage renal disease and cardiovascular morbidity (Minutolo, Agarwal, Borrelli, Chiodini, Bellizzi, Nappi, Cianciaruso, Zamboli, Conte, Gabbai and De Nicola, 2011).

Conclusion. Office blood pressure had no prognostic value, daytime measurements was better and nighttime best. Patients who did not achieve the goal < 140 mmHg had a 12.9 times higher risk of having myocardial infarction and 3.9 times increased risk of developing uremia and 2.7 times for death than the patients who achieved the goal.

Conflict of interest statement. Nothing to declare

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Fig 1. Cumulative survival curves for uremia in relation to achieving goal for nighttime systolic blood pressure (time 1 to 5 hour night). < 140 mmHg stippled line, \geq 140 mmHg black line, OR 4.8 (2.2-10.3), $P < 0.001$.

Fig 2. The relationship between Office and daytime (8-22 h) systolic blood pressure ($R = 0.51$, $p < 0.001$).

Fig 3. The relationship between Office and nighttime (1-5 h) systolic blood pressure ($R = 0.40$, $p < 0.001$).

Fig 4. ROC curve for systolic BP and risk for uremia. Stippled line daytime, fat line nighttimes and thin stippled line office BP.

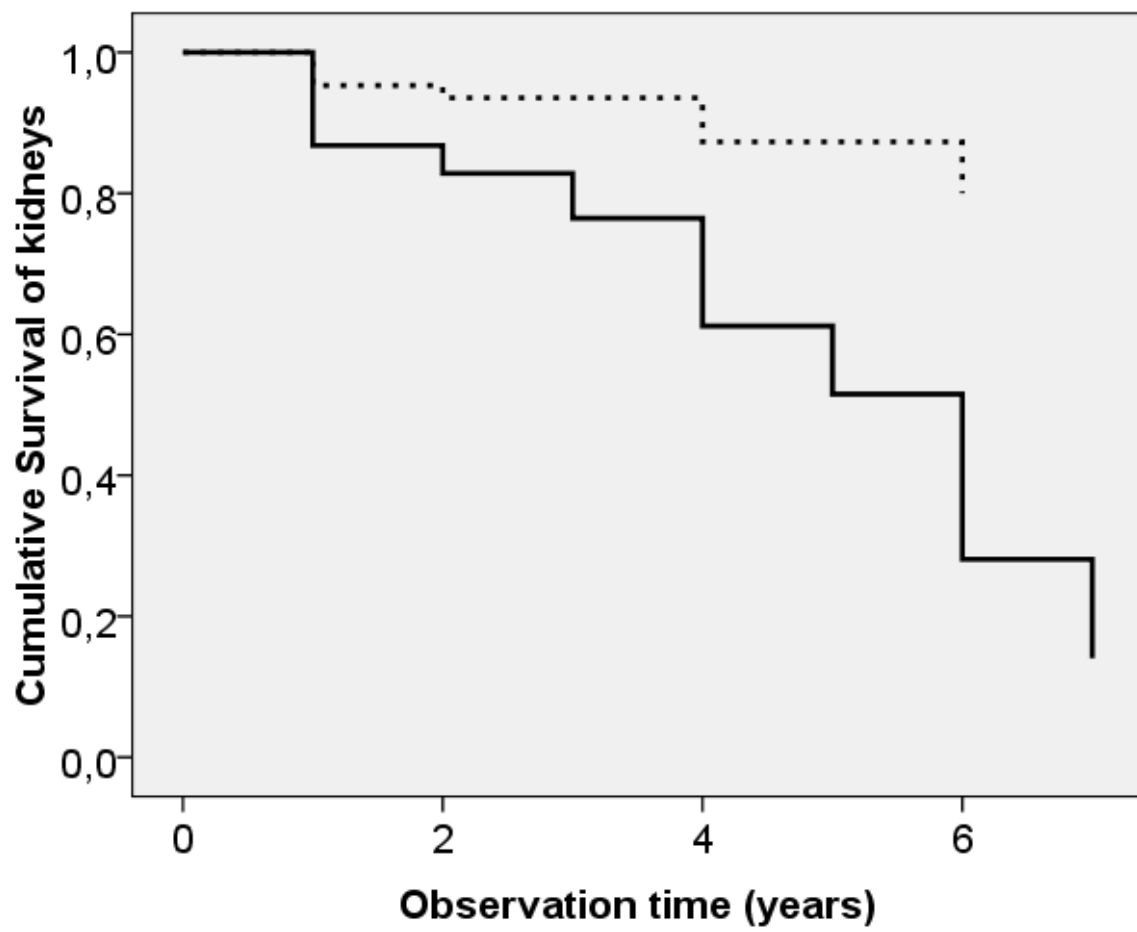
Figure 1

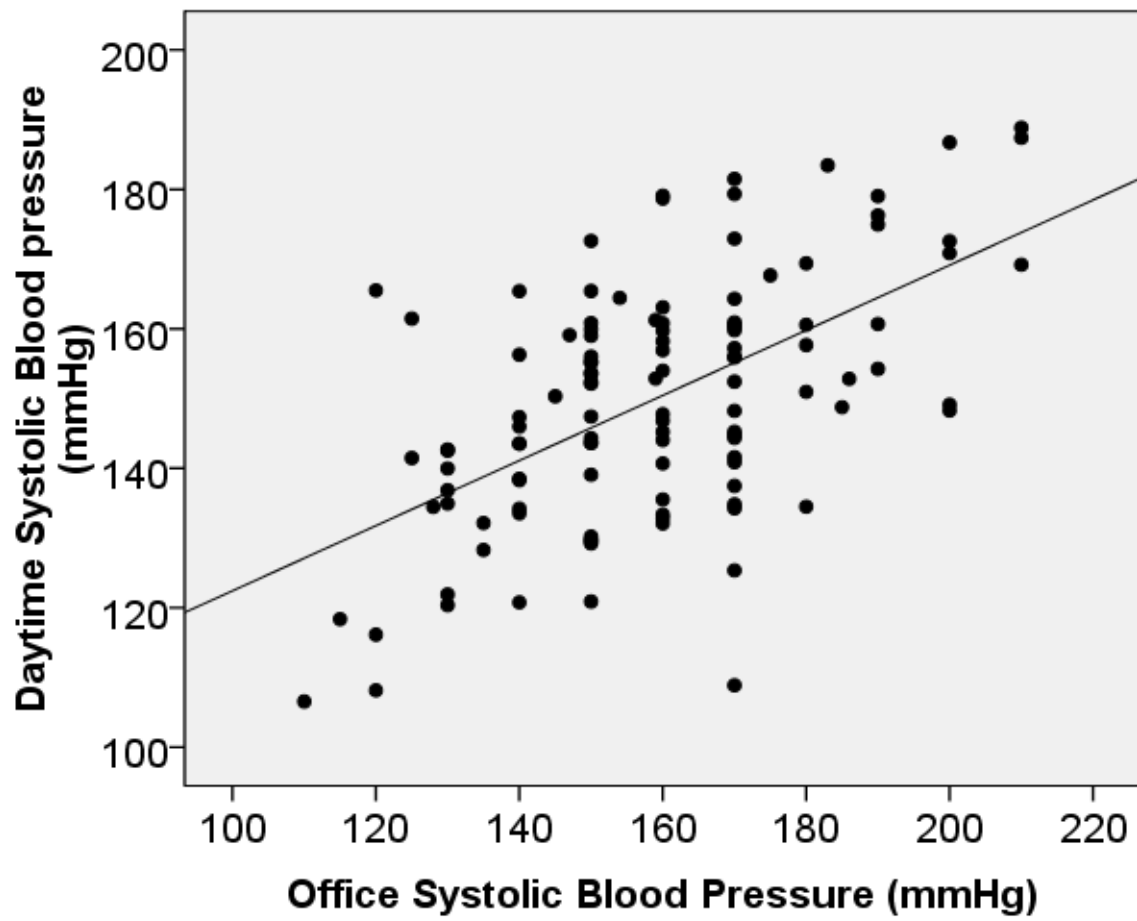
Figure 2

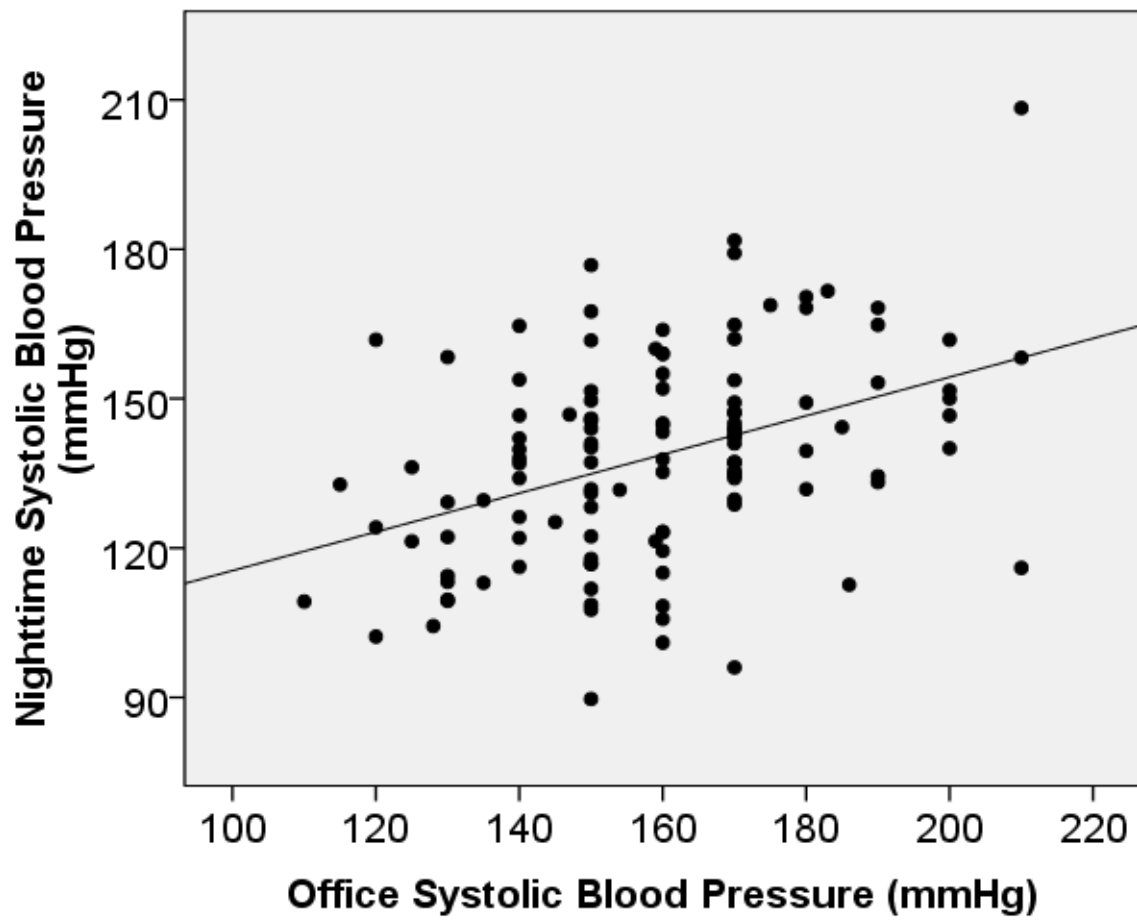
Figure 3

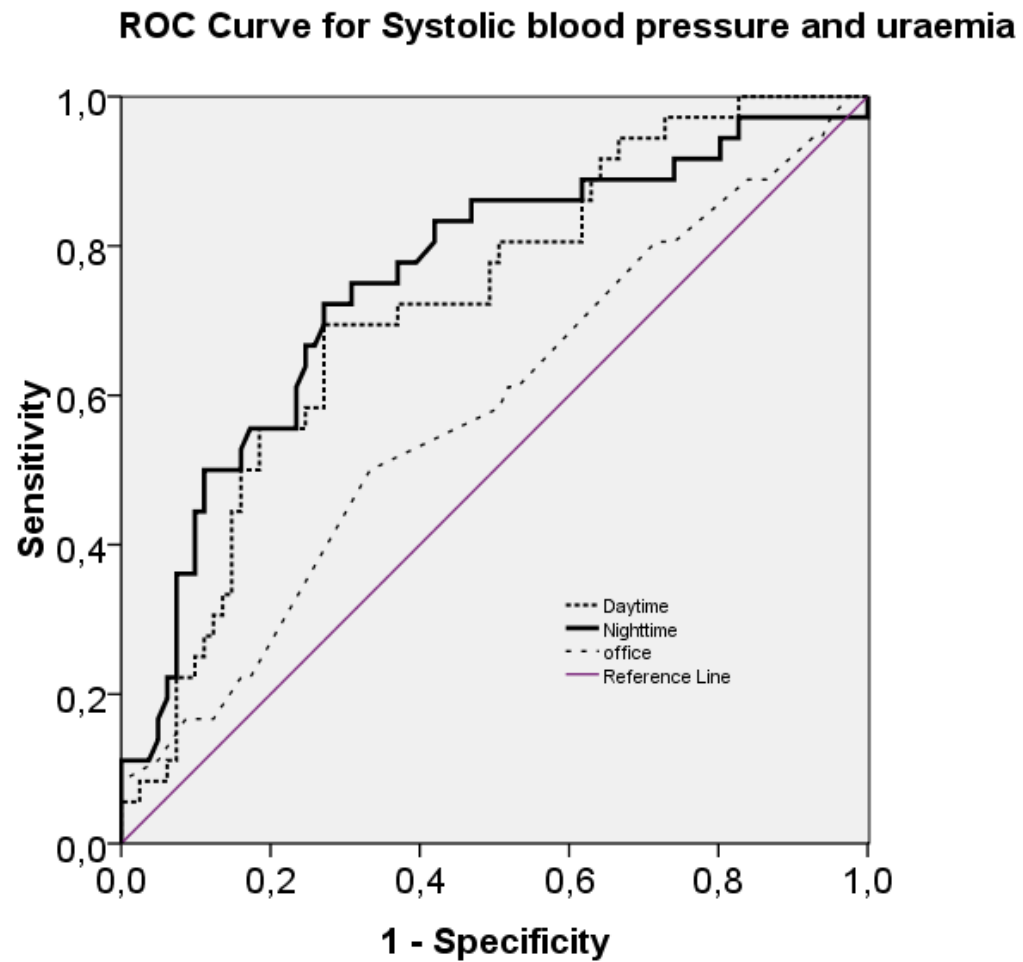
Figure 4

Table 1. Baseline data in 118 type 2 diabetic patients and achievement of goal for nighttime systolic blood pressure < 140 mmHg.

	Goal reached N=61	Goal not reached N=57	P-value
Gender (male/female)	51/10	45/12	0.637
Age (years)	64 (25-83)	65 (40-80)	0.105
Diabetes duration (yrs)	9 (0-37)	15 (1-38)	0.002
Office Systolic BP (mmHg)	150 (110-210)	170 (120-210)	0.000
Office Diastolic BP (mmHg)	80 (60-105)	88 (65-110)	0.237
<u>Systolic BP (mmHg)</u>			
Daytime (8-22)	142 (107-179)	160 (130-189)	<0.001
Nighttime (1-5)	123 (90-140)	152 (140-208)	<0.001
<u>Diastolic BP (mmHg)</u>			
Daytime (8-22)	81 (58-97)	84 (58-102)	<0.001
Nighttime (1-5)	68 (43-88)	78 (59-95)	<0.001
GFR (ml/min/1.73m ²)	73 (14-202)	59 (9-173)	0.039
HbA _{1c} (%)	7.2 (4.7-12.7)	7.5 (4.9-12.1)	0.227
Degree of albuminuria (micro/macro)	22/39	14/43	0.230
U-albumin (mg/l)	368 (13.1-5000)	901 (15-5911)	0.001

Data are given as median and range (min-max)

Table 2. Treatment of 118 type 2 diabetic patients and achievement of goal for nighttime systolic blood pressure < 140 mmHg.

	Goal reached	Goal not reached	P-value
Total on BP treatment	57 (94)	54 (95)	1.0
ACE inhibitors	37 (61)	36 (63)	0.85
ARB	23 (38)	27 (47)	0.352
β blockers	27 (44)	36 (63)	0.044
Ca blockers	19 (31)	26 (46)	0.130
Diuretics	41 (67)	47 (83)	0.09
Statins	37 (61)	37 (65)	0.705
Insulin	46 (75)	52 (91)	0.027

Number of patients and within parenthesis percent. BP = blood pressure. ACE= angiotensin converting enzyme. ARB = Angiotensin receptor blockers.

Table 3. Prognostic significance of nighttime SBP < 140 mmHg, at baseline.

	Goal reached	Goal not reached	Odds ratio and 95% CI	p
<u>Daytime SBP</u>				
Death	9 (28)	18 (21)	0.7 (0.3-1.8)	0.480
Stroke	1 (3)	9 (11)	3.8 (0.5-31.2)	0.215
Myocardial infarction	2 (6)	9 (11)	1.8 (0.4-9.0)	0.454
Heart failure	6 (18)	5 (6)	0.3 (0.1-0.9)	0.049
Uremia	4 (12)	32 (38)	4.4 (1.4-13.6)	0.010
Dialysis	2 (6)	18 (21)	4.2 (0.9-19.1)	0.066
<u>Nighttime SBP</u>				
Death	11 (18)	16 (28)	1.9 (0.7-4.2)	0.198
Stroke	4 (7)	6 (11)	1.7 (0.4-6.3)	0.443
Myocardial infarction	2 (3)	9 (16)	5.5 (1.1-26.8)	0.034
Heart failure	6 (10)	5 (9)	0.9 (0.3-3.1)	0.843
Uremia	9 (15)	27 (47)	5.2 (2.2-12.5)	<0.001
Dialysis	6 (10)	14 (25)	3.0 (1.1-8.4)	0.039

Number of patients and within parenthesis percent. SBP = systolic blood pressure. CI = confidence interval. Odds ratio = Mantel-Haenszels common odds ratio estimate.

Table 4. Prognosis: Risk for complications in relation to having achieved goal for treatment of night time SBP (< 140 mmHg) at baseline, Odds ratio and 95%CI.

	Numbers of patients (n, %)	Odds Ratio and 95% CI	p
Death	27 (23)	2.7 (1.04-6.9)	0.04
Stroke	10 (9)	1.6 (0.4-7.3)	0.52
Myocardial infarction	11 (9)	12.9 (1.6-106.9)	0.017
Heart failure	11 (9)	2.8 (0.6-13.9)	0.19
Uremia	36 (31)	3.9 (1.6-9.5)	0.002
Dialysis	20 (17)	2.7 (0.9-7.9)	0.077

Cox regression analysis with goal for daytime, nighttime and office SBP included.