Percutaneous transluminal renal angioplasty versus surgical reconstruction of atherosclerotic renal artery stenosis: A prospective randomized study

Henrik Weibull, MD, David Bergqvist, MD, PhD, Sven-Erik Bergentz, MD, PhD, Kjell Jonsson, MD, PhD, Lennart Hulthén, MD, PhD, and Per Manhem, MD, PhD, Malmö, Sweden

Purpose: The purpose of this prospective randomized study was to compare percutaneous transluminal renal angioplasty (PTRA) and operation as initial therapy with regard to technical results, primary and secondary patency, and effects on blood pressure and renal function in patients with atherosclerotic unilateral renal artery stenosis.

Methods: Fifty-eight patients who did not have diabetes, who were less than 70 years of age, and who had severe hypertension and significant stenosis were randomized to receive PTRA or operation. Angiography was performed 10 days, 1 year, and 2 years after treatment to verify patency, and blood pressure and renal function were simultaneously evaluated.

Results: Technically, PTRA was successful in 83% and operation in 97% of patients. The primary patency rate after 24 months was 75% in the PTRA group and 96% in the operative group in technically successful cases. The secondary patency rate in the PTRA group was 90% and in the surgical group 97%. To achieve these results four patients in the PTRA group required operation, and one patient in the surgical group required PTRA. Hypertension was cured or improved after additional treatment in 90% of the patients after PTRA and 86% after operation. The corresponding figures for improved or unchanged renal function were 83% and 72%, respectively. After additional treatment, effects on blood pressure and renal function did not differ. Seventeen percent of the patients treated with PTRA required surgical intervention.

Conclusions: PTRA is recommended as first choice of therapy for atherosclerotic renal artery stenosis causing renovascular hypertension if combined with intensive follow-up and aggressive reintervention. (J VASC SURG 1993;18:841-52.)
function were as good as primary results after operation. We have also reported that treatment costs over a 5-year period did not differ between patients undergoing operation or PTRA, regardless of which primary procedure was chosen.\(^7\)

The aim of this prospective, randomized study was to compare results with regard to technical success, primary and secondary patency, and effects on blood pressure and renal function after initial treatment with PTRA or operation in patients with hypertension with unilateral atherosclerotic renal artery stenosis.

**MATERIAL AND METHODS**

The inclusion criteria were (1) patients without diabetes, 70 years of age or less, (2) hypertension (untreated blood pressure 160/100 mm Hg or higher), (3) significant unilateral atherosclerotic renal artery stenosis (localized within 1 cm from the aorta), and (4) S-creatinine level less than 300 mmol/L. All patients' cases were discussed by a surgeon, an interventional radiologist, and an endocrinologist. Both operation and PTRA had to be judged possible to perform on the basis of morphologic appearance. After consensus the patient was randomly assigned to a treatment group.

Between April 1984 and February 1990, 58 patients were randomly assigned by sealed envelopes to initial treatment with PTRA or operation, 29 patients to each group. All consecutive patients were evaluated for the study and included when they fulfilled the inclusion criteria. No other exclusions were made. Patient characteristics are shown in Table I and the groups were well-matched. They did not differ with regard to blood pressure, renal function, or antihypertensive treatment. However, by chance, the operative group had a higher S-creatinine level, but glomerular filtration rate (GFR) did not differ between the groups (\(p = 0.054\), Table II). The diagnosis of renovascular hypertension was based on angiographic findings and determination of renal vein renin ratio between the stenotic and nonstenotic side (Table III).\(^8\) The angiograms were reviewed by two experienced radiologists with a special interest in renal angiography. The angiograms were analyzed with regard to the narrowest diameter of the stenosis, length of the stenosis, distance of the stenosis from the aortic lumen, presence of poststenotic dilation, presence of collaterals, and maximum length of each kidney. The diagnostic angiography and PTRA were separated in time to avoid excessive exposure to contrast media.\(^9,10\)

The following findings were regarded as significant: main renal artery stenosis with a diameter of 2 mm or less\(^11\) and a renal vein renin ratio of the stenotic to the nonstenotic side of 1.5 or greater.\(^12\) Renal vein renin was sampled after withdrawal for at least 1 week of drugs that inhibited renin secretion. To enhance renin production the renal vein blood sampling was performed in supine and 60-degree upright tilted positions.\(^13\) The highest ratio was used in the evaluation.

Obvious collateral circulation, shorter kidney on the stenotic side, and poststenotic dilation were regarded as supportive signs. A stenosis was regarded atherosclerotic if located within the first centimeter from the contrast column in the aorta, usually with a distal stenotic tapering. Thus the stenoses were at least partly located in the aortic wall, that is, including both aortic, ostial, and mixed stenoses according to Cicuto et al.\(^4\) The pressure gradient was measured in most of the patients undergoing PTRA but not in patients undergoing operation because of a potential risk of intimal lesion. There was no difference between the two groups with regard to angiographic findings or renin ratio (Table III).

The techniques for PTRA and operation, as well as the treatment before and after the procedure, have been described in detail.\(^7,14\) To verify patency and absence of restenosis all patients were examined with angiography 7 to 10 days, 12 months, and 24 months after the primary treatment. All patients were seen on an ambulatory basis at least four times a year. Patients showing clinical signs of recurrence, that is, increasing blood pressure or decreasing renal function, underwent angiography as soon as possible.

All patients were scheduled for in-hospital evaluation 3, 12, and 24 months after primary treatment. On these occasions blood pressure was measured repeatedly and the antihypertensive treatment was reduced if possible. Cr-ethylenediaminetetraacetic acid (Cr-EDTA) clearance and S-creatinine levels were measured under standardized conditions at the evaluations before and after the treatment and after 3, 12, and 24 months.

If the primary PTRA procedure failed, surgical reconstruction was planned as fast as possible, usually within a month. If a restenosis was diagnosed at angiography, PTRA was undertaken during the same procedure as a first reintervention in both groups. If repeat PTRA was unsuccessful, a surgical reconstruction was done. Thus the PTRA group includes four patients who also needed operation, and the surgical group includes one patient who also needed PTRA.

Results were evaluated with regard to the treated artery (technical success and patency and need for
Table I. Patient profile

<table>
<thead>
<tr>
<th></th>
<th>PTRA group</th>
<th>Surgical group</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of patients</td>
<td>29</td>
<td>29</td>
<td></td>
</tr>
<tr>
<td>Men/women</td>
<td>20/9 (69%/31%)</td>
<td>14/15 (48%/52%)</td>
<td>0.18</td>
</tr>
<tr>
<td>Age (yr, median and range)</td>
<td>60 (41-69)</td>
<td>54 (38-70)</td>
<td>0.13</td>
</tr>
<tr>
<td>Smoking or previous smoking</td>
<td>14 (48%)</td>
<td>18 (62%)</td>
<td>0.43</td>
</tr>
<tr>
<td>Ischemic heart disease</td>
<td>17 (59%)</td>
<td>14 (49%)</td>
<td>0.60</td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>5 (17%)</td>
<td>7 (24%)</td>
<td>0.75</td>
</tr>
<tr>
<td>Treatment for cardiac decompensation</td>
<td>6 (21%)</td>
<td>8 (28%)</td>
<td>0.76</td>
</tr>
<tr>
<td>Peripheral vascular disease</td>
<td>7 (24%)</td>
<td>6 (21%)</td>
<td>1.00</td>
</tr>
<tr>
<td>Cerebrovascular disease</td>
<td>TIA/RIND</td>
<td></td>
<td></td>
</tr>
<tr>
<td>TIA/RIND</td>
<td>3 (10%)</td>
<td>2 (7%)</td>
<td>1.03</td>
</tr>
<tr>
<td>Cerebrovascular event</td>
<td>2 (7%)</td>
<td>0</td>
<td>0.50</td>
</tr>
<tr>
<td>Multilocular atherosclerosis (angiographic)</td>
<td>6 (21%)</td>
<td>5 (17%)</td>
<td>0.25</td>
</tr>
</tbody>
</table>

TIA, Transient ischemic attack; RIND, reversible ischemic neurologic deficit.

Table II. Profile of hypertension and renal function

<table>
<thead>
<tr>
<th></th>
<th>PTRA group (n = 29)</th>
<th>Surgical group (n = 29)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Highest blood pressure measured without antihypertensive drugs (mm Hg, median and range)</td>
<td>210 (160-280)</td>
<td>222 (170-280)</td>
<td>0.23</td>
</tr>
<tr>
<td>Blood pressure at hospital admission with antihypertensive drugs (mm Hg, median and range)</td>
<td>120 (100-160)</td>
<td>120 (100-160)</td>
<td>0.98</td>
</tr>
<tr>
<td>Patients with more than three antihypertensive drugs</td>
<td>190 (140-250)</td>
<td>200 (140-260)</td>
<td>0.20</td>
</tr>
<tr>
<td>S-creatinine (mmol/L, median and range)</td>
<td>110 (90-130)</td>
<td>110 (80-155)</td>
<td>0.99</td>
</tr>
<tr>
<td>Cr-EDTA (ml/min, median and range)</td>
<td>23 (79%)</td>
<td>24 (83%)</td>
<td>1.06</td>
</tr>
<tr>
<td>S-creatinine (mmol/L, median and range)</td>
<td>95 (67-210)</td>
<td>114 (72-280)</td>
<td>0.032</td>
</tr>
<tr>
<td>Cr-EDTA (ml/min, median and range)</td>
<td>78 (25-135)</td>
<td>62 (23-107)</td>
<td>0.054</td>
</tr>
</tbody>
</table>

Table III. Diagnostic profile

<table>
<thead>
<tr>
<th></th>
<th>PTRA group (n = 29)</th>
<th>Surgical group (n = 29)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Angiographic findings</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stenotic diameter (mm, median and range)</td>
<td>2 (0.8-2.2)</td>
<td>2 (0.8-2.3)</td>
<td>0.88</td>
</tr>
<tr>
<td>Stenotic length (mm, median and range)</td>
<td>5 (2.0-11.0)</td>
<td>6 (3.0-15.5)</td>
<td>0.41</td>
</tr>
<tr>
<td>Poststenotic dilatation (n)</td>
<td>28/29</td>
<td>24/29</td>
<td>0.19</td>
</tr>
<tr>
<td>Collateral circulation (1 to 3 collaterals on angiogram)</td>
<td>17/29 (59%)</td>
<td>18/29 (62%)</td>
<td>1.0</td>
</tr>
<tr>
<td>Length of kidney (cm, median and range)</td>
<td>12.6 (8-16.8)</td>
<td>12.0 (9.3-15.5)</td>
<td>0.54</td>
</tr>
<tr>
<td>Stenotic side</td>
<td>14.1 (11.2-16.7)</td>
<td>13.6 (12.7-16.3)</td>
<td>0.60</td>
</tr>
<tr>
<td>Contralateral side</td>
<td>12.6 (8-16.8)</td>
<td>12.0 (9.3-15.5)</td>
<td>0.54</td>
</tr>
<tr>
<td>Renal venous renin activity ratio</td>
<td>Treated side/contralateral side (median and range)</td>
<td>2.0 (1.4-5.0)</td>
<td>2.0 (1.4-5.1)</td>
</tr>
</tbody>
</table>

reintervention) and with regard to the patient (hypertension and renal function). The stenotic artery was examined with regard to technical success, duration of therapeutic effect, patency, and the need for reintervention. Technical success was defined as total elimination of the stenosis, and the treatment deemed a technical failure if this result was not achieved or when it was not possible to perform PTRA or operation. The final judgment of the technical result was done at the first angiography 7 to 10 days after treatment. Patency was defined as a renal artery without need for reintervention, and reintervention was judged necessary when a restenosis occurred with lumen reduction to half of the diameter or less. Primary results were defined as a therapeutic effect achieved after the first performed intervention, and secondary results as the effect achieved after addition of all therapeutic efforts after restenoses, including operation in the PTRA group and PTRA in the surgical group.

The end point with regard to primary results was restenosis, death, or 24 months after the treatment and with regard to secondary results was death or 24 months after treatment.

For evaluation of results blood pressures referred to were those measured at admission to the hospital.
to reflect the patients’ clinical ambulatory status. Patients were considered cured of hypertension if the diastolic blood pressure was 90 mm Hg or lower without antihypertensive drugs. Patients were improved who had (1) diastolic blood pressure reduced 15 mm Hg or more without antihypertensive drugs, (2) diastolic blood pressure of 90 mm Hg or less with unchanged antihypertensive drugs, but reduced 15 mm Hg or more, (3) diastolic blood pressure 90 mm Hg or less with less antihypertensive medication than required before treatment. The remaining patients were regarded as having failed treatment. Results with regard to renal function were considered (1) improved if the Cr-EDTA clearance was increased more than 15% above the pretreatment level and (2) unchanged if the Cr-EDTA clearance was $\pm 15\%$ and impaired if the Cr-EDTA clearance was more than 15% below the pretreatment level.

**Prerequisites for sample size calculation and statistical methods.** The hypothesis for the study was that initial treatment with PTRA compared with operation would be acceptable as the first therapeutic choice if the following clinical considerations, based on retrospective results, were fulfilled: (1) For surgery, the technical success and 2-year primary patency rate was 96% or greater. (2) For PTRA, technical success rate was 80% or greater and 2-year primary patency rate 75% or greater. (3) PTRA as compared with primary results after operation had the same 2-year secondary patency rate, the same results with regard to blood pressure, and the same effect on renal function.

A one-sided equivalence test was used to investigate whether the patency rates after PTRA and operation could be considered equivalent. Equivalence was defined of two demands: (1) a patency-rate interval consisting of a maximum true difference between the 2-year primary patency rate for PTRA of three out of four patients and that for surgery of 24 out of 25 patients (these figures were a synthesis of retrospective results and clinical considerations) and (2) a minimum deviation from equivalence of 20% as suggested in guidelines of the Food and Drug Administration. The sample size was calculated to a total of 58 patients on the basis of a significance level of 5% and on a power of 80%.

Changes in blood pressure (systolic and diastolic), Cr-EDTA clearance, and S-creatinine level from before treatment through the follow-up evaluation points were analyzed with the Mann-Whitney U test (Wilcoxon). Fisher’s exact test was used to evaluate $2 \times 2$ tables. A $p$ value of less than 0.05 was considered to be statistically significant.

The study was approved by the Ethics Research Committee, Lund University, and informed consent was given in all cases.

**RESULTS**

**Technical results** (Fig. 1). PTRA was technically successful in 24 (83%) of the 29 patients. In the arteries with successful procedures the stenoses were totally repressed and the diameter at the place of the stenosis increased from median 2.0 mm (range 0.8 to 2.2) to 6.5 mm (4.0 to 9.0). The pressure gradient was reduced from median 80/25 mm Hg to 1.5/0 mm Hg after treatment. In two of the failed procedures the stenoses had occluded between the time of diagnostic angiography and the time of PTRA. In both cases successful revascularization was completed within 1 month by operation. In two patients it was impossible to achieve a stable balloon position because of a very narrow stenosis in a sharply angled renal artery. One patient was successfully operated on and the other deteriorated rapidly and further attempts to revascularize were not considered to be indicated. One patient had a stenotic renal artery to a small (8 cm) diseased kidney (not observed at diagnostic angiography) and a normal contralateral kidney. It was impossible to achieve a stable guidewire position and the artery occluded during the procedure. Operative revascularization was not considered to be indicated and a nephrectomy was performed.

In the surgical group the arteries in all 29 patients were revascularized; in 24 arteries with thromboendarterectomy and patch and in 5 with other reconstructions. During the first postoperative night one patient had classic signs of an occlusion, which were unfortunately missed until it was too late. Thus the technical success rate was 83% in the PTRA group and 97% in the surgical group. These findings satisfied the criteria for acceptable technical results and were not significantly different ($p = 0.19$).

**Primary and secondary patency** (Figs. 1 to 3). In the PTRA group 18 (75%) of the 24 successfully treated patients had patent arteries at the end of the follow-up period (24 months). The corresponding figure for "intention to treat" was 62%. In three of the six cases of restenosis increased blood pressure led to diagnosis 10, 11, and 24 months after the primary treatment. In the latter case a contralateral stenosis was also present. In three patients without clinical symptoms and signs, restenoses were diagnosed at the scheduled 12-month angiography. The five recurrences within 1 year were treated with repeat...
Weibull et al.

Technical results | Primary patency at the end of follow-up | Redo | Secondary patency
--- | --- | --- | ---
24 successful, 18 patent, 75% | 5 redo-PTRA | 26 patent, 90% | 2 stenoses (r)
83% | 1 redo-surgery (5 patients) | 1 nephrectomy | 1 no treatment
5 failures | 3 redo-surgery | 1 nephrectomy | 1 no treatment

PTRA 29

58 patients, 58 stenoses
Randomized to treatment with PTRA or surgery

Surgery 29

28 successful, 27 patent, 96%
97% | 1 re-stenosis (1 patient) | 28 patent, 97%
1 failure | 1 no treatment | 1 occluded

Fig. 1. Technical results, primary patency, repeat procedures performed, and secondary patency after additional interventions in PTRA and surgical reconstruction groups.

Fig. 2. Primary and secondary patency illustrated with life-table method. Both primary (after first PTRA or surgical reconstruction including attempts to treat) and secondary (after additional or therapeutic efforts after restenosis and technical failure) results are shown. Op, Operation.

PTRA. In one of these another restenosis developed 2 months later, which was successfully operated on (13 months). All these five patients had patent reconstructions at the end of follow-up.

At the end of follow-up after all redo procedures, including those after technical failures, 26 reconstructions were patent and three were not patent (one patient was dead, one underwent nephrectomy, and one had a stenotic artery), for a secondary patency rate of 90%.

In the surgical group 27 of the 28 successful revascularizations were patent (primary patency rate of 96%). One patient had a restenosis diagnosed by angiography because of increasing blood pressure and decreasing kidney function 4 months after reconstruction. PTRA was successful. The patient improved, but blood pressure rose again after 6 months. Repeat angiography showed a new restenosis, which was redilated successfully. At the end of follow-up the reconstruction was patent. Thus 28
reconstructions were patent and 1 occluded, for a secondary patency rate of 97%.

The observed difference in primary patency rate (PTRA 18 of 24 and operation 27 of 28) was close to the assumed maximum true difference and was statistically significant \((p = 0.05)\) by an efficacy test. The equivalence test result was also statistically significant \((p = 0.025)\). The secondary patency was similar for both treatment options \((p = 0.61)\).

**Contralateral stenoses** (Fig. 3). A total of eight (14%) stenoses developed contralaterally over 24 months in 58 arteries, at a median time of 9 months. Six (10%) occurred within 12 months. There was no difference between the two groups. Four stenoses were found because of signs of increased blood pressure (one in the PTRA group, three in the surgical group) and four were found at scheduled angiographies (two at 12 months and two at 24 months). Four patients were treated with PTRA; three treatments were successful and one failed. The latter patient underwent successful operation within a month. Two patients underwent primary successful surgical reconstruction. Two patients were not treated because of absence of hypertension and maintained renal function. All the others had a patent contralateral artery at the end of follow-up.

**Results with regard to hypertension** (Table IV). Of the 24 de facto treated patients in the PTRA group 3 were judged as cured and 17 had improved by the end of follow-up. Thus the primary results together showed 83% cured and improved patients. Primary results in the surgical group showed 5 cured patients and 21 improved, together 89%. The difference was not significant \((p = 0.52)\).

Secondary results in the PTRA group showed that five patients were cured and 21 improved (90%). Secondary results in the surgical group showed that
five patients were cured and 20 improved (86%), a nonsignificant difference ($p = 1.22$).

There was a significant decrease in both systolic and diastolic blood pressure in both groups ($p < 0.001$), but there were no differences between the groups in primary or secondary results. The number of patients receiving more than three antihypertensive drugs was reduced in the PTRA group from 79% before treatment to 52% after treatment and in the surgical group from 83% to 62%.

**Renal function** (Fig. 4). Primary results in the PTRA group showed that five patients had improved and 18 had unchanged GFR (96%). One patient had decreased GFR at the end of follow-up. Primary results in the surgical group showed that 8 patients had improved, 13 had unchanged (75%), and 7 patients had decreased GFR ($p = 0.083$). Secondary results showed at least unchanged GFR in 83% of the PTRA group versus 72% in the surgical group, which was a nonsignificant difference ($p = 0.53$).

Preoperatively S-creatinine levels were higher in the surgical group ($p = 0.031$), and this difference was maintained at the end of follow-up ($p = 0.026$). On the other hand, GFR was similar in the two groups ($p = 0.054$; Fig. 4).

**Mortality.** One patient died 10 months after a failed PTRA attempt of myocardial infarction and uremia not related to the PTRA procedure.

**Complications.** The procedure-related complications were classified into three categories: major (serious clinical complications), minor (complications with only minor clinical significance), and radiologic-technical (complications noted radiologically without clinical symptoms and signs: applicable to PTRA only). In the PTRA group, five major complications occurred in 29 procedures (17%). One renal artery occluded and nephrectomy was performed. Two patients had to be treated with antibiotics because of septic symptoms. In two patients the renal arteries were perforated and the patients had to be observed in the intensive care unit without further interventions. Minor complications were noted in 11 patients (48%): groin hematoma in four patients, minor retroperitoneal bleeding in two, back pain in three, and reversible renal insufficiency in two. Radiologic-technical complications were noted in 24 patients (83%): intimal damage in 16, subintimal contrast deposition in aorta in 1, pseudoaneurysm at the site of PTRA in 5, and spasm of the renal artery in 2.

In the surgical group, nine patients (31%) had the following major complications: renal artery occlusion in one, pancreatitis in one necessitating laparotomy twice and a 3-month hospital stay, postoperative bleeding with reoperation in one, deep wound infection with surgical drainage of an abscess in one, peripheral embolization in two, cardiac insufficiency in two, and deep venous thrombosis in one. Two minor complications in the form of reversible renal insufficiency were noted.

The frequency of major and minor complications did not differ statistically between the groups ($p = 1.0$).

**DISCUSSION**

Although blood pressure can be controlled with antihypertensive drugs in the majority of patients with renovascular hypertension, there are several reasons for active treatment of significant atherosclerotic renal artery stenosis. First, the natural end point of atherosclerotic renal artery stenosis is occlusion and between 9% and 17% of the stenoses have been reported to occlude within 28 to 56 months. During a 56-month follow-up period of untreated patients Tollefson and Ernst found a progressive narrowing of the stenotic diameter of about 5% per year. The progression is, however, not linear but occurs often rapidly most likely because of plaque rupture or subintimal bleeding, which are well-known in the pathophysiologic nature of coronary thrombosis. Progression occurred in half of the patients without clinical symptoms or signs. Active treatment therefore seems reasonable to save renal parenchyma. Furthermore, the rapid and unpredictable progression also affects the contralateral side. De novo contralateral development of stenosis has been reported in 17% of cases in 28 months and in 27% of cases in 56 months. In the present series contralateral stenoses were seen angiographically in 10% of patients within 12 months and in 14% within 2 years. These arteries

| Table IV. Blood pressure before and 24 months after treatment* |
|-----------------|-----------------|
| **PTRA group**  | **Surgical group** |
| **(n = 29)**    | **(n = 29)**    |
| Blood pressure before treatment | Blood pressure before treatment |
| Systolic        | 190 (140-250)   | 200 (140-260) |
| Diastolic       | 110 (90-130)    | 110 (80-155)  |
| $p < 0.001$     | $p < 0.001$     |
| Blood pressure at the end of follow-up |
| Systolic        | 148 (110-190)   | 155 (115-180) |
| Diastolic       | 90 (65-110)     | 90 (70-105)   |

*All interventions included.*
were free from stenosis before randomization. Thus treatment with potent antihypertensive drugs may mask the progression of the atherosclerotic renal artery stenosis, thereby leading to a risk of loss of renal parenchyma.19,20

The second reason for active treatment of these stenoses is that there are good, long-term results after surgical treatment with regard to primary patency in 80% to 98% of patients30-33 and improved control of blood pressure in 60% to 91%.18,30-33 Renal function improves and stabilizes in 80% to 90% of patients,30,33 and postoperative mortality is low, 0% to 2.5%.30,32

Third, there are good, long-term results after PTRA, especially if secondary results are accepted.6 Moreover, procedure morbidity and mortality are low.14

The aim of this randomized study was to compare PTRA and operation as the initial method of treatment of atherosclerotic renal artery stenosis. Specified criteria were to be fulfilled if PTRA was to be regarded as an initial choice of treatment. The base for these criteria was previous experience with PTRA, as well as what could be regarded as clinically reasonable results. The secondary patency, which reflects the clinical situation, should be as good as the primary patency after operation. There should be no differences between the two treatment options with regard to effects on blood pressure and renal function.

To use conventional statistical methods when studying infrequent diseases is often problematic because of the difficulty of sampling enough cases. Especially problematic with regard to sample size is exclusion of a difference in effect, for example, patency rate, between two therapies. In this study we used a one-sided equivalence test to assess the magnitude of the potential difference between PTRA and operation.15,16 The results showed that the observed difference was close to the maximum expected true difference. The significance (p = 0.025) of the equivalence test indicated that the minimum deviation from equivalence was less than 20%.

Diagnosis was based on results of renal angiography and the renal vein renin ratio. Criteria for angiographic significance of renal artery stenosis were described by Andersson et al.11 A selective renal vein renin ratio of the stenotic to the nonstenotic kidney of 1.5 was applied.12,13,36 One of these criteria had to be fulfilled, but in all but three patients both criteria were met. These two diagnostic criteria, combined with unilateral stenosis, make the diagnosis of renovascular hypertension most reliable.

The technical failure rates of 17% in the PTRA group and 4% in the surgical group were in accordance with earlier studies.5,37 The patient in the surgical group with renal artery occlusion on the night after operation had obvious signs of occlusion, but these were misinterpreted in the intensive care unit. The patient should have been reoperated on, had the surgeon been alarmed in time; when this was done, it was too late.

The technical results were documented during angiography after treatment. Inasmuch as there were no findings that necessitated a new intervention this control could not be recommended as routine. Pressure gradient after intervention was measured.
only in the PTRA group and provides a good documentation of the result of the PTRA procedure.6

The primary patency rate in the whole PTRA group was 75% if de facto treated arteries are included. These figures are on the same level or better than what has been obtained previously.5,6 With intensive follow-up and aggressive reintervention a 90% secondary patency rate was achieved. This is not different from the primary patency rate of 97% in the group primarily assigned to operation. A similar secondary patency rate after PTRA was observed in our previous series.6

Recurrence occurred in both groups, mainly within 12 months; three patients in the PTRA group had no symptoms, but fulfilled the angiographic criteria for reintervention and were therefore retreated. This legitimates the 12-month angiogram after PTRA, but good results after operation make such a routine unnecessary.

The results with regard to reduction in blood pressure were similar in the two groups, and there was a decrease in blood pressure in both primary and secondary results. The results were better than in many series in the literature, particularly for patients treated with PTRA.18,34,35,37 The scheduled angiogram control in our series caught the recurrence before the blood pressure had increased, which could be one explanation of the good long-term effects on blood pressure. Another explanation could be that in the present series the patient type was selected and well defined because of the inclusion criteria.

Renal function was followed up in all patients with a Cr-EDTA determination, which is a better marker of renal function than S-creatinine level and does not fluctuate with food intake and muscle mass. One important question is whether contrast media injures the kidney. We have earlier described reversible renal failure after PTRA and have had the impression that PTRA does impair renal function more than a surgical revascularization.9-10,14 In this series the renal function in the operated group before treatment by chance was inferior to the function in the PTRA group. However, the PTRA trauma, sometimes repeated, and the surgical trauma had similar influences on the renal function. We conclude that contrast media and PTRA do not influence the renal function more than the surgical procedure.

We have previously reported complications of PTRA in detail,14 and the outcome of this series with regard to PTRA was of similar magnitude and type. The radiologic-technical complications were much higher than in the other series. However, we have also reported alterations that are today regarded as a part of the method. In the surgical group major complications seemed to be higher compared with figures after PTRA but the difference was not significant (p = 0.17).

To summarize, this study showed a technical success rate after PTRA of 83% and after operation of 97%. After 24 months the primary patency rate after PTRA of the de facto treated patients was 75%, or 62% with the intention to treat concept, and 96% after operation. The secondary patency rate in the PTRA group was 90%. This was obtained after the first PTRA treatment in 60% of the patients and after repeat PTRA in 15% and in 15% after additional operation. After operation the corresponding patency rate was 97%. There was no difference between the two methods with regard to primary blood pressure response, with regard to influence on renal function, or with regard to secondary results.

Because the criteria to satisfy the hypothesis were fulfilled our conclusion is that PTRA is recommendable as initial therapy for unilateral atherosclerotic renal artery stenosis causing renovascular hypertension if combined with intensive follow-up and aggressive reintervention with PTRA or operation.

We thank Jonas Ranstam, PhD, Department of Community Health Sciences, Malmö General Hospital, for skilled statistical support.

REFERENCES

DISCUSSION

Dr. Ronald J. Stoney (San Francisco, Calif.). This is a preliminary report of a prospective randomized study. In reading the manuscript, I became concerned and, in part, confused by a number of components of the study.

The inclusion criteria are strict and are not representative of patients with atherosclerotic renal artery stenosis. They specifically state that only unilateral disease was admissible for study. Though the study may be focused on a single renal artery lesion, aortorenal atherosclerosis is nearly always bilateral. This prompts my first question to the authors: How many patients were screened to identify this cohort of 58 patients with this rare distribution of renal artery atherosclerosis?

The patients were 70 years old or younger. Currently, treatment of critical renal artery stenosis in older atherosclerotic populations is common and the study parameters...
do not reflect the treatment potential for this pathologic process. It would seem appropriate that in view of this relatively young nondiabetic population with focal renal artery stenosis under study, the authors would specifically limit their conclusions to this study group only.

The two treatment groups showed a significant difference in baseline renal function, with surgical patients having greater renal impairment. All conclusions derived from this study about comparative effects of the two treatment modalities on renal function are, therefore, suspect at best and probably invalid. This would include the conclusion that angiography was no more harmful to renal function in the PTRA group than in the surgical group.

The biostatistical considerations require clarification. The authors hypothesize that PTRA, compared with endarterectomy, would be acceptable as the first therapeutic choice when the maximum true difference between the two treatment arms of the study was 21%. Because the observed difference in primary patency rates between PTRA and operation by their calculations was 21.4% (which is close but not equal to or less than the maximum true difference that they established), I would ask whether the results in the two groups are in fact equivalent?

My major concern with this study is the classification of patients at the time the primary treatment fails. The surgical group is rather simple. There was one early perioperative failure and this was not treated, so 97% of the patients had a technically successful procedure. At the end of the study, only one additional revascularization had failed in the surgical group (patency rate 96%).

In the PTRA group, there were five initial failures for a technical success rate of 83%. At the completion of the study, an additional 6 failures had occurred, for a total of 11 failures within the 24-month study. When the authors applied further treatment to the patients with failed interventions, they calculated secondary patency rates of 97% for operation and 90% for PTRA. It should be noted that fewer than half of the patients with PTRA failures who underwent secondary treatment had, in fact, a second PTRA. Most underwent operation. Retreating patients for a failed intervention is appropriate and was done successfully in a high percentage of patients requiring it in this series. Combining both modalities for retreatment shows only that PTRA is equivalent to renal revascularization when PTRA failures can be treated surgically. In other words, the contralateral treatment modality becomes necessary for continued patency in the PTRA group. At that point in any study when a patient reaches the end point for the specific treatment being analyzed, this should be recognized as a failure of the treatment and reflected in the data analysis.

This study uses its statistics to reach the conclusion that, because the hypothetic biostatistical criteria were fulfilled, PTRA is recommended as the first choice of therapy for atherosclerotic renal artery stenosis. The concerns I have noted and the inconsistencies in this study do not allow me to reach this conclusion when considering the options available for the management of patients with symptomatic aortorenal atherosclerosis.

**Dr. Henrik Weibull.** The question concerning what cohort of patients we have screened is difficult to answer. We are a referral center and the screening procedure to select patients with severe hypertension and with high suspicion of renovascular cause is already passed when the patients are admitted. Out of the patients referred three of four were found to have renovascular hypertension and out of these one of three fulfilled the criteria to be included in the study. The overall frequency of renovascular disease in Sweden is not studied, but between 200 and 300 patients out of the 8 million inhabitants in Sweden are treated actively for renovascular disease every year. Between 30 and 60 of these were treated at Malmö General Hospital every year during the study and roughly one of three had unilateral disease with renovascular hypertension, one of three had renovascular hypertension and bilateral renovascular disease in different combinations, and the rest had renovascular renal insufficiency of different degree.

The present series is highly selected and well-defined as Dr. Stoney mentioned. I think it is important to do studies in this way and of course we only can make conclusions that concern the studied population.

By chance there was a difference between the two groups with regard to baseline values of renal function. However, this difference was maintained in the primary results and I do not think these facts, clearly pointed out, change our conclusions.

With regard to the questions about the biostatistical considerations, the difference between technical success for the two treatment options did not show any significance. The difference with regard to recurrence showed a rate of 21.4% at 2 years, inasmuch as the recurrence rate after operation was lower than in hypothesis (3.6% vs 4%). This differs from the maximum (21%) true difference in the hypothesis by 0.4%, but is acceptable because it is within the hypothesis for the results of PTRA (25%) and better than that for operation.

Concerning Dr. Stoney's last comment on the classifications with regard to secondary patency: primary results were defined as a therapeutic effect achieved after the first performed intervention and secondary results after addition of all therapeutic efforts after restenoses. The primary patency is a good measurement of the technical possibility of a method, but is limited with regard to the reflection of the clinical situation. Secondary patency, on the other hand, reflects the true clinical situation because we always try to choose the best possible treatment option for repeat procedures. With regard to our hypothesis, clearly described in the study, we think this is the best way to describe the results after PTRA and operation, which we think complement each other.

**Dr. John W. Hallett, Jr. (Rochester, Minn.).** Those who have large practices in renovascular disease understand the implications of this study, and I think we must emphasize, as Dr. Stoney did, that these are highly selected
lesions. The follow-up period in the study is very short. It is only 2 years, and one has to question what the results will be at 5 to 7 years. I would ask the authors, in their nonrandomized practice, whether they have any results at 5 to 7 years in patients undergoing PTRA and operation.

My other two questions are these: given a patient with bilateral renal stenosis, would you extrapolate from these results to treat bilateral renal stenosis by PTRA, when most of us would prefer operations? And, given a patient who has need for aortic replacement for aneurysmal or occlusive disease and has a unilateral renal stenosis, do you recommend preoperative balloon dilation before the aortic replacement?

Dr. Weibull. We have previously performed a retrospective nonrandomized study with operation and PTRA and had a median 5-year follow-up time. We found that most recurrences after PTRA occurred within 1 year and after that only sporadic recurrences occurred with the same frequency as after operation. We have also performed a long-term study concerning PTRA only, which confirmed that the recurrence rate is highest within the first year. For the present study we will follow the results consecutively.

Concerning the second question from Dr. Hallet about the possibility to extrapolate from this study to bilateral dilations, I think, from a technical point of view, the results should be the same with unilateral or bilateral lesions. Finally, I think it is possible, in selected cases, to pretreat renal artery stenosis in case of aneurysm or occlusive aortic disease before the aortic reconstruction.