Ambulatory blood pressure profile after carotid endarterectomy in patients with ischaemic arterial disease

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Objective: To assess the circadian blood pressure profile observed 3 months after endarterectomy.

Design: Twenty-five patients undergoing unilateral or bilateral carotid endarterectomy were compared with a control population of 20 patients, matched for age, sex, weight and drug therapy. Casual mean blood pressure measured by mercury sphygmomanometry was similar in both groups.

Results: Non-invasive ambulatory blood pressure monitoring showed that, whereas mean arterial pressure was identical in both groups, the group undergoing surgery had a significant increase in pulse pressure and its variability over 24 h. Such abnormalities predominated during the nocturnal period, in which the reduction in systolic blood pressure was less pronounced in the operated group than in controls. For all parameters there was no significant difference between subjects with unilateral or bilateral endarterectomy.

Conclusion: This study provides evidence that patients with carotid endarterectomy were characterized in the long term by an increase in the pulsatile component of blood pressure and its variability, in association with a disturbance in the physiological circadian rhythm. Such findings were not identified using casual blood pressure measurements.

Journal of Hypertension 1994, **12**:697–702

Keywords: Carotid endarterectomy, hypertension, ambulatory blood pressure, blood pressure variability.

Introduction

Carotid endarterectomy is highly beneficial to patients with recent hemispheric and retinal transient ischaemic attacks or non-disabling strokes and ipsilateral high-grade stenosis of the internal carotid artery [1]. However, in the long term the prognosis of these patients is influenced not only by the severity of cerebrovascular accidents, but also by the other complications of the atherosclerotic disease involving principally the heart. One of the most important risk factors to consider following carotid surgery is hypertension [2,3].

Carotid endarterectomy is known to be often complicated by an instability of the blood pressure either during the operation or in the early postoperative phase [4–7]. These changes in blood pressure are commonly attributed to transient abnormalities of the baroreceptor function, which may be inadvertently damaged during operation, due to removal of the rigid atheromatous plaques from within that region [8,9]. Nevertheless, in the long term the disturbance of blood pressure regulation is no longer observed [8,10]. However, for the long-term evaluation only casual blood pressure measurements using a mercury sphygmomanometer were taken into con-

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Sponsorship: This study was performed with a grant from the Assistance Publique de Paris, the Institut National de la Santé et de la Recherche Médicale (INSERM U 337), the Association Claude Bernard and the Ministère de la Recherche, Paris, France.

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Date of receipt: 11 October 1993; revised: 24 January 1994; accepted: 9 March 1994.

sideration following a long-term survey of carotid surgery.

To assess arterial blood pressure, the mean level and its variability, ambulatory blood pressure measurement is a much more reproducible method than casual blood pressure measurement [11–14]. It correlates more strongly than clinical or casual blood pressure with echocardiographic markers of left ventricular hypertrophy [15,16], non-invasive indices of arterial rigidity [17] and target organ damage in the heart, optic fundi and kidney [18–20].

The purpose of the present study was to evaluate ambulatory 24-h blood pressure measurements in patients following carotid endarterectomy. To evaluate the role of changes in baroreflex function on blood pressure regulation, subjects with either unilateral or bilateral endarterectomy were investigated.

Materials and methods

Patients

Twenty-five patients who underwent unilateral or bilateral carotid endarterectomy were preselected for the present study. Two patients were excluded for practical reasons (living far from the hospital) and one patient was excluded for technical reasons (poor quality of the ambulatory blood pressure recording). Twenty-two patients (14 male, eight female) were included and their results analysed. Their mean ± SD age was 66 ± 9 years, their weight was 73 ± 12 kg and their height was 170 ± 7 cm. Based on arteriographic findings, no patient had a contralateral stenosis of the internal carotid artery (<20%). Their data were compared with those from a further 20 subjects (15 male, five female) who were chosen as a control group without carotid endarterectomy. Their mean ± SD age was 60 ± 13 years, their weight was 70 ± 8 kg and their height was 168 ± 7 cm. Based on conventional continuous Doppler ultrasound and a duplex echo-Doppler system, control subjects had no significant (>20%) stenosis of the internal carotid artery. Informed consent, based on a detailed description of the study, was obtained from all of the patients.

All of the investigations were performed on the same day, 12 weeks after operation. After overnight fasting, blood samples were taken at 0800 h for plasma glucose and lipid determination according to standard techniques; the casual blood pressure was measured with the subject in the supine position, after which all subjects underwent blood pressure monitoring.

Casual blood pressure measurements

Casual blood pressure was measured after 15 min rest in the supine position, using a mercury sphygmomanometer. An average of three measurements was taken for each patient. Korotkoff phase I sounds were used for the determination of systolic blood pressure (SBP), and phase V was used for the evaluation of diastolic blood pressure (DBP). Mean blood pressure was calculated as DBP + $\frac{1}{3}$(pulse pressure).

Blood pressure monitoring

Automated blood pressure monitoring was carried out in each patient using a DIASYS model 200 R monitor (Novacor, Rueil-Malmaison, France) to measure and record blood pressure and heart rate over a full 24-h period [21,22]. The reliability of this method has been discussed in detail previously [23–25]. Recordings were performed every 15 min throughout the 24 h. Ambulatory monitoring was undertaken for a full active day; the patient worked as usual during the day and then went home as usual in the evening. As previously published [17,25], recordings that showed a calculated pulse pressure >100 mmHg, or <20 mmHg with SBP >100 mmHg, were deleted before further data analysis. Each full-day recording was divided into an active (diurnal) period (0700–2200 h) and a non-active (nocturnal) period (2200–0700 h), based on the patients' diaries. Mean values were used for statistical analysis, and variability was assessed on the basis of absolute SD evaluated for each subject [25].

Method for carotid endarterectomy

Surgery was performed under general anaesthesia. The incision was made along the anterior border of the sternocleidomastoid muscle. The common carotid artery was dissected, avoiding injury to the vagus nerve. The carotid bifurcation was then freed completely, care being taken to avoid damaging the carotid sinus and the hypoglossal nerve. Tapes were placed around the carotid arteries. The patient was systematically heparinized with 10 000 u heparin. The common carotid artery was clamped proximally, followed by the internal and external carotid arteries. A bulldog clamp was placed on the superior thyroid artery. An incision was made longitudinally from the common carotid artery to the internal carotid beyond the distal extent of the plaque. The dissection plane was entered at the level of the common carotid, using a smooth spatula. The plaque was then dissected from the bifurcation and the origin of the external carotid artery. Blind endarterectomy was performed in the external carotid artery, the plaque being broken with a clamp 1 cm from the origin of the artery. Dissection of the plaque was then carried out on the internal carotid artery and the distal end of the endarterectomy was visualized completely to avoid any imperfection that could produce a postoperative occlusion. When the arteriotomy was almost closed, the vessels were unclamped and blood flow was restored to the external carotid artery with gentle massage of the bifurcation in order to flush any debris or air into it, rather than into the internal carotid artery. The clamp was

Table 1. Main characteristics of the population.

	Control group (n = 20)	Carotid endarterectomy group (n = 22)
Age (years)	60±13	66±9
Weight (kg)	70±8	73±12
Height (cm)	168±7	170±7
Males/females	15/5	14/8
Stroke or cerebral ischaemic attack, or both (n)	2	22***
Prior myocardial infarctus or angina pectoris, or both (n)	3	5
Congestive heart failure (n)	0	2
Arteriosclerosis obliterans of the lower limbs (n)	2	3
Tobacco consumed (packs/year)	21±13	38±8
Antihypertensive treatment (n)	17	13
Plasma glucose (mmol/l)	5.5±0.6	5.5±0.8
Total plasma cholesterol (mmol/l)	6.0±1.3	5.8±1.0
Plasma high-density lipoprotein (mmol/l)	1.51±0.30	1.11±0.56
Plasma creatinine (mmol/l)	105±30	112±13

Values are expressed as numbers or as means±SD. ***$P<0.001$, versus control.

then removed from the internal carotid artery, allowing restoration of cerebral blood flow. Heparin was neutralized with protamin sulphate, and haemostasis completed.

Statistical analysis

Statistical analysis [26] was performed with statistical software (NCSS; Number Cruncher Statistical Systems, Kaysville, Utah, USA). Descriptive tests were used to express the range values. Comparison of the mean values between the two populations was performed using an unpaired Student's t-test. Comparison of the qualitative parameters was performed using the χ^2-test. Values are expressed as means±SD, and $P<0.05$ was considered statistically significant.

Results

Analysis of the population

Table 1 compares the 22 patients with carotid endarterectomy with the 20 control subjects. Compared with controls, no significant difference was observed, with the exception of a higher incidence of stroke or cerebral ischaemic attacks, or both ($P<0.001$). Of the 20 controls, 17 were treated: nine with β-blocking agents, six with diuretics, three with angiotensin converting enzyme inhibitors, nine with calcium antagonists and two with nitrates. Of the 22 patients with carotid endarterectomy, 14 were treated: three with β-blocking agents, two with diuretics, two with angiotensin converting enzyme inhibitors, six with calcium antagonists and three with nitrates. There was no significant difference in the drug distribution.

Table 2. Casual blood pressure measurements.

	Control group (n = 20)	Carotid endarterectomy group (n = 22)
Blood pressure (mmHg)		
Systolic	142±16	145±23
Diastolic	91±7	80±12***
Mean	108±8	102±11
Pulse pressure	51±15	64±26*
Heart rate (beats/min)	74±10	76±13

Values are expressed as means±SD. *$P<0.05$, ***$P<0.001$, versus control.

Casual blood pressure measurements

Patients with carotid endarterectomy had a higher SBP and pulse pressure ($P<0.05$) and a lower DBP than control subjects (Table 2). The finding concerning DBP was significant ($P<0.001$). However, in both groups blood pressures remained within the normal ranges.

Ambulatory blood pressure measurement

The upper part of Table 3 compares the mean values of blood pressure and heart rate mean levels recorded in the two populations over the three periods. During either of the 24-h periods (diurnal or nocturnal) the mean arterial pressure, DBP and heart rate were not statistically different in patients and controls (Fig. 1). In all three periods patients with carotid endarterectomy exhibited a significant increase in pulse pressure (Fig. 1). During the night patients with endarterectomy were characterized by a less pronounced decrease in SBP than was found in the control subjects. Of the patients, 59% had a night mean SBP >120 mmHg, whereas this was the case for only 37% of the controls ($P=0.03$).

The lower part of Table 3 compares the blood pressure and heart rate variability between the two populations over the three periods. Patients with carotid endarterectomy exhibited a significant increase in pulse pressure variability (due to the increase in variability of SBP and not DBP) in each of the three periods analysed. During the night patients with endarterectomy exhibited a significant increase in SBP variability.

Figure 2 compares the blood pressure measurements in subjects with unilateral or bilateral carotid endarterectomy. The mean age was the same: 67±14 versus 65±5 years, respectively. The mean values of blood pressure and variability were not significantly different in the two groups.

Discussion

In the present study patients with carotid endarterectomy exhibited three dominant features: whereas casual blood pressure was largely within the normal

Table 3. Ambulatory blood pressure measurements.

	24-h period		Diurnal period		Nocturnal period	
	Control group	Carotid endarterectomy	Control group	Carotid endarterectomy	Control group	Carotid endarterectomy
Means						
Blood pressure (mmHg)						
Systolic	123±15	133±15*	130±16	138±18	114±16	127±16*
Diastolic	76±10	72±10	80±10	75±10	70±10	68±12
Mean	91±11	93±7	97±11	96±7	85±11	88±10
Pulse pressure	48±11	61±19**	50±12	63±22*	44±11	58±18**
Heart rate (beats/min)	73±10	74±11	76±11	76±11	68±11	70±13
Variabilities (as expressed by SD)						
Blood pressure (mmHg)						
Systolic	18±4	19±5	15±5	17±5	13±4	17±4*
Diastolic	18±3	18±6	17±4	16±7	15±4	15±5
Mean	13±2	13±3	12±3	11±4	10±3	11±3
Pulse pressure	13±3	17±5**	14±4	17±6*	10±4	14±4**
Heart rate (beats/min)	11±4	12±5	10±4	12±5	9±4	9±4

Values are expressed as means±SD. *$P<0.05$, **$P<0.01$, versus control.

range, ambulatory blood pressure revealed substantial abnormalities of the blood pressure regulation; the ambulatory blood pressure disturbance affected exclusively SBP and pulse pressure, with no significant change in mean arterial pressure, DBP or heart rate; and the nocturnal reduction in SBP and pulse pressure was less pronounced than in the control subjects, and was associated with a significant increase in the variability of these parameters. Since the control subjects in the study had no carotid endarterectomy and no stenosis of the internal carotid artery, and since the distribution of drug treatment was the same in control subjects and patients, the observed blood pressure abnormalities should be analysed taking into account two different findings: the presence or absence of carotid endarterectomy and the characteristic features of the ischaemic arterial disease.

It is generally admitted that local pathological changes, arising after carotid endarterectomy, may affect carotid sinus baroreceptor function and therefore blood pressure regulation [8,9,27]. Endarterectomy results in oedema of the vessel wall. Both this and the resolution of cervical haematoma may result in periarterial fibrosis, thus diminishing sinus wall distensibility. Nevertheless, despite such possible structural modifications, Tyden *et al.* [10] and Dehn and Angell-James [8] did not find any significant change in carotid sinus baroreceptor function and in blood pressure regulation between 8 weeks and 6 months after endarterectomy. In the present study ambulatory blood pressure measurements were performed 12 weeks after endarterectomy. The disturbances in blood pressure regulation were similar whether the subjects had unilateral or bilateral carotid endarterectomy. It is possible that aortic baroreceptors contribute to maintaining the reflex function. Together, these findings do not suggest that carotid endarterectomy itself explains the present observation of long-term abnormality of blood pressure regulation after the surgical procedure.

The principal result of the present study was that the blood pressure changes affected mainly SBP, pulse pressure and their variabilities, whereas mean arterial pressure was affected only very slightly. Studies of pulsatile arterial haemodynamics have repeatedly shown that the blood pressure curve may be divided into two components [28]; a steady component (mean arterial pressure), which is influenced by cardiac output and total vascular resistance, and a pulsatile component (pulse pressure), which is influenced by other independent haemodynamic variables such as ventricular ejection, arterial stiffening and changes in the timing of reflected waves. In the present study there are several findings that suggest that the last two of these mechanisms may be involved. First, distensibility of the vessel wall is known to be reduced by atherosclerosis, both in human carotid arteries [28,29] and in the aorta of experimental atheromatous animals [30]. Secondly, reduced arterial distensibility is a classical pattern in old age, particularly in old subjects with systolic hypertension [28,31]. Thirdly, ambulatory blood pressure measurements are strongly correlated with aortic stiffness, measured from the carotid–femoral pulse wave velocity [17]. Such observations suggest that the increase in SBP and pulse pressure observed in the present patients is related to a reduction in distensibility. Similar observations have been made in old subjects with systolic hypertension, in subjects with arteriosclerosis of the lower limbs [31] and in populations of patients with increased plasma glucose or tobacco consumption [25].

Experimental studies have shown that long cyclic stress (as generated by pulse pressure) alters the arterial wall much more than steady stress (as gener-

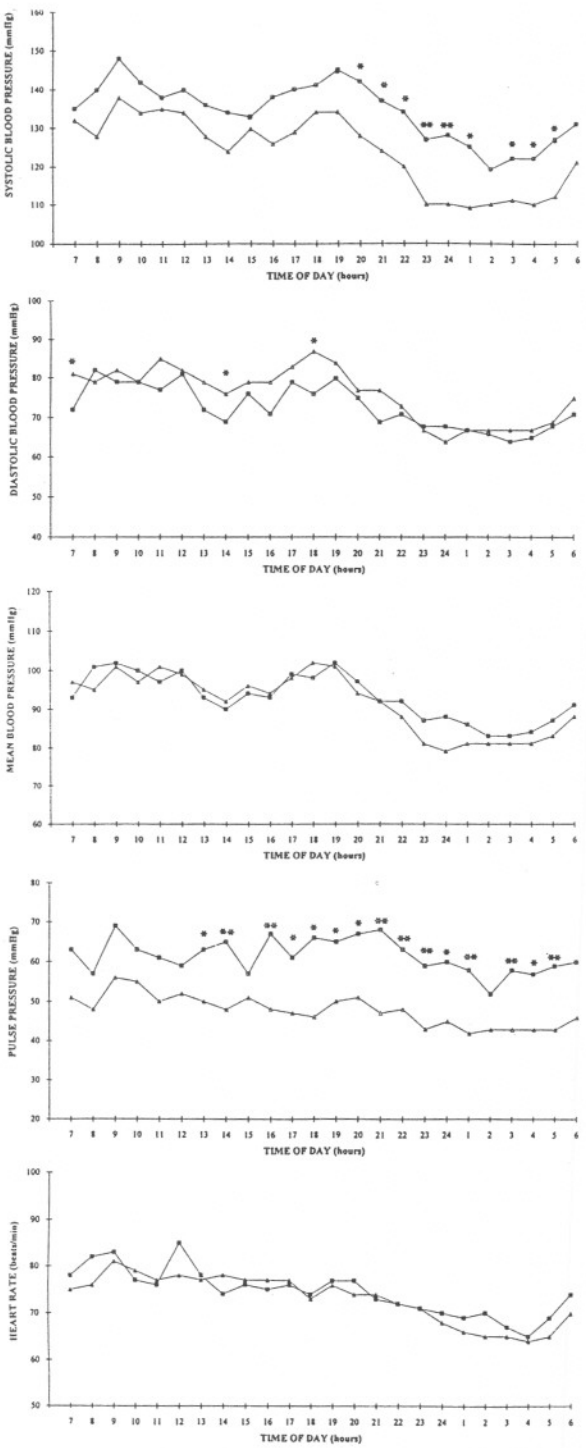

Fig. 1. Circadian curves of hourly blood pressure and heart rate values in patients with carotid endarterectomy (■) and control subjects (▲). For clarity, only mean values and *P* values are presented. $*P<0.05$, $**P<0.001$, versus control.

ated by mean arterial pressure) [28,31]. This important aspect of vascular damage has been particularly emphasized for cerebrovascular injuries [32]. Recent clinical and epidemiological studies have confirmed the important contribution of pulse pressure and cyclic stress to the morbidity and mortality of patients with heart and arterial diseases [33–35]. Taking all of these observations into account, the present study emphasizes that, using ambulatory blood pressure recordings, subjects with carotid endarterectomy are characterized by a disproportionate increase in SBP and pulse pressure, with possible resultant changes in pulsatile stress of the arterial wall. Since it is widely admitted that old subjects with isolated systolic hypertension and increased pulse pressure should be treated by drug therapy [36], the present findings have important clinical applications: the use of blood pressure monitoring for a detailed assessment of blood pressure following carotid endarterectomy, the possible use of antihypertensive drugs and the adaptation of the time of drug intake in such circumstances.

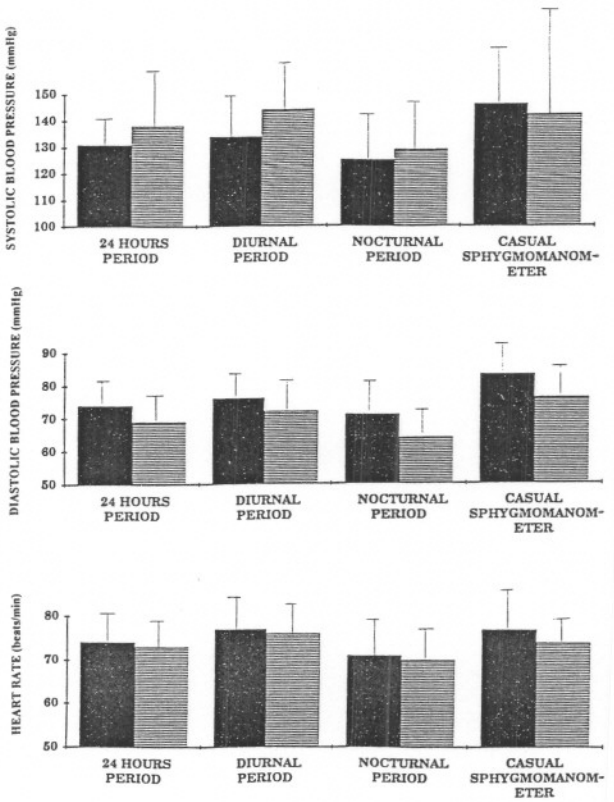

Fig. 2. Comparison of blood pressure and heart rate in subjects with unilateral (■) and bilateral (▤) carotid endarterectomy. No significant differences were observed.

Acknowledgements

The authors thank the Cardiovascular Research and Education Institute for its collaboration, and A. Seban for secretarial assistance.

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