Treatment goals for ambulatory blood pressure and plasma lipids after stroke are often not reached

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ABSTRACT

INTRODUCTION: In Danish health care, secondary prevention after stroke is currently handled mainly by general practitioners using office blood pressure (OBP) assessment of hypertension. The aim of this study was to compare the OBP approach to 24-hour assessment by ambulatory blood pressure (ABP) monitoring. Furthermore, we aimed to record the degree of adherence to recommended therapy goals for blood pressure and plasma lipids.

MATERIAL AND METHODS: In a prospective observational study, 45 stroke patients aged 25-64 years who were participating in specialized intensive outpatient rehabilitation were monitored by OBP and ABP on average 1.3 (0.14-4.3) years post stroke. Furthermore, data on additional risk factors and medication for secondary prevention were collected.

RESULTS: OBP and daytime ABP exceeded the therapy goal of 130/80 mmHg in 71% and 44% of the patients, respectively. ABP exceeded the night-time therapy goal of 115/65 in 57% of cases. Normal dipping at night was found in only 41% (systolic) and 32% (diastolic) of the patients. Considering both day- and night-time blood pressure, antihypertensive medication was absent or inadequate in 60%. Low density lipid (LDL) levels exceeded the recommended limit of 2.5 mmol/l in 49%.

CONCLUSION: For blood pressure (BP) and cholesterol, secondary prevention is far from ideal in post-stroke patients. Compared with OBP, ABP demands more resources, but in turn yields more reliable results and also provides important information about diurnal BP variation. ABP monitoring at least once after stroke should therefore be implemented routinely.

FUNDING: Aase og Einar Danielsens Fond.

TRIAL REGISTRATION: not relevant.

Recurrent stroke rates have declined from annual rates of 8.7% recorded in trials launched in the 1960s to 5.0% in the 2000s [1]. According to the PROGRESS study [2], the risk decreased by 43% through medication reduction of the blood pressure (BP) by 12/5 mm. Nevertheless, taking into account the first-stroke incidence in recent years of approx. 12,000 annually in Denmark, which has 5.6 million inhabitants [3], recurrent stroke remains a considerable public health problem.

In a nationwide population-based follow-up study [4] using data from the Danish National Indicator Project and comprising 28,612 patients hospitalised for ischaemic stroke in 2003-2006, the effectiveness of treatment with antiplatelets, oral anticoagulants, antihypertensives, or statins in routine care was investigated. The cumulated risk of recurrent stroke after a maximum of five years of follow-up was 11.7%. While oral anticoagulant as well as statin treatment was associated with a lower risk of recurrent stroke, use of any type of antihypertensive was associated with a higher or unaltered risk. This surprising finding may reflect unaccounted or residual confounding or lack of BP data.

In a Danish controlled study [5] of 303 patients (mean age 70.2 years), BP was not lowered following four home visits by nurses during the first post-stroke year. The visits included office blood pressure (OBP) measurement and counselling on lifestyle and the need for GP control visits. At follow-up, 62% of patients were hypertensive, both in the intervention and the control group. A Danish population study [6] on GP treatment of 5,413 hypertensive non-stroke patients with a mean age of 65.9 years showed that optimal BP control (OBP < 140/90 mmHg) was achieved in only 29.1%.

In Denmark, post-discharge BP is presently controlled primarily by GPs using OBP, i.e. clinical measurement by a sphygmomanometer or an electronic device. The result may be influenced by many factors, e.g. time of the day, duration of the rest period, duration since latest intake of medicine, physical activity, the impact of the white coat, recent tobacco smoking, caffeine, meals and emotional stress.

The advantages of ambulatory blood pressure (ABP) monitoring, or 24-hour automatic BP reading at regular intervals, versus OBP have been summarized in the 2003 European Society of Hypertension's recommendations [7]: 1) more accurate BP assessment, 2) identification of the "white coat response", 3) BP reflecting the patients´ usual daily activities, 4) more accurate assessment of the effect of medical treatment, 5) identification of patients whose BP does not reduce at night, so-called non-dippers.

The concept of dipping was introduced in 1988 by O'Brien et al [8]. Today, the most widespread definition of non-dipping is a decrease of systolic and diastolic BP of less than 10% from day to night. Dipping from 10 to

Equipment for ambulatory blood pressure monitoring: Special vest with pocket for ambulatory blood pressure recorder (model photo).

19.9% is regarded as normal, 20% or above as extreme, and for so-called reverse dippers, night-time BP is higher than daytime BP.

In a ten-year follow-up study of 1,430 patients [9], the cerebral infarction risk was significantly higher in subjects with a < 10% nocturnal decline in BP than in subjects with a nocturnal decline ≥ 10%.

A total of 575 Japanese patients aged 50+ with sustained hypertension (i.e. hypertension both by OBP and daytime ABP) were followed for an average of 41 months [10]. Brain magnetic resonance imaging disclosed multiple silent infarctions in 53% of extreme dippers, 29% in dippers, 41% in non-dippers, and 49% in reverse dippers. This suggests that extreme dipping was causing silent and clinical cerebral ischaemia through

hypoperfusion during sleep or an exaggerated morning rise of BP. Similarly, reverse dipping might pose a risk for intracranial haemorrhage.

So-called masked hypertension, characterized by a normal OBP but hypertension on ABP monitoring, is a genuine hypertensive condition found in approx. 10% of the adult population and readily detectable by ABP measurement [11].

The present study explored, first, to which extent post-hospital follow-up of OBP was sufficient as part of secondary prevention when evaluated by ambulatory BP monitoring approximately one year post stroke in stroke patients selected for intensive interdisciplinary outpatient rehabilitation; and, second, the pattern of other modifiable risk factors for recurrent stroke.

MATERIAL AND METHODS

From May 2008 to March 2010, 54 consecutive patients with stroke and/or spontaneous subarachnoid haemorrhage (SAH) participating in a special programme comprising intensive interdisciplinary outpatient rehabilitation at the Centre for Brain Injury Rehabilitation in Copenhagen were informed about hypertension as a risk factor and invited to be monitored by ABP. Inclusion criteria were that the patients were personally independent, less than 65 years old, and not so severely injured that return to work was assessed as being impossible.

Nine refused to endure the 24-hour ABP procedure. The GPs of the 45 included patients were informed about the project. Following written consent from the participating patients, the GPs were asked to send recent cholesterol level reports and information about recent medication.

ABP monitoring (ambulatory blood pressure recorder from Rozinn Electronics, Inc.) was started by a single specially trained operator who also performed assessments of body mass index (BMI). Immediately before starting the ABP apparatus, this operator made initial quadruple (left-right-right-left arm) assessments of the OBP using an appropriate cuff size and an Omron electronic device.

Oral and written instruction was given to all participants, who were asked to behave in an everyday fashion during the following 24-hour period at home. A special vest was given to participants, so that they could easily carry the electronic recorder. In cases of hemiparesis, an appropriate cuff was placed on the non-paretic arm. The device automatically measured the BP at 15-min. intervals during daytime (07 a.m. to 11 p.m.) and every half hour at night (11 p.m. to 07 a.m.).

The results were transferred electronically to the Department of Cardiology at Copenhagen University Hospital Hvidovre for evaluation. The results were afterwards sent to the GPs.

📋 TABLE 1

Patient characteristics.

		Mean	Median	Range	Recommended[b]
Demographic variables					
M/F, n (%)	32 (71)/13 (29)	–	–	–	–
Age distribution, M/F, n					
25-44 yrs	6/6	–	–	–	–
45-64 yrs	26/7	–	–	–	–
Stroke diagnosis, M/F, n (%)					
Cerebral infarction		19/11(67)	–	–	–
Cerebral haemorrhage		9/0 (20)	–	–	–
Subarachnoid haemorrhage		4/2 (13)	–	–	–
Diagnosis of diabetes		6/0 (13)	–	–	–
Special cardial risk factor, M/F, n (%)[a]		4/1 (11)	–	–	–
Conc. of lipid variables, mmol/l					
Total cholesterol		4.51	4.30	2.3-8.0	< 4.5
HDL		1.50	1.31	0.7-2.8	–
LDL		2.60	2.40	1.1-4.9	< 2.5
Triglycerides		1.52	1.12	0.5-4.4	–
Lifestyle factors					
Body mass index, kg/m²		26.4	24.8	17.6-43.3	< 25[c]
Smoking, M/F, n (%):		9/2 (24)	–	–	–

F = female; HDL = high density lipids; LDL = low density lipids; M = male.
a) Atrial fibrillation or valvular problems.
b) [12].
c) [13].

Definition of a therapy goal for antihypertensive medication

The patients' post-stroke OBP and ABP results were rated in accordance with the recommendations from the European Society of Hypertension as optimal and, for OBP, adopted by the Danish Stroke Society as therapy goals for patients after stroke, all in mmHg [7, 12] as follows:

OBP: systolic/diastolic < 130/80 mmHg
Daytime ABP: systolic/diastolic < 130/80 mmHg
Night-time ABP: systolic/diastolic < 115/65 mmHg

Ethics: The regional ethics committees in Denmark evaluate only biomedical studies.
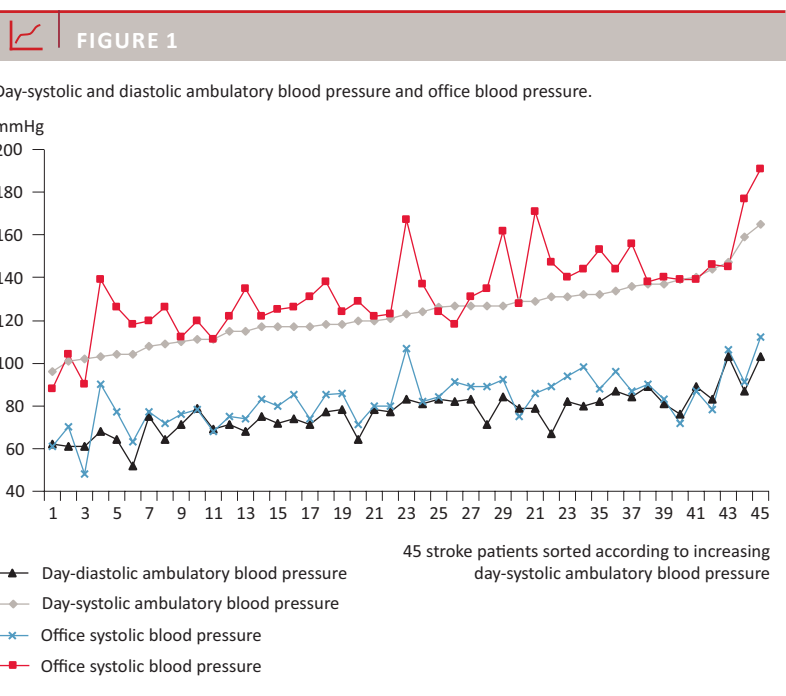
Trial registration: not relevant.

RESULTS

Table 1 shows baseline characteristics including gender, age and diagnosis at recent stroke/SAH debut for the 45 included participants. Of these, 37 were first-stroke cases. The median age at ictus for the 32 participating males was 55 years, and for the 13 females 45 years; and the upper age limit was 64 years. Of the nine patients who refused to participate, three were males aged 44, 45 and 51 years; five were females aged 45-54 years and one was a 21-year-old female.

Table 1 also shows the proportions of patients who had been diagnosed with diabetes and special cardial risk factors, lipid variables, and relevant lifestyle factors.

OBP assessment and ABP monitoring at the Centre for Brain Injury Rehabilitation took place at an average 1.3 (0.14-4.3) years post stroke.

Figure 1 shows individual correspondence between daytime systolic /diastolic OBP and daytime systolic /diastolic ABP. In most cases, OBP was higher than ABP, but to a highly variable extent.

FIGURE 1

Day-systolic and diastolic ambulatory blood pressure and office blood pressure.

- Day-diastolic ambulatory blood pressure
- Day-systolic ambulatory blood pressure
- Office systolic blood pressure
- Office systolic blood pressure

45 stroke patients sorted according to increasing day-systolic ambulatory blood pressure

However, in seven patients, systolic OBP was lower than daytime systolic ABP, but there were no cases in which systolic OBP was normal and systolic ABP exceeded the therapy goal of 130 mmHg, i.e. no masked systolic hypertension. In one case, diastolic OBP was lower and diastolic ABP higher than the therapy goal of 80 mmHg, i.e. masked diastolic hypertension.

Table 2 shows the mean, median and range for systolic and diastolic daytime OBP as well as daytime systolic/diastolic ABP and night-time systolic/diastolic ABP. OBPs are averages of the quadrupled measurements. The average number of daytime ABP readings was 48; the average number of night-time ABP readings was 16.

Table 3 shows that daytime OBP and ABP was ≥ 130/80 mmHg in 32 and 20, or 71% and 44% of the patients, respectively. Furthermore, and night-time ABP was ≥ 115/65 mmHg in 25 (57%) cases. Totally, the day-and/ or night-time ABP goals were exceeded in 27 (60%) cases.

Out of 32 patients with hypertension by OBP, only 20 had hypertension by daytime ABP, i.e. sustained hypertension. Seven had isolated nightly hypertension.

Table 4 shows the distributions between different groups of dipping; 41%/32%, respectively, were systolic/diastolic normal dippers, but 41%/36%, respectively, were systolic/diastolic non-dippers. All of the six patients with diabetes mellitus were both systolic and diastolic non-dippers. Of the six patients with SAH, five were normal and one was an excessive dipper. Non-dippers (0-4.9%) had the highest mean age. Apart from this observation, these small groups yielded no association between dipper status and age, gender or kind of stroke (cerebral haemorrhage versus infarction).

TABLE 2

Blood pressure measurements. Mean, standard deviation, median and range for systolic and diastolic office blood pressure as well as daytime systolic/diastolic ambulatory blood pressure in 45 stroke patients and night-time systolic/diastolic ambulatory blood pressure in 44 stroke patients. The values are mmHg.

	Mean ± SD	Median	Range
Systolic office blood pressure	134 ± 20	131	88-191
Daytime SyABP	124 ± 15	124	96-165
Night-time SyABP	109 ± 16	108	85-157
Diastolic office blood pressure	83 ± 12	83	48-112
Daytime DiABP	77 ± 10	79	52-103
Night-time DiABP	66 ± 11	66	44-99

ABP = ambulatory blood pressure; DiABP = diastolic ambulatory blood pressure; OBP = office blood pressure; SD = standard deviation; SyABP = systolic ambulatory blood pressure.

TABLE 3

Blood pressure measurements. Number (%) of stroke patients with office blood pressure (OBP) and ambulatory blood pressure (ABP) equal to or exceeding 130/80 mmHg (daytime) and/or 115/65 mmHg (night-time).

	Blood pressure, systolic/diastolic, mmHg					
	OBP ≥ 130/80	day-ABP ≥ 130/80	night-ABP ≥ 115/65	OBP ≥ 130/80; day-ABP < 130/80	OBP ≥ 130/80; day-ABP ≥ 130/80	night-ABP ≥ 115/65; day-ABP < 130/80
Isolated systolic hypertension	4	1	0	–	–	–
Isolated diastolic hypertension	8	6	11	–	–	–
Both systolic and diastolic hypertension	20	13	14	–	–	–
Total	32 of 45 (71)	20 of 45 (44)	25 of 44 (57)	–	–	–
Isolated office hypertension	–	–	–	12	–	–
Sustained (daytime) hypertension	–	–	–	–	20	–
Isolated night-time hypertension	–	–	–	–	–	7

TABLE 4

Blood pressure measurements. Dipping status (n = 44).

	Systolic		Diastolic	
	patients, n (%)	mean age, yrs	patients, n (%)	mean age, yrs
Reverse dipping	0	–	0	–
Non-dippers (0-4.9%)	5 (11)	55.8	5 (11)	55.8
Non-dippers (5-9.9%)	13 (30)	47.8	11 (25)	49.4
Normal dipping (10-19.9%)	18 (41)	51.5	14 (32)	47.7
Excessive dipping (≥ 20%)	8 (18)	46.0	14 (32)	50.2

FIGURE 2

Ambulatory blood pressure x 100 versus day-systolic ambulatory blood pressure.

45 stroke patients patients sorted according to increasing day-systolic ambulatory blood pressure

- ◆ Day-systolic ambulatory blood pressure
- ■ Systolic night/day ambulatory blood pressure x 100
- ✕ Diastolic night/day ambulatory blood pressure x 100

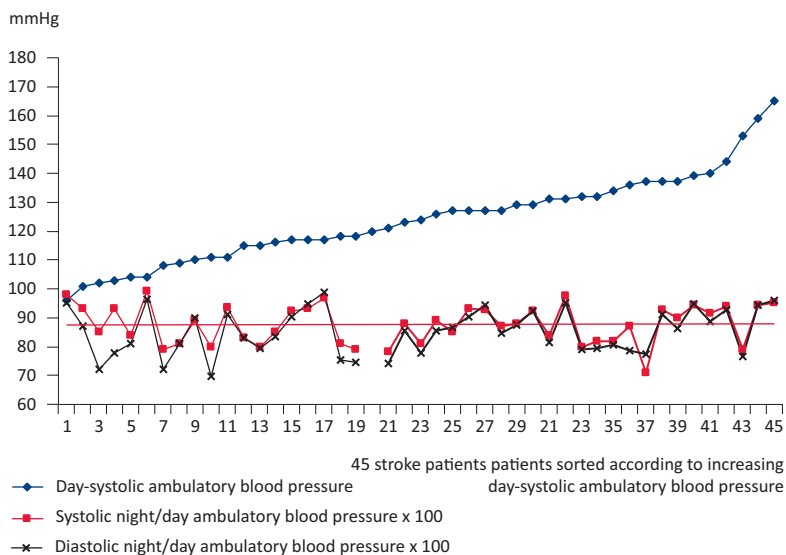**Figure 2** shows individual systolic and day-to-night dips expressed as night/day ABP ratio × 100; according to the equation: dip% = 100 (1 − night/day ratio). Thus, for normal dippers, the night-time ABP is between 80.1% and 90% of the daytime ABP; for non-dippers, it is between 90.1% and 100%; and for extreme dippers ≤ 80%. As shown by the trend line, the systolic night/day ratio did not vary systematically with increasing systolic daytime ABP. Mean systolic dipping was 12.4%, median systolic dipping 12%, range 1-29%.

Diastolic dip-percentages were similar to the systolic percentages; however, extreme dipping was more frequent for the former group. Once again, the night/day ratio did not vary systematically with increasing diastolic daytime ABP. Mean diastolic dipping was 14.9%, median diastolic dipping 14%, range 1.4-30%.

Out of 45 patients, 27 (60%), had systolic and/or diastolic BPs exceeding therapy goals; yet 14 of these took no antihypertensive medication; for the remaining 13, their antihypertensive medication was obviously insufficient. Only eight (18%) fulfilled the BP therapy goals without medication. LDL exceeded 2.4 mmol/l in 22 (49%) patients, which indicates absent (13 patients) or insufficient (nine patients) medication. In this group, there were thus also only eight patients (18%) who fulfilled the therapy goal without medication.

DISCUSSION

To the best of our knowledge, the present study is the first to investigate post-stroke ABP in Denmark. The most important limitation is the small patient number due to strong selection of the study population. However, an ABP monitoring study [14] of 187 first-ever consecutive hypertensive stroke survivors found lack of effective BP regulation at four months after ictus in more than half of the patients. Diabetes mellitus and functional independence were main factors contributing to inadequate BP control. The more functionally independent the patients were, the worse was medication compliance.

As illustrated by Tables 2-4, our results confirm other studies in the sense that secondary prevention was far from ideal. Important reasons for this may be the generally short stays in hospital in the acute phase,

which may not allow for proper adjustment of long-term medical secondary prevention, lagging cooperation between hospital and GPs, lack of compliance in the patient group or individual limitations because of haemodynamic factors.

Furthermore, there may be a need for the more accurate and informative ABP assessments as a supplement to the usual OBP assessments.

Given BP variability over time, it seems optimistic to consider occasional OBPs representative. Self-control by home-measurement is more satisfactory than occasional OBP performed by the GP. But even when self-control is used, information about night-time pressure remains totally absent, even though the literature has established that night-time pressure constitutes a more important risk factor for stroke than daytime pressure [15]. A study [16] in untreated essential hypertensives found night-time hypertension to be more frequent than non-dipping. The same was the case in the present study including stroke patients: while 25 of 44 patients (57%) had a night-time BP exceeding the therapy goal, 41% were systolic and 36% were diastolic non-dippers.

Several modifiable factors may influence night-time ABP: several studies link a non-dipping pattern to the obstructive sleep apnoea syndrome, as recently reviewed [17]. One study [18] found poor sleep quality and stressful status to be closely associated with increased activation of the sympathetic nervous system, both being independent predictors of non-dipping hypertension. In another study [19], treatment with Zolpidem converted many non-dippers with a poor sleep quality into dippers. An important aspect may be the lag of appreciation of chronotherapy [20].

CONCLUSION

The present work confirms other studies: Much remains to be done with regard to improvement of medical secondary prevention after stroke. In particular, OBP alone appears to be insufficient for proper BP follow-up. Compared with OBP, ABP demands more resources, but yields more reliable results and also information about diurnal BP variation. Because of the prognostic importance of this and the special vulnerability of stroke patients, ABP monitoring at least once after stroke should be implemented routinely.

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