Baseline renal function and surgical revascularization in atherosclerotic renal arterial disease in the elderly

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■ From 1975 to 1984, 107 patients ≥60 years of age had surgical revascularization at the Cleveland Clinic for correction of atherosclerotic renal arterial disease. To evaluate the effect of baseline renal function (RF) on outcome in older patients, the patients were retrospectively divided according to their preoperative serum creatinine levels into Group I, ≤1.4 (N=26), and Group II, ≥1.5 (N=81). Extrarenal atherosclerosis was more frequent in Group II (*P*<.005). Higher rates of complications were seen both in Group II and with extrarenal atherosclerosis, but these associations did not achieve statistical significance (*P*=.07). Baseline RF did not affect results, but after revascularization, the fall in diastolic blood pressure was greater in Group I (28.2 ± 4.4 mmHg *v* 17.4 ± 1.8 mmHg, *P*<.05). No such effect was noted in systolic blood pressure or in the frequency of cure or improvement *v* failure. Operative mortality for the entire group was 2.8%.

☐ INDEX TERMS: ATHEROSCLEROSIS; RENAL ARTERY DISEASE; VASCULAR SURGERY ☐ CLEVE CLIN J MED 1989; 56:415–421

SURGICAL REVASCULARIZATION (SR) of the renal arteries is a well-established treatment for renal arterial disease (RAD), which is a potentially reversible cause of both renovascular hypertension and renal failure. Both preoperative renal impairment and atherosclerosis have been considered important determinants of SR operative mortality, morbidity, and success rate.[1,2]

In spite of the success of percutaneous transluminal renal angioplasty (PTRA), SR remains an important therapeutic alternative in a significant number of selected patients in whom atherosclerosis is the cause of RAD. In fact, newer surgical techniques that obviate operation on a badly diseased aorta, coupled with routine preoperative screening and correction of existing coronary or cerebrovascular disease, have made SR of RAD safer and more successful than it was in earlier times.[3] In recent years, SR is being more commonly used in the growing population of older patients, in whom atherosclerosis is virtually the only cause of RAD.[4–6]

We conducted this investigation to evaluate the effect of baseline renal function (RF) (either impaired or normal) on outcome following SR in a group of older patients who had atherosclerotic RAD.

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TABLE 1
BASELINE PATIENT CHARACTERISTICS BY DEGREE OF RENAL FUNCTION*

	Group I†	Group II†	P
Age (yr)	65.2 ± 0.7	65.9 ± 0.5	NS
Sex			
Male	11 (42.3)	48 (59.3)	NS
Female	15 (57.7)	33 (40.7)	
Duration of hypertension (yr)	10.5 ± 2.8	9.9 ± 1.1	NS
Initial systolic BP (mmHg)	198.3 ± 6.3	191.8 ± 3.6	NS
Initial diastolic BP (mmHg)	107.5 ± 3.8	100.8 ± 1.7	NS (.07)
Number of medications	2.8 ± 0.2	3.1 ± 0.1	NS
Solitary kidney			
No	22 (84.6)	68 (83.9)	NS
Yes	4 (15.4)	13 (16.1)	
Renal artery disease			
Unilateral	8 (30.8)	15 (18.5)	NS
Bilateral	18 (69.2)	66 (81.5)	
Initial serum creatinine level (mg/dL)	1.2 ± 0.0	2.8 ± 0.2	.0001
Follow-up time (yr)	2.1 ± 0.5	1.6 ± 0.2	NS

*Values expressed either as mean ± SEM or as absolute numbers. Numbers within parentheses represent the relative value or percentage of the absolute value.
†Group I = baseline serum creatinine level ≤1.4 mg/dL (N = 26). Group II = baseline serum creatinine level ≥1.5 mg/dL (n = 81).

MATERIALS AND METHODS

We retrospectively reviewed the records of patients 60 years of age and older who underwent SR at the Cleveland Clinic between January 1975 and December 1984 for RAD. We selected the age of 60 years as a lower limit, following the World Health Organization classification of older people,[7] recognizing that any demarcation between the mature and the elderly is arbitrarily fixed by socioeconomic events rather than by physiological changes. Atherosclerosis was the sole cause of RAD in all subjects.

Patients had been selected for SR on the judgment of their attending physicians. The usual indications were: poorly controlled hypertension despite maximum antihypertensive therapy, intolerance to antihypertensive medications, high-grade bilateral renal artery stenosis, high-grade stenosis to a solitary kidney, or a kidney that was at least 9 cm in combination with either clinical evidence of progressive deterioration of RF or any of the other conditions. Thus, indications for SR were either hypertension, renal failure (or the threat of renal failure), or both.

There were 107 patients who underwent SR and met the above criteria, and these were arbitrarily divided according to baseline preoperative serum creatinine levels into Group I, ≤1.4 mg/dL (N=26), and Group II, ≥1.5 mg/dL (N=81). All relevant data available from patient records were tabulated and later entered into a computer for future analysis. Part of the methodology included here has been previously described.[5,6]

Pre-revascularization baseline data included: demographic information, duration of hypertension, blood pressure (BP), number of antihypertensive medications, serum creatinine, presence or absence of bilateral RAD or of a solitary kidney, and extent of atherosclerosis. Atherosclerosis was classified as renal when limited to the renal artery or extrarenal when clinically overt extrarenal atherosclerosis was present in addition to RAD, as manifested by one or more of the following: coronary arterial disease with myocardial infarction, angina pectoris, congestive heart failure, or abnormal coronary angiogram; extracranial cerebrovascular occlusive disease with stroke, transient ischemic attacks, or abnormal carotid angiogram; peripheral vascular disease with intermittent claudication; or atherosclerotic involvement of the abdominal aorta with or without aneurysm formation.

Also at baseline each of the above variables that define extrarenal atherosclerosis was analyzed independently, such as heart disease, atherosclerotic cerebrovascular occlusive disease, peripheral vascular disease, and presence or absence of concomitant atherosclerotic involvement of the abdominal aorta.

Post-therapy variables were: number of antihypertensive medications, serum creatinine, BP, operative mortality (defined as any death either occurring within the first 30 days postoperatively or judged to have resulted from the operation regardless of the time interval), postoperative complications occurring within 30 days of the procedure, and late complications.

Data were obtained at the most recent follow-up visit

TABLE 2
BASELINE EXTRARENAL EVIDENCE OF ATHEROSCLEROSIS BY DEGREE OF RENAL FUNCTION

	Group I*	Group II*	*P*
Extent of atherosclerosis			
Renal	7 (26.9)	4 (4.9)	<.005
Extrarenal	19 (73.1)	77 (95.1)	
Heart disease			
Present	14 (53.9)	56 (69.1)	NS
Absent	12 (46.1)	25 (30.9)	
Involvement of the aorta			
Present	15 (88.2)	54 (93.1)	NS
Absent	2 (11.8)	4 (6.9)	
Cerebrovascular disease			
Present	13 (50.0)	44 (57.9)	NS
Absent	13 (50.0)	32 (42.1)	
Peripheral vascular disease			
Present	11 (44.0)	35 (46.7)	NS
Absent	14 (56.0)	40 (53.3)	

*Group I = baseline serum creatinine level ≤1.4 mg/dL (N = 26). Group II = baseline serum creatinine level >1.5 mg/dL (N = 81).

(6 to 83 months post-treatment). Mean follow-up time for the group was 1.74 ± 0.2 years (mean ± SEM).

Post-treatment RF results were evaluated according to these categories: Improvement was defined as a decrease in serum creatinine of at least 20% from pretreatment levels. Stable was defined as a post-treatment serum creatinine level within ±20% of the pretreatment level. Deterioration was defined as a post-treatment serum creatinine level 20% or more above the pretreatment value.

Post-revascularization hypertension results were evaluated according to these categories: Patients were considered cured if the most recent BP was ≤140/90 mmHg on no medications, improved if there was either a decrease ≥15 mmHg in diastolic BP on the same or fewer medications or a decrease <15 mmHg but normotensive on medications, and a failure if none of these criteria were met.

Baseline and postoperative RF data were available for all patients. In the majority of records reviewed, all of the other baseline and post-SR variables were also available. However, for some records, information regarding these variables was either incomplete or missing for retrospective analysis, in part because some patients immediately returned to the care of their referring physicians and were lost to follow-up.

Statistics

The above pre- and post-revascularization variables were analyzed using the SAS computer program (Statistical Analysis Institute, Carey, NC). For comparisons of qualitative-nominal data, we used the chi-square test. For analysis of tables with small expected frequencies, we used the Fisher's exact test (two-tail) for 2×2 tables and the exact chi-square test (Fortran program) for larger tables. For the comparison of quantitative data, we employed the unpaired t-test. Finally, the Wilcoxon rank-sum test was used if the data did not follow a normal distribution.

RESULTS

Baseline patient characteristics

When patients were divided into Groups I and II on the basis of level of baseline RF, the two groups differed otherwise only on the extent of atherosclerosis. Although renal atherosclerosis confined to the kidney was less commonly seen than extrarenal atherosclerosis in both groups, extrarenal atherosclerosis was more frequent in Group II: 95.1% *v* 73.1% (*P*<.005) (*Tables 1* and *2*). The range of pre-SR serum creatinine levels was 0.9 to 13.5 mg/dL, and the mean baseline serum creatinine level ± SEM was 1.2 + 0.0 mg/dL for Group I and 2.8 ± 0.2 mg/dL for Group II (*P*<.0001). The age range was 60 to 76 years. There was only one black patient in the population of patients studied.

While there was a tendency toward bilateral RAD in Group II (81.5% *v* 69.2%), this did not achieve statistical significance (*P*=.19). Also, both mean systolic (198.3 ± 6.3 mmHg *v* 191.8 ± 3.6 mmHg) and mean diastolic (107.5 ± 3.8 mmHg *v* 100.8 ± 1.7 mmHg) BP tended to be higher in Group I but did not achieve statistical significance (*P*=.37 and *P*=.07, respectively). These groups did not differ significantly by age, sex, duration of hypertension, number of antihypertensive medications, or by presence of heart disease or of a soli-

TABLE 3
EFFECT OF SURGICAL REVASCULARIZATION ON RENAL FUNCTION AND HYPERTENSION BY BOTH BASELINE RENAL FUNCTION AND EXTENT OF ATHEROSCLEROSIS

	Group I*	*P*	Group II*	Renal	*P*	Extrarenal
Renal function results						
Stable or improved	25 (96.2%)	NS	70 (86.4%)	11 (100%)	NS	84 (87%)
Worsened	1 (3.8%)		11 (13.6%)	0 (0%)		12 (13%)
Hypertension treatment results						
Cured or improved	25 (96.2%)	NS	66 (88%)	9 (90.0%)	NS	82 (90.1%)
Failure	1 (3.8%)		9 (12%)	1 (10.0%)		9 (9.9%)

*Group I = baseline serum creatinine level ≤1.4 mg/dL (N = 26). Group II = baseline serum creatinine level ≥1.5 mg/dL (N = 81).

TABLE 4
EFFECT OF SURGICAL REVASCULARIZATION ON RENAL FUNCTION AND HYPERTENSION IN PATIENTS WITH EXTRARENAL ATHEROSCLEROSIS DIVIDED BY BASELINE RENAL FUNCTION

	Group I*	*P*	Group II*
Renal function results			
Stable or improved	18 (94.7%)	NS	66 (85.7%)
Worsened	1 (5.3%)		11 (14.3%)
Hypertension treatment results			
Cured or improved	18 (94.7%)	NS	64 (88.9%)
Failure	1 (5.3%)		8 (11.1%)

*Group I = baseline serum creatinine level ≤1.4 mg/dL (N = 26). Group II = baseline serum creatinine level ≥1.5 mg/dL (N = 81).

tary kidney. Although some of the data were missing in some of the patients' records, these subgroups also differed neither by history of cerebral or peripheral vascular disease nor by the presence or absence of concomitant involvement of the aorta.

In summary, after dividing the patients by level of baseline RF, we obtained fairly homogeneous groups, thus avoiding as much as possible the potential influence of concomitant factors (such as heart disease) that may confound the independent influence of the baseline RF on the outcome following SR.

Effect of surgical revascularization on RF

The degree of baseline RF did not seem to affect significantly the outcome on RF following SR (P=.29) (*Table 3*), although obviously postsurgical serum creatinine levels remained different between both groups (1.1 ± 0.1 mmHg *v* 2.3 ± 0.2 mg/dL, P=.0001). Of the patients in Group II, 86.4% had stable or improved RF following SR, whereas 3.8% of the patients in Group I had deteriorated function.

Since at baseline more patients from Group II had extrarenal atherosclerosis, we also analyzed the results by dividing all patients by extent of atherosclerosis (renal *v* extrarenal) before SR. As shown in *Table 3*, this particular baseline variable had no significant impact on the outcome of RF following SR (P=.6). Similar results were obtained when only patients with extrarenal atherosclerosis were considered and divided by baseline RF (*Table 4*, P=.45). The number of patients with renal atherosclerosis was too small for meaningful analysis.

Effect of surgical revascularization on hypertension

In the group of 101 patients from whom BP records following SR were available, the mean fall in diastolic BP was greater and the mean diastolic BP was lower in Group I than in Group II: 28.2 ± 4.4 mmHg *v* 17.4 ± 1.8 mmHg, P<.05, and 79.8 ± 1.5 mmHg *v* 83.2 ± 0.8 mmHg, P<.05, respectively. Neither the mean systolic BP (143.5 ± 3.7 mmHg in Group I *v* 149.6 ± 2.1 mmHg for Group II) nor the mean fall in systolic BP (55.1 ± 7.6 mmHg *v* 42.5 ± 4.0 mmHg for Groups I and II, respectively) was statistically different.

Even though there was some tendency for more failures (12% *v* 3.8%) and fewer cured or improved hypertensive patients (88% *v* 96.2%) in Group II, this was not significant (*Table 3*, P=.45). Also, the extent of atherosclerosis did not affect hypertension following SR (*Tables* 3 and 4). Similarly, the change in the mean number of antihypertensive medications was not different between the two groups: 1.4 ± 0.2 *v* 1.3 ± 0.1 for Groups I and II, respectively.

Complications and mortality after SR

Although complication rates tended to be higher following SR in Group II (23.7% *v* 7.7%) and in the sub-

TABLE 5
FREQUENCY OF COMPLICATIONS BY BOTH BASELINE RENAL FUNCTION AND EXTENT OF ATHEROSCLEROSIS

	Group I*	*P*	Group II*	Renal	*P*	Extrarenal
Postoperative complications						
Without	24 (92.3%)	.07	61 (76.3%)	10 (90.9%)	NS	75 (79%)
With	2 (7.7%)		19 (23.7%)	1 (9.1%)		20 (21%)
Late complications						
Without	19 (73.1%)	NS	57 (72.1%)	9 (81.8%)	NS	67 (71.3%)
With	7 (26.9%)		22 (27.9%)	2 (18.2%)		27 (28.7%)

*Group I = baseline serum creatinine level ≤1.4 mg/dL (N = 26). Group II = baseline serum creatinine level ≥1.5 mg/dL (N = 81).

group of patients with extrarenal atherosclerosis and abnormal RF simultaneously (25% *v* 5.3%), this trend did not achieve statistical significance (*P*=.07) (*Tables* 5 and 6).

In order of frequency, the major perioperative complications after SR were: peripheral arterial emboli, postoperative renal failure with or without dialysis, sepsis, myocardial infarction, congestive heart failure, cerebrovascular accident, gastrointestinal bleeding, splenectomy, pancreatitis, hepatic necrosis with gangrene of the gallbladder, retroperitoneal hematoma, and pneumonia. The late complication rates among the patients who were available for longer follow-up (N=105) were not affected by either baseline serum creatinine level or by the extent of atherosclerosis (*Tables* 5 and 6).

Early perioperative mortality in the whole group was always related to a concomitant septic process. The perioperative mortality rate after SR was 2.8% (3/107).

TABLE 6
FREQUENCY OF COMPLICATIONS IN PATIENTS WITH EXTRARENAL ATHEROSCLEROSIS DIVIDED BY BASELINE RENAL FUNCTION

	Group I*	P	Group II*
Postoperative complications			
Without	18 (94.7%)	.07	57 (75%)
With	1 (5.3%)		19 (25%)
Late complications			
Without	13 (68.4%)	NS	54 (72%)
With	6 (31.2%)		21 (28%)

*Group I = baseline serum creatinine level ≤1.4 mg/dL (N = 26). Group II = baseline serum creatinine level ≥1.5 mg/dL (N = 81).

DISCUSSION

In the Cooperative Study of Renovascular Hypertension, in 1975,[1] the important determinants of operative mortality were: cause of the disease, presence of coronary artery disease, complexity of the renal operative procedure linked to the mean occlusion time of the renal artery, concurrent extrarenal surgery, and presence of bilateral renal functional impairment. In fact, in the Cooperative Study, the presence of preoperative renal impairment (serum creatinine ≥1.4 mg/dL) was associated with a mortality of 22.5% compared with a mortality of 5.3% in patients with normal RF. The cause of death in 19 of the 34 patients who died was perioperative uremia, and decreased RF before SR was demonstrated in two-thirds of these 19 patients.

In our study, this influence of preoperative renal impairment was not as clear and definite. Although there was a tendency for higher rates of complications in Group II, this trend did not achieve statistical significance (*P*=.07). Also, baseline RF did not affect the outcome of SR on RF. Obvious differences may explain the disparate results between the two studies: progress in surgical techniques allowing shorter operating time, advances in perioperative care, such as invasive hemodynamic monitoring, and a better pharmacological armamentarium all combine to diminish the potential for renal ischemia. Furthermore, dialytic intervention was not as readily available before the early 1970s as it has become in recent years.

In this investigation, baseline RF seemed to have some effect on postoperative hypertension. In Group I, despite a baseline tendency for higher diastolic BP, the mean fall in diastolic BP post-SR was significantly greater than in Group II (*P*<.05). However, when hypertension outcome was evaluated by systolic BP or by categorical results (cure or improvement *v* failure), no difference was found. The somewhat worse effect on BP with higher serum creatinine levels may be explained by a more volume- than renin-dependent hypertension since serum creatinine levels following SR remained higher in this group. On the other hand, the variability of BP so commonly seen in elderly patients and the limitations of a retrospective study (such as different observers and the lack of a standardized method of BP measurement) may make the categorical definition of hypertension results a better measure of hypertension outcome than the mean fall of BP after SR. If mean fall in blood pressure is used as the dependent variable, baseline RF did not significantly affect hypertension results.

Since we included only patients 60 years or older, the comparison between normal and abnormal serum creatinine levels in this study may actually be one between different levels of renal impairment. It is well known that in older patients serum creatinine levels allow underestimation of the real glomerular filtration rate such that a "normal" serum creatinine level may not represent normal RF.[8]

At baseline, extrarenal atherosclerosis was associated with higher serum creatinine levels. This is not surprising because one differential diagnosis that must be taken into account when one encounters unexplained azotemia with hypertension in the elderly is atheromatous ischemic RAD. The latter is characterized by clinical evidence of significant atherosclerotic disease in other extrarenal vessels and urinary protein excretion of <1 g/24 h, and should be considered when other diagnoses have already been ruled out.[9] More importantly, this entity may be associated with renal cholesterol microemboli and other complex intrarenal lesions, such as multiple stenoses of intrarenal vasculature, that may explain the azotemia.[10]

One should also expect to find a higher frequency of complications in this group because of the greater potential for systemic cholesterol emboli manifested as several of the major perioperative complications described above, such as cerebrovascular accident, gastrointestinal bleeding, or peripheral arterial emboli. However, in our study, only a borderline, if any, association was noted between frequency of complications and the subgroup with extrarenal atherosclerosis and higher serum creatinine levels (P=.07). Even more important, mortality after SR was only 2.8% in this population and was always associated with a septic process.

In the cooperative study, 28 of the 34 deaths occurred in patients with atherosclerosis, and the overall operative mortality rate for patients with atherosclerotic RAD was 9.3% *v* 3.4% for patients with fibromuscular hyperplasia. Although age per se was not a major risk factor, the mean age of patients who died was 50.0 years, compared with 44.3 years in the survivors. At the Cleveland Clinic, a 2% mortality rate was achieved between 1974 and 1980. This was attributed to preoperative screening, correction of existing coronary or cerebrovascular occlusive disease, and methods of revascularization that obviate operation on a badly diseased aorta.[3]

At our institution, the mean age of patients presenting with atherosclerotic RAD has increased from 55 years between 1975 and 1980 to 61 years between 1981 and 1984.[4] The issue of age is of great importance for two reasons. First, it is clinically relevant. As the "graying" of the American population continues, physicians will be spending more time attending older patients. It is estimated that while physicians now spend 40% of their practice time with patients older than 65, in 40 years, this will increase to 75%.[11] Second, hypertension and atherosclerosis remain the most important causes of death in the elderly.

Renovascular hypertension in the elderly also appears to be more common than has been generally suspected. Of 128 patients over age 60 seen in Copenhagen who had diastolic BP >110 mmHg, 7% had renovascular hypertension.[12] We have shown that old age in itself is not a contraindication for SR, and that in a highly selected older population in whom medical therapy has failed, SR can be safely performed and is an effective mode of therapy.[5,6] Also, at our institution, the operative mortality or clinical outcome following SR for atherosclerotic RAD in patients 65 years and older has not been different from that of the younger group.[4–6]

Once the decision for interventional treatment with either SR or PTRA has been made, which of the two modalities should be selected for the elderly patient remains a controversial issue. To our knowledge, no randomized and prospective study comparing these two methods has been done. Besides other potential complications, both modalities increase risk of inducing cholesterol embolism. The simplicity of the procedure, lower cost, and less inconvenience for the patient make PTRA a very appealing method of therapy for the elderly. However, newer surgical techniques, coupled with routine preoperative screening for other vascular diseases, have made SR a reasonable alternative even in the older population.

PTRA generally gives excellent results when atherosclerotic RAD involves non-ostial and well-localized lesions to the first and second third of the main renal artery,[13] with patency rates of 81% to 93% for follow-up periods of three to six years.[14] However, the results of PTRA have been less satisfactory for these lesions: ostial (with a success rate of less than 25%, total occlusion of the main renal artery, in segmental branches, in sharp angle with the aorta, in a lengthy stenosis, and in those associated with severe atheromatosis of the aorta.

CONCLUSION

In this retrospective study of older patients, first, both abnormal baseline RF per se and extrarenal atherosclerosis with high baseline serum creatinine levels were associated with higher rates of complications, but this relationship did not achieve statistical significance. Second, baseline RF had no impact on RF results, but did have some impact on BP. Third, SR can be considered a safe and successful therapeutic alternative in a highly selected population of elderly patients.

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