Clinical and biochemical criteria in the detection of renal artery stenosis

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Objective To investigate methods to diagnose renal artery stenosis (RAS) among the general hypertensive population.

Methods We studied the value of clinical and biochemical characteristics at the outpatient clinic to identify subjects with a renal artery narrowing of more than 50% of the luminal surface among 1047 hypertensive patients. Included in the analysis were: blood pressure, age, sex, body mass index, endogeneous creatinine clearance, smoking and plasma renin activity.

Results Among the 1047 patients, 355 were selected for angiography. In this subgroup 104 patients (29%) had RAS. The subjects with RAS had significantly higher diastolic and systolic blood pressures than did those without stenosis. Forward stepwise logistical regression analysis showed that systolic blood pressure, stimulated plasma renin activity and smoking were the most predictive independent screening variables for the presence of RAS. Yet, none of these characteristics or their combinations were sufficiently sensitive to distinguish reliably between patients with essential hypertension and those with RAS. Sytolic blood pressure >160 mmHg or diastolic blood pressure >100 mmHg on automatic (Dinamap) recording as criteria selected a subgroup of patients with a RAS prevalence of 30%.

Conclusions By using blood pressure screening criteria a subgroup of hypertensive patients with a high prevalence of RAS can be formed in whom further invasive tests for RAS are indicated and efficient.

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Introduction

At present the only method to diagnose renal artery stenosis (RAS) with certainty is angiography [1,2]. The low prevalence of RAS among the general hypertensive population renders angiography, considering its cost and invasive nature, inappropriate as a screening procedure. However, the definitive treatment modalities presently available for this condition mandate a proper search for RAS among hypertensive subjects [3].

Extensive studies of alternative non-invasive methods have not yet provided a replacement for angiography [4–6]. Most of the screening methods investigated proved not to be sufficiently reliable because of their relatively low sensitivities [3].

Therefore, clinical criteria are applied to select from among the general hypertensive population those subjects who have a high likelihood of stenosis and to restrict invasive diagnostic interventions to these patients. By doing so, on the one hand the number of diagnostic interventions is limited and on the other hand the diagnosis of renovascular disease is not overlooked in too great a proportion of patients. Many different clinical criteria are applied in this selection procedure [7]. Although age, blood pressure and physical characteristics such as flank bruits are generally accepted [7], their accuracy in this respect is not known.

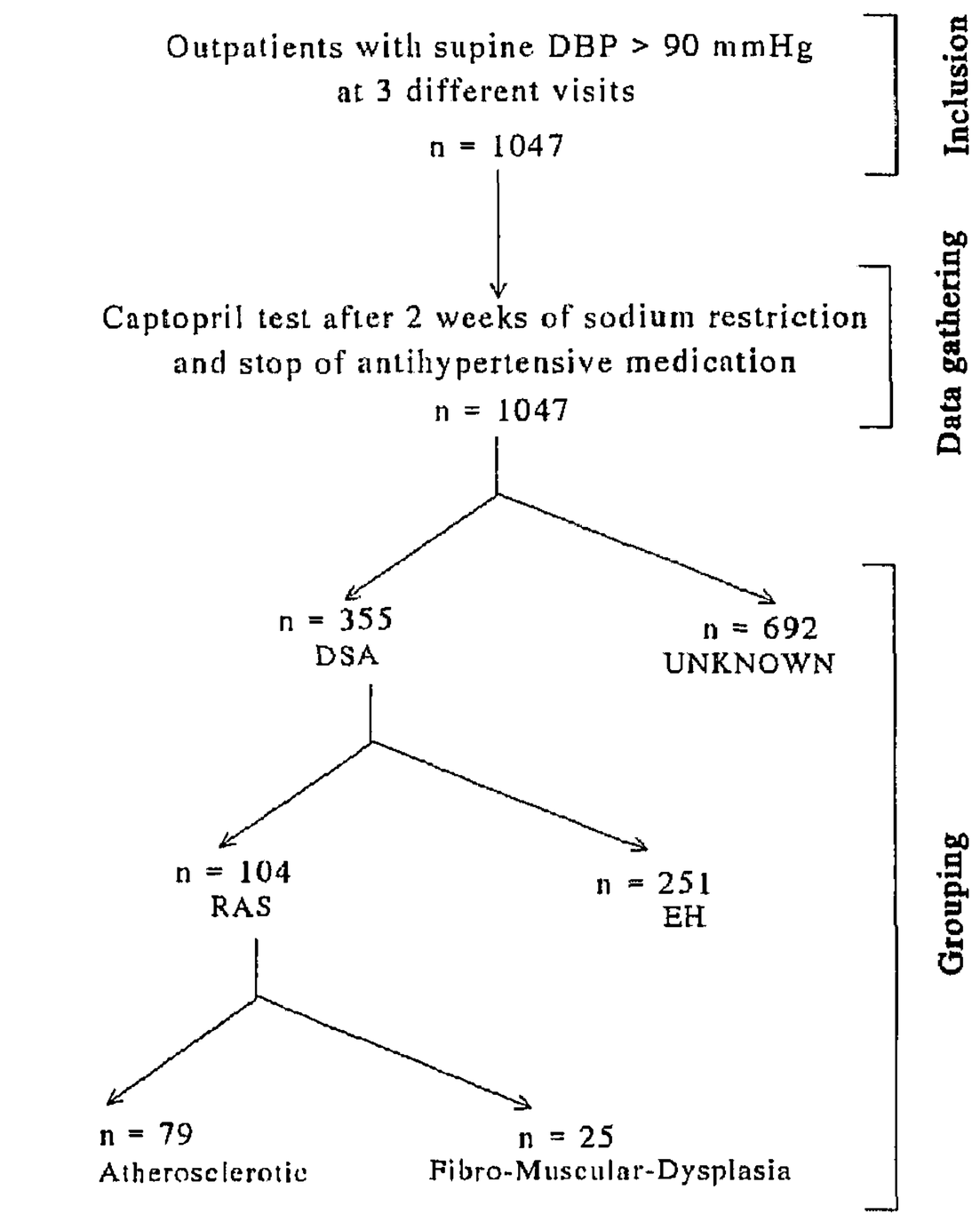
With the determination of the best predictive selection criteria for RAS, the management of hypertensive patients can be improved and the size of subgroups selected for angiography can possibly be reduced. We studied the values of various clinical and biochemical criteria in this respect in a group of 1047 hypertensive patients of the outpatient clinic of our tertiary referral hospital.

Methods

Patients

From the outpatient clinic, 1047 newly referred hypertensive patients were investigated by a prospectively designed protocol. Patients were referred by general practioners or internists from other hospitals. The outline of the procedure is depicted in Figure 1. The clinical and biochemical characteristics studied were: age, blood pressure, body mass index (BMI), sex, endogenous creatinine clearance (ECC) computed by the formula of Cockroft [8], plasma renin activity (PRA) [9], serum potassium concentration [10], smoking, malignant hypertension, abdominal bruits, claudication of the legs, congestive heart

Fig. 1.



The outline of the procedure that resulted in the three groups of patients.

failure, and a history of myocardial infarction, angina pectoris, cerebrovascular accident, low age at onset of hypertension and resistance to therapy of the hypertension. Hypertension was diagnosed when mean of three consecutive supine sphygmomanometer diastolic blood pressure readings at the outpatient clinic on three different visits was above 90 mmHg [11].

Data gathering

When hypertension had been established, the first step in the diagnosis of all of the patients consisted of a so-called captopril test. This test was performed after the subjects had stopped both antihypertensive medication and sodium restriction for at least 2 weeks. The procedure was performed at the outpatient clinic, during which the patients remained supine in a quiet room. Their blood pressure was recorded every 3 min by an automatic blood pressure device (Critikon Dinamap 1846 SX, Critikon, Tampa, Florida, USA) throughout the procedure. Blood samples for creatinine and PRA determination were extracted after 20 min of supine rest by the patient. Sixty minutes after the administration of an oral dose of 25 mg captopril, samples for PRA determination were again extracted. In order to standardize the blood pressure data, only the blood pressure recordings obtained using the Dinamap device were used in the analysis. The average of the three blood pressure readings just before captopril administration was taken as the baseline blood pressure. If the obtained data listed above were unreliable or missing because of technical failure, then these data were omitted and a missing value was entered in the analysis. Therefore, the total number of observations is not 1047 for all of the characteristics presented.

Patients with other causes of secondary hypertension were excluded from this study. The presence of secondary hypertension was investigated by determination of serum concentrations of electrolytes, aldosterone [12] and catecholamines [13]; urine excretions of creatinine, metanephrines and protein were also determined, and urine microscopy was performed.

Grouping

In a subgroup of 355 patients arterial digital subtraction angiography (DSA) of the renal arteries was performed. The following criteria were used in the selection of these patients [1]: the presence of an abdominal bruit above the renal artery or in the flank; the onset of hypertension having been before the age of 20 years or after the age of 45 years; accelerated or malignant hypertension, hypertensive encephalopathy or an established referral diastolic blood pressure (DBP) over 115 mmHg by sphygmomanometry; and treatment-resistant hypertension, characterized by a DBP over 95 mmHg despite adequate two-regimen antihypertensive medication and good compliance. The results of the captopril test' were not used as a selection criterion for angiography. The angiographies of the renal arteries were performed on an outpatient basis by arterial digital subtraction angiography and the results were studied by experienced radiologists. Only patients with a narrowing of more than 50% of the luminal surface measured by angiography were considered to have RAS.

By applying the above criteria a subgroup was formed in which a DSA was performed and the presence or absence of RAS thereby ascertained. Thus the value of clinical and biochemical criteria to discriminate between essential hypertension and hypertension with RAS in this subgroup could be investigated.

To study the univariate relationship between the clinical and biochemical data and the prevalence of RAS, values of these parameters were grouped into classes. Within these classes the prevalence of RAS was determined and trends in the differing prevalence of RAS between these classes were analysed.

In order to investigate the potential role of the above-mentioned selection criteria in the detection of RAS, a separate analysis was performed in those patients who underwent arteriography. Differences between patients with RAS based on atherosclerosis or fibromuscular dysplasia (FMD) were also investigated.

Statistical analysis

The differences in the continous variables in the whole group of hypertensive patients were analysed by using Student's t-test or Wilcoxon's rank sum test. $P<0.05$ was considered statistically significant. All of the tests were two-sided. The discriminating power of the clinical and biochemical data in detecting the presence of RAS was investigated using a forwards stepwise logistical regression analysis. In the first analysis all of the parameters were included for those patients who had undergone angiography and for whom all of these data were available. In the second analysis claudication of the legs and abdominal bruits were omitted because these parameters cannot be used as screening parameters owing to their low frequency of occurrence in the hypertensive population. Differences between subgroups were tested using a c^2-test. Values are expressed as means ± SD or as medians (25–75% ranges) unless indicated otherwise.

Results

Patients were referred for various reasons, of which failure to respond to antihypertensive medication was most common. On the basis of outpatient clinic blood pressure measurements in 1047 Caucasian patients, a diagnosis of hypertension was made. In these 1047 patients a hypertension work-up was performed and their data analysed. In 37 patients the three baseline automatic blood pressure readings were considered insufficiently accurate to use in the analysis. The reasons for this were technical problems with the equipment and included movement by the patients. For the analysis of characteristics other than blood pressure the data for these patients were used when appropriate. The eight patients with malignant hypertension were treated with dihydropyridine calcium antagonists during evaluation. In all of the other patients antihypertensive medication was discontinued for at least 2 weeks.

Whole-group characteristics

The entire group consisted of 492 male and 555 female patients with a mean BMI of 26.5 ± 4.7 kg/m^2. The mean blood pressure measured using the Dinamap device was 154 ± 24/92 ± 14 mmHg. The serum creatinine concentration averaged 90.7 ± 38.5 mol/l and the calculated ECC averaged 94.3 ± 35.6 ml/min. There were only slight differences in blood pressure and renal function between men and women (Table 1).

Table 1 Clinical and biochemical characteristics of 1047 hypertensive patients

	All patients (n = 1047)	Women (n = 555)	Men (n = 492)
Age (years)	48 ± 13	48 ± 14	49 ± 12
Body mass index (kg/m^2)	26.5 ± 4.7	26.6 ± 5.6	26.3 ± 3.6
Systolic blood pressure (mmHg)	154 ± 24	153 ± 24	155 ± 24
Diastolic blood pressure (mmHg)	92 ± 14	90 ± 14**	93 ± 14
Serum creatinine level (mol/l)	91 ± 39	80 ± 23**	103 ± 48
Endogenous creatinine clearance rate (ml/min)	94 ± 36	91 ± 38**	98 ± 32
Serum potassium level (mmol/l)	3.8 ± 0.4	3.8 ± 0.4**	3.9 ± 0.4
PRA1 (nmol/l per h)	0.9 (0.4–1.6)	0.8 (0.4–1.6)	1.0 (0.4–1.9)
PRA2 (nmol/l per h)	1.1 (0.4–2.8)	0.9 (0.4–2.3)	1.3 (0.6–3.5)

Values are expressed as means ± SD or medians (25%–75% ranges). PRA1, plasma renin activity at baseline; PRA2, plasma renin activity 60 min after captopril therapy. Blood pressures were obtained by automatic blood pressure registration. **$P<0.01$, versus men.

Differences arising from the presence of RAS

Of the 355 patients in whom angiography was performed, RAS was present in 104 (29%). Bilateral stenosis was present in 10 patients. The established prevalence of RAS in the entire group was therefore at least 10%.

For further analysis three different groups were formed: a group with RAS, a group without RAS henceforth referred to as essential hypertensives and a group in whom DSA had not been performed and the presence of RAS had not been determined (Fig. 1). The characteristics of the first two subgroups were compared and are listed in Table 2 together with the values for the third group. SBP and DBP were significantly higher in the RAS group than they were in the essential hypertension group (Table 2). Renal function represented by ECC was significantly lower in the group with RAS than it was in the group without RAS.

The baseline PRA was significantly higher in the patients with RAS. Furthermore, the captopril-stimulated PRA reached significantly higher levels in the RAS group than it did in the essential hypertension group. The median increase in PRA was 2.7 nmol/l per h (0.2–17.7) [median (25 and 75% quantiles)] in the patients with RAS and

Table 2 Clinical and biochemical characteristics of three subgroups of hypertensive patients (patients with renal artery stenosis, patients with essential hypertension and patients characterized as of unknown status because renal angiography had not been performed)

Total	Renal artery stenosis (n = 104)	Essential hypertension (n = 251)	Unknown status (n = 692)
Age (years)	50 ± 12*	46 ± 13	49 ± 13
Body mass index (kg/m^2)	24.5 ± 4.0*	26.3 ± 4.9	26.8 ± 4.7
Systolic blood pressure (mmHg)	170 ± 25*	157 ± 23	151 ± 23
Diastolic blood pressure (mmHg)	100 ± 14*	96 ± 15	89 ± 13
Serum creatinine level (mol/l)	107 ± 61*	91 ± 41	88 ± 32
Endogenous creatinine clearance rate (ml/min)	78 ± 29*	95 ± 29	97 ± 38
Serum potassium level (mmol/l)	3.8 ± 0.4	3.8 ± 0.4	
PRA at baseline (nmol/l per h)	2.0 (0.9–3.4)*	1.0 (0.4–2.0)	0.8 (0.4–1.4)
PRA after 25 mg captopril (nmol/l per h)	4.8 (1.2–22.2)*††	1.3 (0.4–3.9)††	1.0 (0.4–2.0)††

Values are expressed as means ± SD or medians (25%–75% quantiles). PRA, plasma renin activity. Blood pressures were obtained by using an automatic blood pressure measuring device. *$P<0.05$, versus essential hypertensives; ††$P<0.01$, versus PRA at baseline.

Table 3 Renal artery stenosis in classes of characteristics of 1047 hypertensive patients

Characteristic	n	DSA (RAS)
Age (years)		
<30	102	40 (7)
30–40	156	51 (8)
40–50	278	100 (33)
50–60	287	95 (30)
60–70	178	61 (23)
>70	46	8 (3)
Total	1047	355 (104)
Body mass index (kg/m²)		
<20	51	22 (8)
20–22.5	139	61 (23)
22.5–25	207	81 (32)
25–27.5	240	75 (19)
27.5–30	154	44 (8)
30–35	137	38 (11)
35–40	36	14 (1)
>40	16	4 (0)
Total	980	339 (102)
Diastolic blood pressure (mmHg)		
<70	50	11 (1)
70–80	128	25 (5)
80–90	278	60 (18)
90–100	273	102 (25)
100–110	173	73 (21)
>110	91	58 (22)
Total	993	330 (92)
Systolic blood pressure (mmHg)		
<120	47	10 (1)
120–140	239	58 (11)
140–160	348	116 (22)
160–180	231	83 (28)
180–200	106	48 (23)
>200	35	23 (11)
Total	1006	338 (96)
Endogenous creatinine clearance (ml/min)		
<70	205	81 (38)
>70	793	261 (64)
Total	998	342 (102)

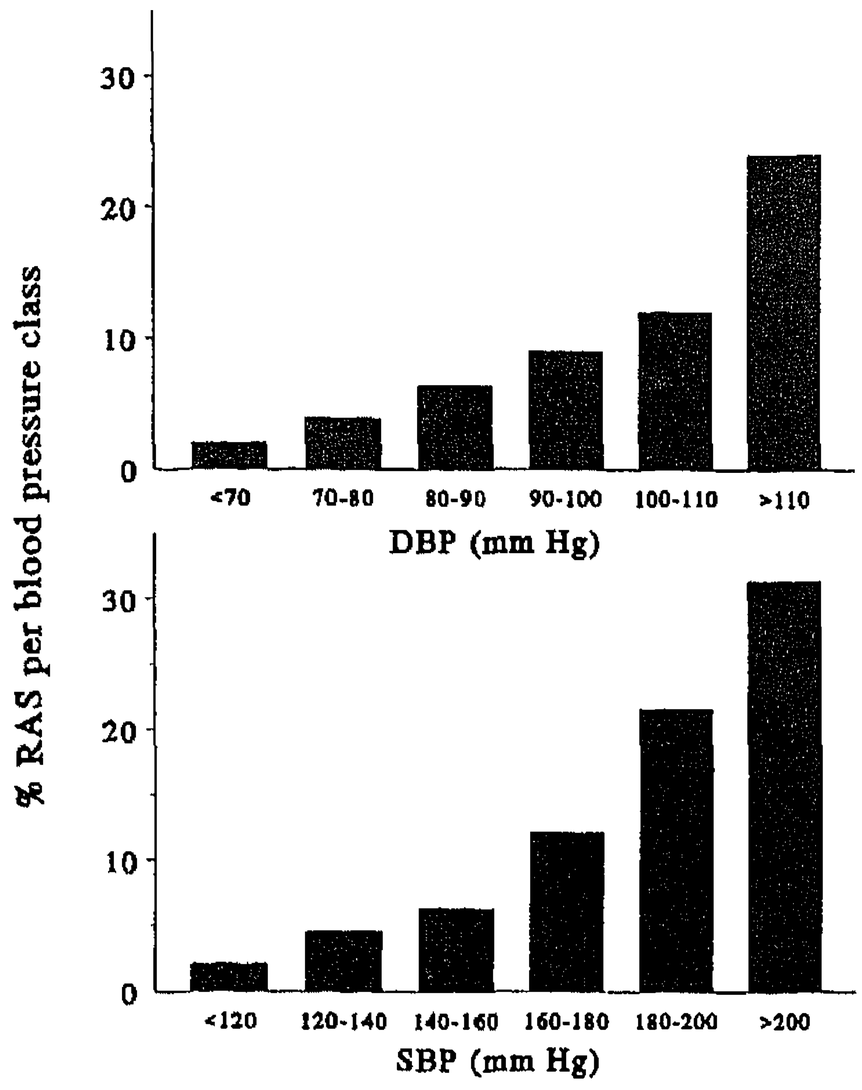
DSA, digital substraction angiography; RAS, renal artery stenosis.

0.3 nmol/l per h (0.0–1.7) in the subjects with essential hypertension ($P<0.01$, Table 2). Also, the relative median increases in PRA of 140% (24–381) and 25% (0–108) in the RAS and essential hypertension groups, respectively, were significantly different ($P<0.01$). Both baseline and stimulated PRA were lower in the group which had not undergone angiography than they were in the other groups. The absolute median increase in PRA in the group with unknown RAS status was 0.09 nmol/l per h (−0.03 to 0.65, Table 2), which is a relative change from baseline of 12% (−5 to 58).

Differences based on classes of characteristics

The prevalence of RAS increased with higher DBP and SBP (Table 3, Fig. 2). Also, in the class with a low ECC, the overall RAS prevalence of 19% was more than twice as high as that in the class with a higher ECC (8%). The RAS prevalence showed a small but insignificant rise with increasing age (Fig. 3). Although the prevalence of RAS was highest in the lower BMI classes, there was no significant inverse correlation.

Fig. 2.



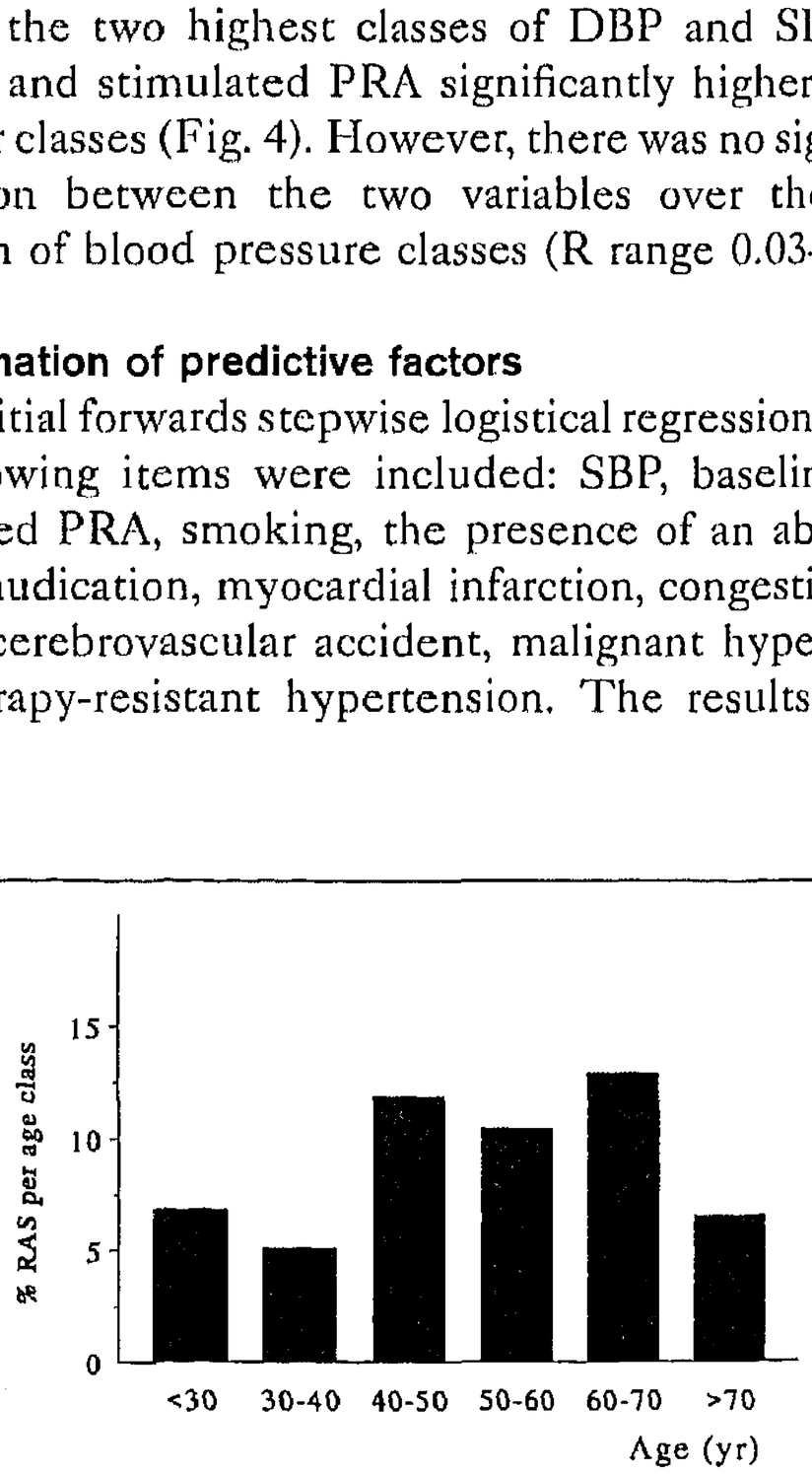
The percentage of patients with renal artery stenosis (RAS) detected by angiography per blood pressure class for diastolic blood pressure (DBP) and systolic blood pressure (SBP). Blood pressure classes were compiled from all of the 1047 hypertensive patients.

Only in the two highest classes of DBP and SBP were baseline and stimulated PRA significantly higher than in the other classes (Fig. 4). However, there was no significant correlation between the two variables over the entire spectrum of blood pressure classes (R range 0.03–0.12).

Discrimination of predictive factors

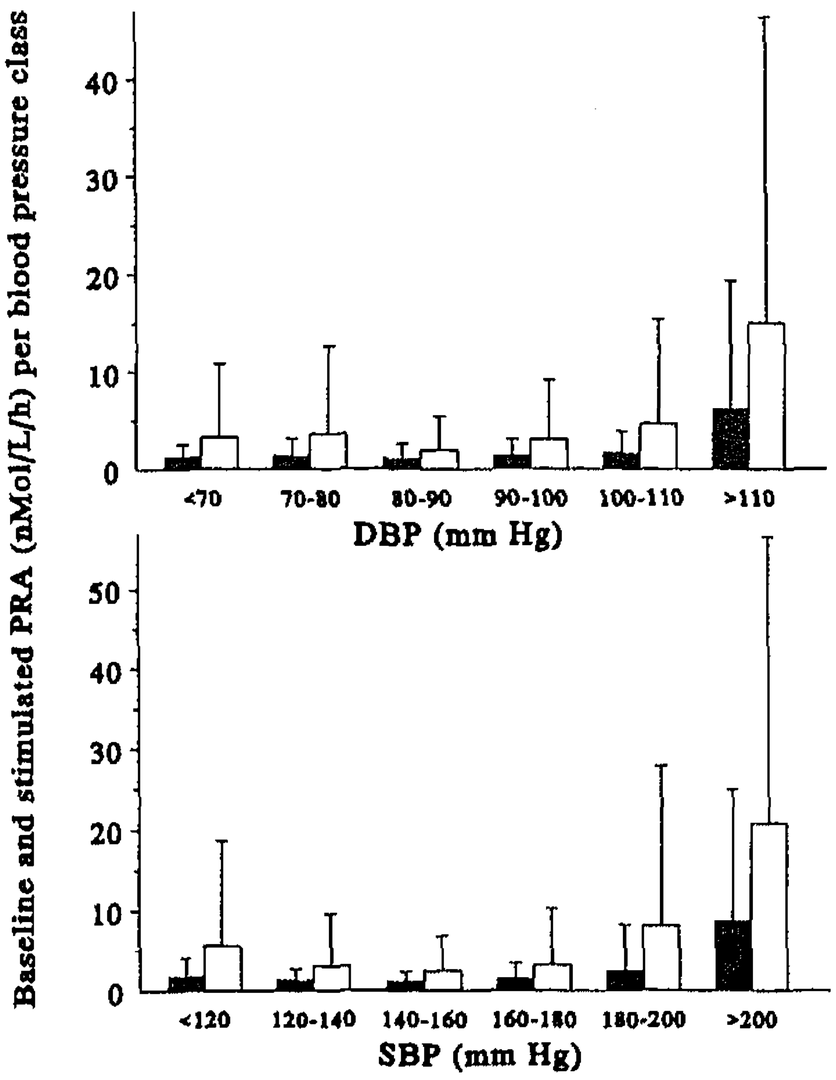
In the initial forwards stepwise logistical regression analysis the following items were included: SBP, baseline PRA, stimulated PRA, smoking, the presence of an abdominal bruit, claudication, myocardial infarction, congestive heart failure, cerebrovascular accident, malignant hypertension and therapy-resistant hypertension. The results for the

Fig. 3.



The percentage of patients with renal artery stenosis (RAS) detected by angiography per age class. Age classes were compiled from all of the 1047 hypertensive patients.

Fig. 4.



The mean (SD) baseline (■) and stimulated (□) plasma renin activity (PRA) per blood pressure class for diastolic blood pressure (DBP) and systolic blood pressure (SBP). Blood pressure classes were compiled from all of the 1047 hypertensive patients.

Table 4 **Outcomes of different selection criteria for the detection of renal artery stenosis applied to 355 patients who had undergone angiography of whom 104 had renal artery stenosis**

Criterion	Sensitivity (%)	Specificity (%)
Logistic regression formula 1	52	85
Logistic regression formula 2	44	84
Müller criteria [14]	30	92
DBP > 100 mmHg	44	66
SBP > 160 mmHg	64	63
DBP > 100, SBP > 160 mmHg	40	77
ECC < 70 ml/min	37	82
Serum potassium concentration < 3.5 mmol/l	17	86
PRA1 > 5 nmol/l per h	21	91
ΔPRA > 2 nmol/l per h	61	74
ΔPRA > 3 nmol/l per h	51	80
PRA1 > 2.5 nmol/ per h and ECC < 70 ml/min	23	93
PRA1 > 2.0 nmol/l per h and Δ%PRA > 150% and SBP > 140 mmHg	34	93
PRA1 > 2.5 nmol/l per h and SBP > 140 mmHg	43	81
PRA1 > 2.0 nmol/l per h and Δ%PRA > 150%	42	90
Smoking	73	52
Claudication	29	94
Congestive heart failure	3	98
Myocardial infarction	7	94
Abdominal bruits	23	94
Cerebrovascular acccident	3	97
Malignant hypertension	2	97
Therapy resistance	61	50
Low age at onset of hypertension	6	90

DBP, diastolic blood pressure; SBP, systolic blood pressure; PRA1, baseline plasma renin activity; ΔPRA, change in PRA after captopril therapy; Δ%PRA, percentage of ΔPRA from PRA1; ECC, endogenous creatinine clearance rate.

group in which all of the patients had undergone angiography showed that the stimulated PRA (PRA2), smoking, claudication, abdominal bruits and therapy resistance all contributed independently to the probability of having RAS ($P<0.05$). From the logistical regression analysis, the intercept and coefficients with standard error and P-value for the remaining variables were obtained: intercept = 2.67 ± 0.3 ($P<0.001$), stimulated PRA 0.0549 ± 0.0125 ($P<0.001$), smoking 0.728 ± 0.3175 ($P = 0.02$), claudication 1.6557 ± 0.4404 ($P<0.001$), abdominal bruits 1.4779 ± 0.4629 ($P<0.01$) and therapy resistance 0.7711 ± 0.3189 ($P = 0.02$). An estimate for the probability of having RAS can be computed as

$$\text{prob(RAS)} = Z/(1 + Z),$$

where $Z = \exp[-2.67 - 0.054 \times \text{PRA2} + 0.73 \times \text{smoking} + 1.66 \times \text{claudication} + 1.48 \times \text{abdominal bruits} + 0.77 \times \text{therapy resistance}]$.

If it is decided that RAS is present when this computed probability exceeds 50%, then, upon resubstitution into the equation of the patients who underwent angiography, this formula has a sensitivity of 52% and a specificity of 85% (Table 4). The positive and negative predictive values are 59 and 81%, respectively.

A second forwards stepwise logistical regression analysis in which claudication, abdominal bruits and malignant hypertension were omitted, showed that SBP, stimulated PRA (PRA2) and smoking contributed independently to the probability of having RAS ($P<0.05$). The stimulated PRA had the strongest relationship with RAS ($P<0.001$). From the logistical regression analysis, the intercept and coefficients with standard error and P-value for the remaining variables were obtained: intercept = 4.32 ± 0.99 ($P<0.001$), stimulated PRA 0.0527 ± 0.0125 ($P<0.001$), smoking 0.9481 ± 0.3016 ($P<0.01$) and SBP 0.0748 ± 0.00597 ($P = 0.01$). Here Z can be computed as

$$Z = \exp[-4.32 - 0.053 \times \text{PRA2} + 0.95 \times \text{smoking} + 0.01 \times \text{SBP}]$$

If it is decided that RAS is present when the computed probability exceeds 50%, then, upon resubstitution into the equation of the patients who underwent angiography this formula has a sensitivity of 44% and a specificity of 84% (Table 4). The positive and negative predictive values are 53 and 78% respectively.

When the criteria of Müller [14], which are often cited in the literature with test results of 100% sensitivity and 100% specificity, were applied to the same population, this resulted in a sensitivity of 31%, a specificity of 92%, a positive predictive value of 61% and a negative predictive value of 76% in the detection of RAS (Table 4). Table 4 illustrates that neither PRA changes nor blood pressure criteria alone or in combination with other clinical data were of additional value in detecting RAS.

Table 5 incidence of selection criteria for angiography in patients with essential hypertension versus those with renal artery stenosis and renal artery stenosis caused by atherosclerosis versus renal artery stenosis caused by fibromuscular dysplasia (FMD)

Criterion	Essential hypertension (n = 251)	Renal artery stenosis		
		All (n = 104)	Atherosclerosis (n = 79)	FMD (n = 25)
Age (years)	46 ± 12ttt	50 ± 12	54 ± 10	40 ± 15*
Smoking	109 (43)ttt	69 (66)	65 (82)	9 (36)*
Potassium concentration (mmol/l)	3.8 ± 0.4	3.8 ± 0.4	3.8 ± 0.5	3.9 ± 0.3
Potassium concentration <3.5 mmol/l	31 (12)	16 (15)	15 (19)	4 (16)
Men	119 (47)	57 (55)	50 (63)	7 (28)
Women	132 (53)	47 (45)	29 (37)	18 (72)
Claudication	14 (6)ttt	27 (26)	27 (34)	2 (8)*
Congestive heart failure	5 (2)	3 (3)	5 (6)	0 (0)
Myocardial infarction or angina pectoris	13 (5)	7 (7)	9 (11)	1 (4)
Cerebrovascular accident	7 (3)	3 (3)	3 (4)	0 (0)
Age at onset <20 years	24 (10)	6 (6)	2 (3)	8 (32)*
Abdominal bruits	14 (6)ttt	22 (21)	14 (18)	10 (40)*
Malignant hypertension	6 (3)	2 (2)	3 (4)	0 (0)
Resistance to therapy	115 (46)	57 (55)	54 (67)	11 (44)

Number of patients per group, percentage between brackets (%). *$P<0.05$, versus renal artery stenosis caused by atherosclerosis; ttt$P<0.001$, versus renal artery stenosis.

Table 5 shows the results of the analysis of markers for RAS in patients who had undergone DSA and for whom all of these data were available. The group with RAS was divided into two by ascribing the cause of the stenosis to atherosclerosis or to FMD. The serum potassium concentration was equal in all groups and not correlated with RAS. There were significantly more men and smokers in the group with RAS caused by atherosclerosis ($P<0.001$) than there were in the group with RAS caused by FMD. Members of the latter group were significantly younger ($P<0.01$). Claudication ($P<0.05$) was significantly commoner among the patients with RAS caused by atherosclerosis, whereas female sex ($P<0.001$), a low age at onset of hypertension ($P<0.05$) and the presence of an abdominal bruit ($P<0.05$) were associated with RAS caused by FMD.

Discussion

The mean supine baseline blood pressure in the 1047 hypertensive patients included in this study was 154 ± 24/92 ± 14 mmHg. These values were obtained during a standardized procedure using a Dinamap automatic blood pressure measuring device. The Dinamap device is based on an oscillometric principle that registers blood pressure values 3–10 mmHg lower than corresponding sphygmomanometric measurements, both for DBP and for SBP [15–17]. Especially in hypertensive ranges the values are lower [18]. In our clinic, the Dinamap device measures on average DBP 6 ± 7 mmHg lower and SBP 11 ± 9 mmHg lower than the usual sphygmomanometric method (unpublished data). The presented data therefore underestimate the actual blood pressures of the patients in this study.

Some remarkable differences in blood pressure were present among the three groups of patients, i.e. those with RAS, those with essential hypertension and those in whom angiography had not been performed. Although the most important selection criterion for angiography was the blood pressure, the subjects with RAS still had a significantly higher blood pressure than did those with essential hypertension. This emphasizes the importance of blood pressure criteria in the selection of patients for angiography. The multivariate analysis to investigate the relationship of various criteria to the presence of RAS also showed blood pressure to be one of the three independent discriminators for the presence of RAS.

Among the patients with SBP > 157 mmHg or DBP > 97 mmHg, on Dinamap recording, the prevalence of RAS was 30%. SBP > 170 mmHg or DBP > 105 mmHg measured by sphygmomanometry can be considered equivalent to the Dinamap recordings. So, in patients with these blood pressure levels after 2 weeks without antihypertensive therapy without a sodium-restricted diet, further diagnostic action to detect RAS is warranted, considering this high prevalence of RAS.

The logistical regression formulae show that the PRA after angiotensin converting enzyme inhibition has statistically the strongest relationship with the presence of RAS. However, as has been shown repeatedly, this increase in PRA cannot be used as a screening criterion for the presence of RAS in the individual patient because the sensitivity in this respect is too low [4]. In the present study we used different interpretations of the rise in PRA after captopril therapy in relation to the presence of RAS. At no point could the rise in PRA be used to detect RAS in the individual patient because the sensitivities remained low. By relying on changes in PRA a great number of stenoses would remain undetected. For the same reason none of the other patient characteristics could be used as a screening criterion for the presence of RAS. Neither did combinations of PRA and other studied criteria provide an acceptable sensitivity for detecting RAS. Also, the formulae of Müller [14] and our own logistic regressions gave no satisfactory results in this large population (Table 4).

The first logistic regression analysis showed that, besides PRA, claudication and abdominal bruits are strong predictors for the presence of RAS. This is not surprising and these clinical findings have long been used on a more or less intuitive basis as selection criteria for angiography. Congestive heart failure, myocardial infarction, cerebrovascular accident, malignant hypertension and a low age at onset of hypertension also showed a high specificity for RAS. However, their prevalence among this group was very minor, because of which they can of course not be used in the screening for RAS. Therefore, in order to find useful screening criteria, a second regression analysis was performed in which claudication and abdominal bruits

were omitted. Besides the already-mentioned PRA, SBP turned out to be an independent predictor for RAS. In both analyses smoking also turned out to be an independent predictor for the presence of RAS. In contrast to abdominal bruits and claudication, smoking is very common in the hypertensive population leading to a very low specificity when it is used as a selection criterion (Table 4), which renders smoking unsuitable as a screening selection criterion. So, the blood pressure is the most useful and practical clinical clue to the presence of secondary hypertension in this study.

The actual prevalence of RAS in the entire hypertensive population of this study is at least 10%. Given the prevalence described in various studies, it can be assumed that the number of patients with a stenosis in the group not examined arteriographically could only have been low [19,20]. So, we can use the prevalence established in our patients as a reference point for further discussion.

What diagnostic tools are presently available to detect RAS? Performing arteriography in all of the 1047 patients to disclose RAS in 10% is not a realistic option. A cost-effective non-invasive screening procedure would be preferrable. In this respect non-invasive imaging techniques are an option. Doppler ultrasonography performed in the entire group would be costly at the gain of discovering RAS in at most 60% of the patients with proved RAS [5, 21,22]; in this study, in only 62 of 104 patients. Magnetic resonance angiography of the renal arteries shows RAS and with application of the latest developments in the technique gives very reliable results, but to use it as a screening procedure would be very costly [6,23]. Diethylenetriamine pentaacetic acid or technetium 99m mercaptoacetyltriglycine renographies have an overall sensitivity for RAS of approximately 70% [24,25]. Thus, screening of all of the present patients with these renographies would have resulted in about 70 of the 104 patients with RAS being detected and a superfluous scan performed in 943 patients. An objection against this interpretation might be that, with renography, only those patients with stenosis are detected that have true renovascular hypertension, defined by cure or improvement of blood pressure after removal of the stenosis [26]. However, multiple large-scale studies have clarified that the sensitivity of renography in this respect is even lower than that for stenosis as such [3,27].

Newer procedures using acetylsalycilic acid, based on the renin- and prostaglandin-dependences of high blood pressure in patients with RAS, are bound to suffer from the same drawbacks as did previous procedures based on the renin-dependence of high blood pressure in the case of RAS and can only be judged in more detail by further studies [28].

At present, the most adequate practical clinical approach to seek RAS in hypertensive patients is the use of blood pressure criteria to identify a subgroup with a high prevalence of RAS. In such a group it is worthwhile to perform renal angiography if there are reasons to suspect secondary hypertension. In doing so the clinician has to bear in mind that RAS in some patients is not detected. A reasonable safety net is introduced if any difficulty in the treatment of a hypertensive patient or a decrease in renal function during treatment is regarded as a clinical criterion for further diagnostic study to detect RAS. The present study shows that blood pressure criteria are more adequate means to select hypertensive patients for diagnosis of RAS than are various sophisticated combinations of clinical and biochemical parameters.

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