THE EFFECT OF BALLOON ANGIOPLASTY ON HYPERTENSION IN ATHEROSCLEROTIC RENAL-ARTERY STENOSIS

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ABSTRACT

Background Patients with hypertension and renal-artery stenosis are often treated with percutaneous transluminal renal angioplasty. However, the long-term effects of this procedure on blood pressure are not well understood.

Methods We randomly assigned 106 patients with hypertension who had atherosclerotic renal-artery stenosis (defined as a decrease in luminal diameter of 50 percent or more) and a serum creatinine concentration of 2.3 mg per deciliter (200 μmol per liter) or less to undergo percutaneous transluminal renal angioplasty or to receive drug therapy. To be included, patients also had to have a diastolic blood pressure of 95 mm Hg or higher despite treatment with two antihypertensive drugs or an increase of at least 0.2 mg per deciliter (20 μmol per liter) in the serum creatinine concentration during treatment with an angiotensin-converting–enzyme inhibitor. Blood pressure, doses of antihypertensive drugs, and renal function were assessed at 3 and 12 months, and patency of the renal artery was assessed at 12 months.

Results At base line, the mean ($\pm$SD) systolic and diastolic blood pressures were 179$\pm$25 and 104$\pm$10 mm Hg, respectively, in the angioplasty group and 180$\pm$23 and 103$\pm$8 mm Hg, respectively, in the drug-therapy group. At three months, the blood pressures were similar in the two groups (169$\pm$28 and 99$\pm$12 mm Hg, respectively, in the 56 patients in the angioplasty group and 176$\pm$31 and 101$\pm$14 mm Hg, respectively, in the 50 patients in the drug-therapy group; $P=0.25$ for the comparison of systolic pressure and $P=0.36$ for the comparison of diastolic pressure between the two groups); at the time, patients in the angioplasty group were taking 2.1$\pm$1.3 defined daily doses of medication and those in the drug-therapy group were taking 3.2$\pm$1.5 daily doses ($P<0.001$). In the drug-therapy group, 22 patients underwent balloon angioplasty after three months because of persistent hypertension despite treatment with three or more drugs or because of a deterioration in renal function. According to intention-to-treat analysis, at 12 months, there were no significant differences between the angioplasty and drug-therapy groups in systolic and diastolic blood pressures, daily drug doses, or renal function.

Conclusions In the treatment of patients with hypertension and renal-artery stenosis, angioplasty has little advantage over antihypertensive-drug therapy. (N Engl J Med 2000;342:1007-14.)

EXPERIMENTS conducted by Goldblatt and colleagues[1] on the effects of renal-artery constriction in animals led to the recognition that renal-artery stenosis may cause hypertension. Initially, surgical revascularization was the only treatment for renal-artery stenosis,[2,3] but percutaneous transluminal balloon angioplasty,[4] with or without stent placement, later supplanted surgery as the preferred treatment.[5] In uncontrolled, retrospective studies of balloon angioplasty, 36 to 100 percent of patients with hypertension had some reduction in blood pressure, with the highest rates of response in patients with fibromuscular dysplasia,[6] but in few patients, however, was blood pressure restored to normal levels. In two small, randomized studies, the benefit of balloon angioplasty was even smaller,[7,8] suggesting that the general enthusiasm for this procedure may not be justified.

We report the results of a multicenter, randomized, controlled comparison of balloon angioplasty and antihypertensive-drug therapy for the treatment of atherosclerotic renal-artery stenosis associated with hypertension and normal or mildly impaired renal function.

METHODS

This prospective, randomized study was conducted at 26 centers in the Netherlands between January 1993 and November 1998. The study was designed to identify patients with hypertension caused by renal-artery stenosis and to evaluate their treatment. The current report focuses on the treatment phase of the study, in which 106 patients with atherosclerotic renal-artery stenosis were randomly assigned to undergo balloon angioplasty of the renal artery (without stent placement) or to receive antihypertensive-drug therapy. The study was approved by the institutional review board at each participating center, and all patients provided written informed consent.

The diagnostic phase of the study involved 1205 patients, 18 to 75 years old, who had been referred to the participating centers because of difficult-to-treat hypertension associated with normal

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or mildly impaired renal function (defined as a serum creatinine concentration of ≤2.3 mg per deciliter [200 μmol per liter]). The diagnostic workup included a medical history, a physical examination, and laboratory studies, renal scintigraphy after the administration of captopril, and renal arteriography.[9] Patients were excluded if they had cancer, hypertension caused by a condition other than renovascular disease (e.g., renal parenchymal disease, primary aldosteronism, or hypercortisolism) or unstable coronary artery disease or heart failure, or if they were pregnant. Renal arteriography was performed in 543 patients because their diastolic blood pressure, measured at three consecutive outpatient visits one to three weeks apart, was at least 95 mm Hg despite treatment with a standardized regimen of two antihypertensive drugs or because their serum creatinine concentration on the second or third visit had risen by at least 0.2 mg per deciliter (20 μmol per liter) during treatment with an angiotensin-converting–enzyme inhibitor. Of these 543 patients, 169 were found to have ostial or nonostial renal-artery stenosis (defined as a decrease in luminal diameter of ≥50 percent) and thus were considered candidates for the treatment phase.

Patients were excluded from the treatment phase of the study if they had any of the following: a single functioning kidney and a serum creatinine concentration greater than 1.7 mg per deciliter (150 μmol per liter); an affected kidney that was less than 8.0 cm long, as determined by ultrasonography; total occlusion of the renal artery; an aortic aneurysm necessitating surgery; or renal-artery stenosis due to fibromuscular dysplasia. One hundred six patients were eligible for the treatment phase and were randomly assigned to undergo balloon angioplasty or to receive antihypertensive-drug therapy. Block randomization was used to ensure that the groups contained roughly equal numbers of patients, with stratification according to institution and several clinical variables.[10] Stratification variables were the serum creatinine concentration (<1.4 mg per deciliter [120 μmol per liter] vs. ≥1.4 to 2.3 mg per deciliter), the type of antihypertensive-drug therapy received during the diagnostic phase of the study (amlodipine and atenolol vs. enalapril and hydrochlorothiazide), and the extent of renal-artery stenosis (unilateral vs. bilateral). Randomization was performed by computer at the coordinating center (Erasmus University Hospital, Rotterdam), without investigators' knowledge of patients' groups at the time of assignment.

Treatment and Follow-up

Patients assigned to the drug-therapy group and, if necessary, those assigned to the angioplasty group, received antihypertensive-drug therapy according to a stepwise protocol, with a target diastolic blood pressure of less than 95 mm Hg. Drug therapy consisted of the two-drug regimen the patient had been receiving during the diagnostic phase of the study; if necessary, a dose could be increased or another drug added.

Blood pressure was measured by standard sphygmomanometry every one to three months, and always at months 3 and 12, with the patient seated after a five-minute rest; at each visit, three measurements were made at least one minute apart, and the values were recorded to the nearest 2 mm Hg and then averaged.[11] Three and 12 months after randomization, blood pressure was also measured with an automatic device (Datascope, Montvale, N.J.) at 5-minute intervals for 60 minutes. In addition, at 3 and 12 months, serum creatinine was measured and renal scintigraphy was performed after the administration of captopril.[12] In both the angioplasty group and the drug-therapy group, renal arteriography was repeated at 12 months.

Patients assigned to the angioplasty group were given 300 mg of aspirin daily, starting the day before angioplasty and continuing for six months. Antihypertensive-drug therapy was discontinued on the day of the procedure to prevent hypotension and was subsequently resumed if necessary. If, after three months, the patient's diastolic pressure was 95 mm Hg or higher or the serum creatinine concentration had risen by at least 0.2 mg per deciliter, the treating physician decided whether to recommend a second balloon angioplasty, stent deployment, or bypass surgery.

Patients assigned to the drug-therapy group underwent balloon angioplasty if, after three months, their diastolic pressure was 95 mm Hg or higher despite treatment with three or more drugs or if there was evidence of progressive renovascular occlusive disease. Progressive renovascular occlusive disease was defined as an increase of at least 0.2 mg per deciliter in the serum creatinine concentration or worsening of the time–activity renogram on scintigraphy; worsening was defined as a change in the time–activity curve from type 1 or 2 to type 3, 4, or 5 or a change in the curve from type 3 to type 4 or 5 (type 1 indicates minor abnormalities, type 2 delayed excretion with washout, type 3 delayed excretion without washout, type 4 renal failure with measurable uptake by the kidney, and type 5 renal failure without measurable uptake).[13] Lipid-lowering medication was prescribed for any patient who had a serum cholesterol concentration greater than 251 mg per deciliter (6.5 mmol per liter).

Renal Arteriography, Renal Scintigraphy, and Balloon Angioplasty

Arteriography was performed before the beginning of the treatment phase and at 12 months by the femoral approach with the digital-subtraction technique. The images were then assessed at each participating center by the radiologist who had performed the arteriography. All arteriograms were subsequently evaluated by three independent radiologists, who graded the images according to the severity of stenosis, expressed in steps of 10 percent decreases in luminal diameter. The median value of these three grades was then calculated.

Renal scintigraphy was performed with use of technetium-99m–labeled mercaptoacetyltriglycine. The nuclear-medicine specialists who assessed the renal scintigrams were asked to report the results in terms of the probability of renovascular disease (low, indeterminate, or high), according to a consensus report on the diagnosis of renovascular disease by renal scintigraphy.[14] Scintigrams judged to indicate a high or indeterminate probability of renovascular disease were considered abnormal.

Outcome Measures

The primary outcome measures were the systolic and diastolic blood pressures at 3 and 12 months after randomization. The secondary outcome measures were the numbers and defined daily doses of antihypertensive drugs (one defined daily dose is the average maintenance dose per day for adults),[15] the serum creatinine concentration, the creatinine clearance according to the formula of Cockcroft and Gault,[16] the results of renal scintigraphy, the presence or absence of patency of the renal artery (where patency was defined as stenosis of <50 percent), and the incidence of complications.

In a separate analysis, outcomes were assessed in terms of blood-pressure responses in the two groups. In this analysis, improvement was defined as either (1) a decrease of 10 mm Hg or more in diastolic pressure with either no change or a decrease in the number of drugs or (2) a decrease in the number of drugs without a change in diastolic pressure; worsening was defined as either (1) an increase of 10 mm Hg or more in diastolic pressure with either no change or an increase in the number of drugs or (2) an increase in the number of drugs without a change in diastolic pressure; and cure of hypertension was defined as a diastolic blood pressure of less than 95 mm Hg without use of antihypertensive drugs.

Statistical Analysis

Results are given as means ±SD or as medians and ranges. Results at 12 months were analyzed according to the intention-to-treat principle. In addition, results at 3 and 12 months in the drug-therapy group were analyzed according to whether patients underwent angioplasty after three months. Two-sided comparisons between groups were made with Student's t-test or the Mann–Whitney test. Chi-square testing was used for analysis of categorical data. A paired t-test was used to compare the blood-pressure

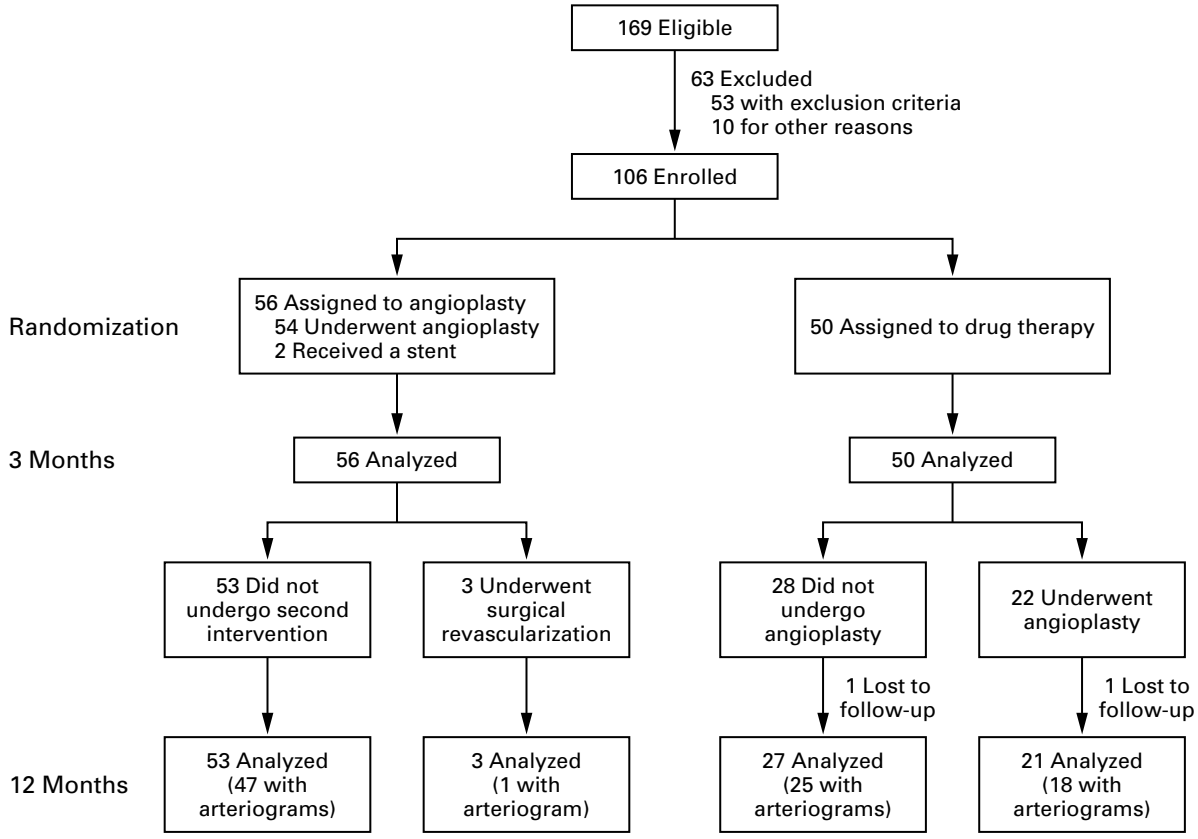

Figure 1. Design of the Study.

values measured at the 3-month and 12-month follow-up visits with the values measured at base line.

RESULTS

Of the 169 patients with renal-artery stenosis, 53 were excluded on the basis of the prespecified exclusion criteria and 10 patients were excluded for other reasons (prominent aortic plaques in 2, a serum creatinine concentration >2.3 mg per deciliter in 1, lack of informed consent in 4, and withdrawal by the internist in 3). Of the remaining 106 patients, 56 were randomly assigned to balloon angioplasty and 50 to antihypertensive-drug therapy (Fig. 1). At base line, the blood-pressure levels and doses of antihypertensive drugs (means of the values obtained at the three visits during the diagnostic phase) were similar in the two groups, as were other base-line characteristics (Table 1). Likewise, in the subgroup of patients with impairment of renal function related to the use of angiotensin-converting–enzyme inhibitors, the blood-pressure levels and drug doses in the patients randomly assigned to balloon angioplasty were similar to those in the patients assigned to antihypertensive-drug therapy.

Renal Arteriography

To be included in the study, patients were required to have unilateral or bilateral renal-artery stenosis of at least 50 percent, as judged by the radiologist who had performed the arteriography. In 10 of the 106 patients included (5 in the angioplasty group and 5 in the drug-therapy group), however, the stenosis was judged to be less than 50 percent by the panel of three independent radiologists.

Of the 56 patients in the angioplasty group, 2 received a stent in addition to undergoing angioplasty (1 because of a small aneurysm in the distal segment of the renal artery and the other because the radiologist had not adhered to the protocol). Balloon angioplasty failed for technical reasons in three patients with unilateral stenosis and on one side in one patient with bilateral stenosis. After three months, surgical revascularization was performed in two of the patients in whom angioplasty had failed and in one patient in the angioplasty group who had persistent hypertension (diastolic pressure, ≥95 mm Hg).

Renal arteriography was repeated 12 months after balloon angioplasty in 48 of the 56 patients assigned

TABLE 1. BASE-LINE CHARACTERISTICS OF THE PATIENTS.*

VARIABLE†	ANGIOPLASTY GROUP (N=56)	DRUG-THERAPY GROUP (N=50)
Clinical data		
Male sex — no. (%)	37 (66)	28 (56)
Age — yr	59±10	61±10
Body-mass index	25.4±3.5	25.2±3.1
Cigarette smoking		
Former or current — no. (%)	46 (82)	35 (70)
Pack-years among those who smoked	22±14	25±17
Abdominal bruit — no./total no. (%)	12/56 (21)	12/48 (25)
Diabetes mellitus — no. (%)	3 (5)	3 (6)
Onset of hypertension <2 yr before enrollment — no. (%)	19 (34)	17 (34)
Blood pressure — mm Hg		
Systolic	179±25	180±23
Diastolic	104±10	103±8
Antihypertensive drugs		
No. of defined daily doses	3.3±1.1	3.2±1.5
No. of drugs	2.0±0.8	2.0±0.9
Regimen (no.)		
Amlodipine and atenolol	18	13
Enalapril and hydrochlorothiazide	22	23
Other	16	14
Laboratory and angiographic data		
Serum creatinine — mg/dl		
Median	1.2	1.3
Range	0.9–2.2	0.5–2.3
Serum creatinine ≥1.4 mg/dl — no. (%)	18 (32)	21 (42)
Creatinine clearance — ml/min	67±23	60±24
Serum cholesterol — mg/dl	244±31	247±46
Serum cholesterol >251 mg/dl — no./total no. (%)	22/56 (39)	18/45 (40)
Abnormal renal scintigrams — no./total no. (%)	35/54 (65)	32/49 (65)
Stenosis		
Bilateral — no. (%)	13 (23)	11 (22)
<70% — no. (%)	12 (21)	15 (30)
Average decrease in luminal diameter — %	76±20	72±18
Inclusion criteria		
Hypertension resistant to standard medication — no. (%)	49 (88)	38 (76)
Renal-function impairment related to angiotensin-converting–enzyme inhibitors — no. (%)‡	7 (12)	12 (24)

*Plus–minus values are means ±SD. To convert the values for serum creatinine to micromoles per liter, multiply by 88.4. To convert the values for serum cholesterol to millimoles per liter, multiply by 0.026. Because of rounding, not all percentages total 100.

†For some variables, the total number of patients (denominator) is less than the total number in the group because tests were not performed in all patients. The body-mass index is the weight in kilograms divided by the square of the height in meters.

‡In the subgroup with renal-function impairment related to the use of angiotensin-converting–enzyme inhibitors, the systolic blood pressure was 164±25 mm Hg and the diastolic blood pressure 98±10 mm Hg among patients assigned to angioplasty, and the respective systolic and diastolic pressures were 160±20 and 98±5 mm Hg among the patients assigned to drug therapy; these patients were receiving 2.9±0.4 and 2.9±1.1 defined daily doses, respectively.

to that group; 4 patients declined to undergo the procedure, and it was not requested for 3 of the patients in whom balloon angioplasty had failed and for 1 of the patients who had undergone surgical revascularization. Of these 48 patients, 23 had at least 50 percent stenosis of the treated artery, but none had total occlusion.

Of the 50 patients in the drug-therapy group, 28 were treated exclusively with antihypertensive drugs during the 12-month follow-up period. Of the remaining 22 patients, balloon angioplasty was performed after the three-month follow-up in 14 patients because of persistent hypertension despite treatment with three or more drugs and in 8 patients because of progressive renovascular occlusive disease (as indicated by an increase of 0.2 mg per deciliter or more in the serum creatinine concentration or worsening of the time–activity curve on renal scintigraphy). At the time of angioplasty, the arteriograms of 3 of the 22 patients who underwent angioplasty showed total occlusion, so the procedure had to be aborted.

Renal arteriography was repeated 12 months after randomization in 43 of the 50 patients initially assigned to the drug-therapy group. Arteriography showed stenosis of 50 percent or more in 31 of the 43 patients (72 percent), stenosis that had progressed to total occlusion in 4 patients (9 percent), and stenosis of less than 50 percent in 8 patients. Of the 25 patients who underwent repeated arteriography and who had been treated exclusively with drug therapy, 5 had an increase in stenosis of 20 percentage points or more, 16 had no change, and 4 had a regression of stenosis of 20 percentage points or more.

Blood Pressure

Mean systolic and diastolic blood pressure at three months did not differ significantly between the angioplasty and drug-therapy groups (Table 2). At 12 months, intention-to-treat analysis revealed no significant differences in systolic and diastolic blood pressure between the drug-therapy group (of which 22 patients underwent balloon angioplasty after 3 months) and the angioplasty group. The doses of antihypertensive drugs used by patients in the angioplasty group were significantly lower than those used in the drug-therapy group at 3 months, but this difference was no longer significant at 12 months. Among patients with renal-function impairment related to the use of angiotensin-converting–enzyme inhibitors, the blood-pressure levels at 3 and 12 months were similar in the drug-therapy and angioplasty groups.

Among the patients who were randomly assigned to the drug-therapy group, the systolic and diastolic blood pressures were higher at base line and at the three-month follow-up visit in patients who underwent balloon angioplasty after three months than in those who did not (Table 3). Blood pressure decreased after angioplasty but was still higher at 12

TABLE 2. OUTCOMES AT 3 AND 12 MONTHS IN THE ANGIOPLASTY AND DRUG-THERAPY GROUPS.*

VARIABLE	ANGIOPLASTY GROUP (N=56)	DRUG-THERAPY GROUP (N=50)	P VALUE
Outcomes 3 months after randomization			
Blood pressure — mm Hg†			
Systolic	169±28	176±31	0.25
Diastolic	99±12	101±14	0.36
Blood pressure by automatic device — mm Hg			
Systolic	160±26	163±27	0.61
Diastolic	89±14	88±13	0.73
Antihypertensive drugs			
No. of defined daily doses	2.1±1.3	3.2±1.5	<0.001
No. of drugs	1.9±0.9	2.5±1.0	0.002
Serum creatinine — mg/dl			0.05
Median	1.2	1.3	
Range	0.7–1.9	0.6–2.6	
Creatinine clearance — ml/min	70±25	59±23	0.03
Abnormal renal scintigrams — no./total no. (%)	17/47 (36)	28/40 (70)	0.002
Outcomes 12 months after randomization			
Blood pressure — mm Hg‡			
Systolic	160±26	163±25	0.51
Diastolic	93±13	96±10	0.25
Blood pressure by automatic device — mm Hg			
Systolic	152±20	162±27	0.07
Diastolic	84±10	88±13	0.13
Antihypertensive drugs			
No. of defined daily doses	2.5±1.7	3.1±2.3	0.10
No. of drugs	1.9±0.9	2.4±0.9	0.002
Serum creatinine — mg/dl			0.11
Median	1.2	1.2	
Range	0.6–1.9	0.6–8.2	
Creatinine clearance — ml/min	70±24	62±27	0.11
Abnormal renal scintigrams — no./total no. (%)	19/53 (36)	25/44 (57)	0.04
Complications during follow-up — no. of patients			
Occlusion of affected artery	0	8	
Rupture of affected artery	0	0	
Increase of ≥50% in serum creatinine	2	6	
Embolization of cholesterol crystals	0	2	
Groin hematoma necessitating transfusion or surgery	2	4	
Other§	2	4	

*Plus–minus values are means ±SD. To convert the values for serum creatinine to micromoles per liter, multiply by 88.4.

†P<0.001 for the comparison with systolic and diastolic pressure at randomization in the angioplasty group; P=0.16 for the comparison with systolic pressure at randomization and P=0.13 for the comparison with diastolic pressure at randomization in the drug-therapy group.

‡P=0.001 for the comparison with systolic and diastolic pressure at three months in the angioplasty group; P=0.001 for the comparison with systolic pressure at three months and P=0.002 for the comparison with diastolic pressure at three months in the drug-therapy group.

§Other complications were symptomatic hypotension at the time of angioplasty in one patient in the angioplasty group and angina pectoris in one patient and myocardial infarction in one patient in the drug-therapy group.

months in the patients who underwent this procedure than in the patients who received drug therapy alone. The doses of drugs did not change significantly after angioplasty, and at 12 months they were similar in the two subgroups.

Although there was no significant difference between groups in mean blood-pressure levels, a favorable effect in the angioplasty group could be identified when outcomes were categorized according to blood-pressure response, as defined in the Methods section. At 12 months, blood-pressure control had improved in 38 of the 56 patients in the angioplasty group (68 percent) and in 18 of the 48 patients in the drug-therapy group who had complete follow-up (38 percent). Conversely, blood-pressure control had worsened at 12 months in 5 patients in the angioplasty group (9 percent) and 16 patients in the drug-therapy group (33 percent) (P=0.002). Hypertension was considered cured at 12 months in 4 of the 56 patients in the angioplasty group (7 percent) and in none of the patients in the drug-therapy group.

In the 54 patients in the angioplasty group in whom

TABLE 3. BASE-LINE CHARACTERISTICS AND OUTCOMES IN PATIENTS IN THE DRUG-THERAPY GROUP ACCORDING TO WHETHER THEY UNDERWENT ANGIOPLASTY AFTER THREE MONTHS.*

VARIABLE	DRUG THERAPY WITH ANGIOPLASTY AFTER 3 MONTHS (N=22)	DRUG THERAPY ALONE (N=28)	P VALUE
Base-line characteristics			
Blood pressure — mm Hg			
Systolic	185±22	176±24	0.21
Diastolic	107±7	101±9	0.02
Antihypertensive drugs			
No. of defined daily doses	3.6±1.8	2.8±0.9	0.05
No. of drugs	2.3±1.0	1.8±0.8	0.08
Serum creatinine — mg/dl			0.56
Median	1.3	1.2	
Range	0.9–2.3	0.5–2.2	
Creatinine clearance — ml/min	55±21	63±26	0.22
Abnormal renal scintigrams — no./total no. (%)	14/21 (67)	18/28 (64)	0.86
Outcomes 3 months after randomization			
Blood pressure — mm Hg			
Systolic	190±33	164±24	0.004
Diastolic	111±13	94±9	<0.001
Antihypertensive drugs			
No. of defined daily doses	3.7±1.6	2.8±1.2	0.03
No. of drugs	2.8±1.1	2.2±0.8	0.02
Serum creatinine — mg/dl			0.65
Median	1.2	1.3	
Range	0.8–2.2	0.6–2.6	
Creatinine clearance — ml/min	58±21	60±24	0.75
Abnormal renal scintigrams — no./total no. (%)	10/16 (62)	18/24 (75)	0.49
Outcomes 12 months after randomization			
Blood pressure — mm Hg			
Systolic	169±25†	159±24‡	0.16
Diastolic	102±9†	91±9‡	<0.001
Antihypertensive drugs			
No. of defined daily doses	3.3±2.8	3.0±1.8	0.74
No. of drugs	2.5±1.1	2.4±0.8	0.81
Serum creatinine — mg/dl			0.33
Median	1.3	1.2	
Range	0.6–8.2	0.6–2.0	
Creatinine clearance — ml/min	58±26	65±27	0.42
Abnormal renal scintigrams — no./total no. (%)	10/19 (53)	15/25 (60)	0.63

*Plus–minus values are means ±SD. To convert the values for serum creatinine to micromoles per liter, multiply by 88.4.

†$P<0.001$ for the comparison with systolic and diastolic pressure in this subgroup at three months.

‡$P=0.26$ for the comparison with systolic pressure and $P=0.32$ for the comparison with diastolic pressure in this subgroup at three months.

angioplasty was technically successful, including the 2 patients who also received a stent, neither the blood-pressure levels nor the defined daily doses of antihypertensive drugs at 3 and 12 months were related to the severity of renal-artery stenosis at randomization; the blood-pressure levels and the drug doses of the 32 patients with greater than 70 percent stenosis did not differ from those of the 20 patients with stenosis of 70 percent or less (data not shown). Blood pressure and drug doses in the angioplasty group also were not correlated with the presence or absence of stenosis of 50 percent or greater at 12 months: among the 26 patients (23 in whom arteriography was repeated and 3 in whom arteriography was not repeated and in whom there was technical failure) with at least 50 percent stenosis after 12 months, the mean (±SD) systolic and diastolic blood pressures were 162±21 and 91±11 mm Hg, respectively, during treatment with 2.3±1.3 defined daily doses, as compared with 159±32 mm Hg ($P=0.79$) and 96±16 mm Hg ($P=0.14$), respectively, during treatment with 2.9±2.0 defined daily doses ($P=0.13$) among the 25 patients with less than 50 percent stenosis. In addition, in the angioplasty group, the presence of an abnormal scintigram at entry did not predict the blood-pressure level: there were no significant differences in blood pressure or defined daily doses of antihypertensive drugs between patients with a normal

scintigram at entry and those with an abnormal scintigram.

Renal Function and Results of Scintigraphy

At 3 months, the median serum creatinine concentration in the angioplasty group was lower and the mean creatinine clearance higher than the respective values in the drug-therapy group, but at 12 months the values for these variables were similar in the two groups, according to intention-to-treat analysis. The percentage of abnormal scintigrams was lower in the angioplasty group than in the drug-therapy group at both 3 and 12 months (Table 2).

DISCUSSION

The aim of our study was to determine whether balloon angioplasty offers any advantage over drug therapy in the treatment of patients with hypertension associated with atherosclerotic renal-artery stenosis. We found that both approaches resulted in similar decreases in blood pressure, but that angioplasty reduced the need for one additional antihypertensive drug given in its usual daily dose. Fewer drugs were used in the angioplasty group than in the drug-therapy group in part because of the design of the study, and thus this difference does not constitute proof of the efficacy of angioplasty. The blood pressure in this group might have been lower if the patients had received as many antihypertensive drugs as the patients in the drug-therapy group. In very few of the patients in the angioplasty group was hypertension cured.

Several factors may account for the limited efficacy of balloon angioplasty in our study. Angioplasty is followed by restenosis in a high proportion of patients,[17-19] which may adversely affect the blood-pressure response. However, we found no difference after one year in the blood-pressure response between patients with stenosis and those without stenosis. Stent placement as an adjunct to angioplasty has been reported to lower the incidence of restenosis,[20,21] but in one study the use of a stent did not result in greater improvement in blood pressure or renal function after six months than did angioplasty without stenting,[20] a finding consistent with our results. Whether stenting is better than balloon angioplasty, in terms of long-term control of blood pressure and improvement in renal function, is not known.

Another explanation for the disappointingly small effect of balloon angioplasty on blood pressure in our study may be the fact that a substantial number of patients in the drug-therapy group underwent balloon angioplasty after three months because their hypertension persisted despite treatment with three or more drugs or because they had signs of progressive occlusive renovascular disease. As a result, follow-up data on the effects of drug therapy alone in these patients were available only at three months. When the patients who had initially been assigned to the drug-therapy group but who later underwent balloon angioplasty were evaluated as a separate subgroup, it appeared that angioplasty had had a favorable effect on blood pressure. The important point is that blood pressure was not higher at 12 months in the drug-therapy group as a whole than in the angioplasty group. Therefore our results cannot be used as an argument against the more conservative, drug-based treatment.

Our method of selecting patients may also have affected the results. Of the 106 patients, 10 (5 in each group) had stenosis of the renal artery that was judged by an independent panel of three radiologists to be less than 50 percent. Some investigators consider stenosis to be hemodynamically important only if the diameter is reduced by more than 60 percent[22,23] or by more than 70 percent.[13,24] However, we found no correlation between the blood-pressure response and the severity of renal-artery stenosis at base line.

Our study was designed primarily to assess the influence of balloon angioplasty on the control of blood pressure, but our data also provide information about the effect of this intervention on renal function. Renal function appeared to be better in the angioplasty group than in the drug-therapy group at 3 months, but not at 12 months. The long-term effects of angioplasty on renal function remain to be determined.

We conclude that it is still prudent to restrict balloon angioplasty (with or without the use of a stent) to patients whose hypertension persists despite treatment with three or more drugs or who have progressive occlusive renovascular disease (as indicated by an increase in the serum creatinine concentration or worsening findings on the renal scintigram).

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APPENDIX

The other members of the Dutch Renal Artery Stenosis Intervention Cooperative (DRASTIC) Study Group are as follows: *Rotterdam* — P.P.N.M. Diderich, L.C. van Dijk, F.M.E. Hoekstra, F.J.M. Klessens-Godfroy, T.L.J.M. van der Loos, A.H. van den Meiracker, H.Y. Oei, P.J. Wismans; *Amersfoort* — S.J. Eelkman Rooda, C.A.M.J. Gaillard; *Nijmegen* — R.A.M.J. Claessens, J.W.M. Lenders, T. Thien; *Alkmaar* — J.A.C.A. van Geelen; *Deventer* — C.J. Doorenbos; *Dordrecht* — J. van der Meulen, P. Smak Gregoor; *Maastricht* — P.W. de Leeuw, P.N. van Es, M.M.E. Krekels, A.A. Kroon; *Spijkenisse* — F. van Berkum, R. Lieverse; *Leiden* — J.H. Bolk, P. Chang, A. Cohen, A.A.M.J. Hollander; *Beverwijk* — G. Schrijver; *Sittard* — F. de Heer, F.L.G. Erdkamp; *Enschede* — R.M. Brouwer, W.A.H. Koning; *Amsterdam* — G.A. van Montfrans, K.J. Parlevliet, J.C. Roos, J. Silberbusch; *Delft* — W. Hart; *Den Haag* — E.J. Buurke; *Nieuwegein* — H.H. Vincent; *Goes* — F.L. Waltman; *Zwolle* — G. Kolsters; *Hilversum* — S. Lobatto.

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