Renal revascularization in Takayasu arteritis–induced renal artery stenosis

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Purpose: **This study was undertaken to define the long-term effects of renal revascularization on blood pressure, and renal and cardiac function in patients with Takayasu arteritis–induced renal artery stenosis (TARAS).**

Methods: **Twenty-seven patients (25 women; mean age, 27 years) with TARAS underwent intervention. Primary, primary assisted, and secondary patency rates were determined, and the late effects on blood pressure, renal and cardiac function, and survival were analyzed.**

Results: **All patients had hypertension (mean blood pressure, 167/99 mm Hg; 2.5 antihypertensive medications per patient). Mean estimated glomerular filtration rate in patients not receiving hemodialysis was 76 mL/min, and in five patients serum creatinine concentration was greater than 1.5 mg/dL. Three patients were hemodialysis-dependent, and two had intractable congestive heart failure. Forty interventions were performed, including 32 aortorenal bypass procedures, two repeat implantations, four nephrectomies, and two transluminal angioplasty procedures. Postoperative morbidity was 19%. There were no deaths. During follow-up (mean, 68 months), three graft stenoses, all due to intimal hyperplasia, and three graft occlusions occurred. Two of three graft stenoses were successfully revised. At 1, 3, and 5 years of follow-up, primary patency was 87%, 79%, and 79%, respectively; primary assisted patency was 93%, 89%, 89%, respectively; and secondary patency was 93%, 89%, and 89%, respectively. Intervention resulted in a decrease in blood pressure to a mean of 132/79 mm Hg ($P < .0001$), and the need for antihypertensive medications was reduced to one per patient ($P < .01$). Mean glomerular filtration rate increased to 88 mL/min ($P < .005$), and two patients no longer required hemodialysis. Congestive heart failure resolved in both patients, and did not recur. There were three deaths during follow-up, with 5-year and 10-year actuarial survival of 96% and 80%, respectively.**

Conclusions: **Renal revascularization to treat TARAS is durable, has a salutary effect on blood pressure, and enhances long-term renal and cardiac function. This response establishes renal revascularization as a successful and durable intervention for TARAS, and a benchmark to which other therapies should be compared. (J Vasc Surg 2004;39:749-57.)**

Takayasu arteritis (TA) is a nonspecific granulomatous inflammatory arteriopathy of unknown cause that results in occlusive obliteration or less commonly aneurysm degeneration of large and medium-sized elastic arteries. The disease was first described in 1908 by Takayasu,[1] a Japanese ophthalmologist, in a young female patient with retinal neovascularization and absent radial pulses. Subsequent descriptions of the disease have emphasized the "pulseless" syndrome, with involvement of the brachiocephalic arteries. However, less attention has been paid to involvement of other segments of the aorta, the visceral arteries, and in particular the renal arteries. Unrecognized TA-induced renal artery stenosis (TARAS) can result in malignant hypertension, severe renal dysfunction, cardiac decompensation, and premature death.[2] The morbidity associated with delayed diagnosis requires greater awareness, and more aggressive diagnostic evaluation and treatment in patients with TARAS.

In 1990 we reported our initial experience with TA,[3] focusing on the beneficial effects of surgical revascularization in a variety of anatomic locations in appropriately selected patients. The present study was undertaken to evaluate the outcome of intervention specifically for TARAS, with emphasis on the long-term effects of revascularization on blood pressure, renal function, cardiac function, and survival.

METHODS

Between 1977 and 2003, 27 patients with TARAS received treatment at the Keck School of Medicine of the University of Southern California. The diagnosis of TA was established by the presence of at least three criteria, as outlined by the American College of Rheumatology[4]: age at onset younger than 40 years, extremity claudication, decreased brachial artery pulse, differential of greater than 10 mm Hg in upper extremity systolic pressure, subclavian or abdominal aortic bruit, and focal angiographic aortic or branch vessel abnormality. Patient demographic data, use of steroid or immunosuppressant agents, erythrocyte sedi-

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Table I. Patient characteristics

Parameter	*n %*
Sex	
Female	25 (93)
Male	2 (7)
Race	
Asian	5 (19)
White	4 (15)
Hispanic	18 (67)
Age at diagnosis (y) (mean ± SEM)	27 ± 2.5
Follow-up (mo)	
Mean	68
Range	1-154

mentation rate (ESR), extrarenal sites of arterial involvement and previous vascular procedures; preoperative blood pressure (BP), number of antihypertensive medications, serum creatinine concentration (SCr), cardiac function, and angiographic and computed tomography (CT) findings; procedures performed at our center, associated 30-day morbidity and mortality; postoperative BP, SCr, cardiac function, graft patency, and mortality were collected through review of patient records and imaging studies.

Primary study end points were comparison of preoperative BP and medication requirements, estimated glomerular filtration rate (GFR), SCr, cardiac function, and morphologic features with those documented at last follow-up; patency of the renal revascularization; and patient survival.

BP was obtained with a sphygmomanometer in the office or hospital setting in a limb clinically free of or least involved with TA. Hypertension was defined as systolic BP greater than 140 mm Hg or diastolic BP greater than 90 mm Hg,[5] or current use of antihypertensive medications. Renal function was determined with the SCr concentration (mg/dL), and estimated GFR with the Cockcroft-Gault method.[6] Renal dysfunction was defined as SCr 1.5 mg/dl or greater,[7] or the need for hemodialysis. Congestive heart failure was diagnosed with the Framingham clinical criteria.[8] Left ventricular hypertrophy (LVH) was documented with transthoracic echocardiography as an increased wall mass index.[9]

Aortography that included the ascending aorta, aortic arch, and descending and abdominal aorta was performed in all patients before surgical or endovascular intervention. When aortograms suggested significant longitudinal aortic involvement, such as patent but irregular aortic contour, CT with intravenous contrast medium was performed to define the extent of aortic wall thickening. This information was used along with the intraoperative findings to locate the aortic anastomosis in the least diseased aortic segment. Unilateral renal revascularization was accomplished through a subcostal incision and a retroperitoneal approach. Simultaneous bilateral renal revascularization was achieved through a midline incision and transperitoneal exposure. A left seventh interspace thoracoabdominal approach was reserved for patients with concomitant thoracic aortic involvement that required repair. Revascularization was accomplished in most cases with bypass grafts. Autogenous saphenous vein was the preferred graft, with prosthetic grafts and hypogastric artery reserved for patients without suitable vein. The aorta or an aortic branch vessel with minimal inflammatory involvement, or an aortic graft when present, was used for graft inflow. Distal graft anastomoses were placed in grossly normal renal artery distal to the inflammatory process. Ex vivo techniques were used in kidneys with significant branch vessel involvement. Nephrectomy was performed when extensive inflammatory involvement of the renal artery precluded vascular reconstruction. Renal revascularization was followed by serial duplex ultrasound scanning, magnetic resonance angiography, or aortography in all patients. In patients with suspected occlusion or stenosis at noninvasive imaging, aortography was performed for confirmation.

Use of data from patient charts for purposes of this study was approved by the institutional review board. Continuous variables are expressed as mean ± SEM, and mean values were compared with paired two-tailed Student *t* tests. Significance was attributed at $P < .05$. Patency rates for revascularization were based on postoperative serial imaging studies and confirmation aortograms. Patency rates and patient survival were estimated with life table analysis.

RESULTS

Patient demographic data are shown in Table I. Ninety-three percent of patients were women, and 67% were Hispanic. All patients had received steroid therapy for TA at some point in the course of the disease, and 13 were receiving steroid therapy at the time of intervention. Immunosuppression with cyclosporine or methotrexate had been used in 14 patients. Two patients were receiving methotrexate, one was receiving cyclosporine, and one was receiving azathioprine at the time of renal revascularization. Eight patients had previously undergone 11 renal interventions at outside facilities, including seven percutaneous angioplasty procedures, three aortorenal bypass procedures, and one nephrectomy. All revascularizations had failed. Fourteen patients had undergone interventions in nonrenal vascular beds, including three ascending aortic replacements, three aortocarotid bypass procedures, three aortoiliofemoral bypass procedures, two cardiac valve replacements, and one carotid-subclavian bypass procedure.

Pre-intervention ESR was 26.2 ± 5.1 mm/h (range, 4-114 mm/h), and in 12 patients ESR was greater than 10 mm/hr at the time of intervention. At presentation, all 27 patients had hypertension, with BP 167 ± 6/99 ± 5 mm Hg, requiring 2.5 ± 0.3 medications per patient. Three patients were dialysis-dependent. In the remaining 24 patients mean SCr was 1.2 ± 0.1 mg/dL, and estimated GFR was 76 ± 4.5 mL/min. In five of the 24 patients SCr was greater than 1.5 mg/dL. LVH was documented in 16 patients, and refractory congestive heart failure secondary to systolic ventricular dysfunction in two patients. Aortography demonstrated focal occlusive renal artery disease

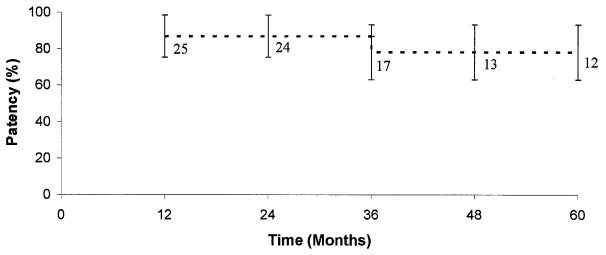

Fig 1. Primary patency (graft patency without intervention), with 95% confidence intervals, by life table analysis, after revascularization to treat Takayasu arteritis–induced renal artery stenosis. Numbers represent number of patent grafts followed up at each time point. Patency at 1, 3, and 5 years was 87%, 79%, and 79%, respectively.

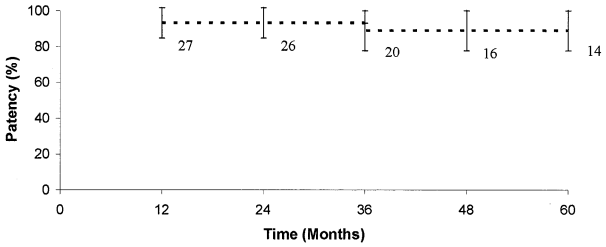

Fig 2. Primary assisted patency (graft patency including revised patent but stenotic grafts) and secondary patency (graft patency including revised stenotic and occluded grafts, with 95% confidence intervals, by life table analysis, after revascularization to treat Takayasu arteritis–induced renal artery stenosis. Numbers represent number of patent grafts followed up at each time point. Patency at 1, 3, and 5 years was 93%, 89%, and 89%, respectively.

consistent with TA in all patients, with coexisting aneurysm dilatation in two patients. Eleven renal arteries were occluded, and the remainder were stenotic. The descending thoracic aorta was involved in two patients, and the femoral arteries in three patients.

Thirty-six kidneys were revascularized. Renal revascularization was accomplished with use of bypass grafts in 32 kidneys, renal artery reimplantation in two kidneys, and percutaneous transluminal angioplasty in two kidneys. Origin of the bypass grafts was the infrarenal aorta in 19 patients, an aortic graft in five, the suprarenal abdominal aorta in four, the thoracic aorta in two, and a visceral artery in two. Bypass grafts were autogenous (19 saphenous vein, one hypogastric artery) in 20 patients, and prosthetic in 12 patients. Renal branch vessel reconstruction was required in five bypass procedures, with one requiring ex vivo technique. Four nephrectomies were performed, two at the time of contralateral renal revascularization, one before contralateral revascularization, and one as the sole procedure. Five aortic reconstructions and one inferior mesenteric artery reimplantation were also performed at the time of revascularization. Postoperative morbidity (19%) included wound infection (n = 2), myocardial infarction (n = 1), retroperitoneal hematoma requiring repeat exploration (n = 1), and mesenteric ischemia requiring superior mesenteric artery revascularization (n = 1). There were no postoperative deaths.

Mean follow-up was 68 ± 9 months (range, 3-154 months). Long-term steroid therapy was maintained in seven patients, and immunosuppressant therapy in one patient. During postoperative follow-up, three (8%) graft stenoses were documented, at 4, 9, and 29 months, respectively (mean, 14 months), and three (8%) graft occlusions occurred, at 3, 3, and 32 months, respectively (mean, 13 months). The six graft failures occurred in five patients. At the time of graft failure, two patients were receiving steroid therapy and three were not receiving any therapy. Two stenoses and two occlusions occurred in prosthetic grafts, and one each in autogenous grafts. Graft stenoses were successfully revised with percutaneous angioplasty in one patient, and surgical revision of a distal anastomotic stenosis in the second patient. The third graft was replaced with a prosthetic aortorenal graft. In both surgical interventions, histopathologic examination of the stenosis showed intimal hyperplasia without any evidence of arteritis. All three patients had normal renal function and well-controlled BP at last follow-up.

There were three graft occlusions in two patients. One patient was receiving hemodialysis at the time of the original procedure. The revascularization was remarkable for extensive inflammatory involvement of both renal arteries, which made branch vessel reconstruction necessary. After occlusion of both grafts, further revascularization was not attempted. The patient continued to require hemodialysis, and died of complications of renal failure 9 months after surgical intervention. In the other patient, repeat revascularization with splenorenal bypass was successful, but eventually renal failure developed, and the patient died 9 years after the initial procedure, of a cardiac event. Primary patency of the renal revascularization at 1, 3, and 5 years was 87%, 79%, and 79%, respectively (Fig 1). The corresponding primary assisted patency rates were 93%, 89%, and 89%, respectively, and secondary patency rates were 93%, 89% and 89%, respectively (Fig 2; Tables II-V, online only).

At last follow-up, mean BP had decreased to 132 ± 4/79 ± 2 mm Hg ($P < .01$), and the requirement for antihypertensive medications was reduced to 1 ± 0.2 drugs per patient ($P < .01$). Ten patients had normal BP without any antihypertensive medications, two patients had no improvement in BP or change in medication requirements, and the remaining 15 patients improved (BP, ≤140/90, with decreased medication requirements). In the 24 patients who were not dialysis-dependent preoperatively, SCr decreased to 1 ± 0.1 mg/dL ($P < .05$), and estimated GFR improved to 88 ± 5 mL/min ($P < .05$). In all but two patients SCr was less than 1.5 mg/dL. Two of three dialysis-dependent patients no longer required hemodialysis. Preoperative and postoperative echocardiograms were available for 21 patients for comparison. Documented regression of LVH occurred in nine patients (33%), and hypertrophy developed in two patients (7%) during follow-

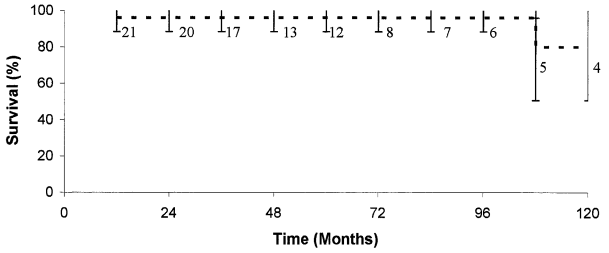

Fig 3. Patient survival, with 95% confidence intervals, by life table analysis, after revascularization to treat Takayasu arteritis–induced renal artery stenosis. Numbers represent number of patients followed up at each time point. Survival at 5 and 10 years was 96% and 80%, respectively.

up. Congestive heart failure resolved in both patients, and did not recur.

Of the 27 patients who underwent treatment of TARAS, 14 (52%) continue to be followed; 10 patients (37%) were lost to follow-up, at a mean of 70 ± 11 months; and three patients (11%) died. Three patients had uncomplicated pregnancies and childbirth after successful revascularization. Two patients with failed interventions died, as described above, and a third patient died 14 years after successful revascularization, as a result of a transfusion reaction. Actuarial survival at 5 and 10 years was 96% and 80%, respectively (Fig 3).

DISCUSSION

Published information concerning the long-term outcome of renal revascularization to treat TARAS comes from India, the Far East, and France. These reports vary considerably in their focus, may or may not define the criteria used to diagnose TARAS, often do not analyze separately the results of intervention for TARAS and interventions in other arterial beds, and analyze only the outcomes of BP and renal artery or graft patency.

Data regarding endovascular renal procedures to treat TARAS are limited, with only three studies of any size, all from India.[10-12] In one study of 20 patients who underwent 33 angioplasty procedures to treat TARAS, Sharma et al[10] reported a technical success rate of 85%, with clinical BP improvement in 82%. Selective angiographic follow-up at a mean of 8 months demonstrated recurrent stenosis in 21%. A follow-up experience from Sharma et al[11] described the results in 62 patients with TARAS. Immediate technical success and positive BP response was 95% and 89%, respectively. Cure of hypertension was demonstrated in 23% of patients. Mean follow-up was 22 months, and a recurrent stenosis rate of 16% was angiographically documented in patients with recurrent hypertension. The degree of BP response is not provided, and discussion of renal function and cardiac function is not included. Tyagi et al[12] studied 54 patients with 75 renal lesions from TARAS. An 89% technical success rate was reported, and a 14% recurrent stensois rate was documented at 14 months of follow-up.

Reported results of surgical revascularization to treat TARAS have, for the most part, focused on the use of bypass grafts, inasmuch as the transmural injury of TA does not lend itself to endarterectomy or open angioplasty.[13] Keiffer et al[14] reported surgical revascularization of 37 renal arteries in 24 patients. Ancillary procedures such as aortic reconstruction (87%) and visceral revascularization (71%) were common. There was one postoperative death. At a mean follow-up of 61.3 months, hypertension was cured in 12 patients (63%) and improved in 31%. Remedial renal revascularization was required in four patients during follow-up. Two other series, one by Lagneau et al[13] and the other by Pokrovsky et al,[15] report similar surgical success, with hypertension cured in 55% to 63% of patients and improved in 17% to 45%, at follow-up of 5 to 14 years. As with endovascular therapy, the end points of renal function and cardiac function were not studied.

Given the beneficial effects we previously reported for surgical revascularization in TA,[3] we have preferentially treated TARAS with open surgical techniques. However, one patient in our current series did undergo successful staged bilateral angioplasty and has required no further intervention. Angioplasty was used in this patient because of her young age, relatively early onset of TARAS with stabilization with steroid therapy, and some regression of renal stenosis. The first angioplasty procedure was performed when the patient was 13 years of age, and the second a year later. Medical management has included prednisone and methotrexate, and the patient is now 20 years old, without evidence of recurrent stenosis. In contrast, seven other angioplasty procedures performed at outside institutions before surgical revascularization failed, and one resulted in loss of a kidney.

On the basis of our limited experience and that discussed above, it appears that the results of endovascular therapy can be optimized when TARAS is limited and somewhat reversible with medical therapy. Longstanding, chronic TA, the most common clinical scenario seen at our institution, produces full-thickness vessel injury, an inelastic fibrotic arterial wall, and a significant incidence of occlusion. Renal artery occlusion was documented in 30% of the patients reported by Lagneau et al,[13] and a similar percentage was noted in our study. Both factors, the pathologic findings and rate of occlusion, limit the use of angioplasty. Whether the advances in endovascular technology, including the use of stents in the renal position, will expand the indications for endovascular treatment of TARAS, as it has for atherosclerotic disease, remains to be established.

Inherent to any discussion of surgical treatment of TARAS is the natural history of TA and the role of medical management. In previous reports concerns have been expressed that intervention for TA before or without medical therapy may compromise the surgical results[16] because of progression of the inflammatory process. In the present study, approximately 50% of patients were receiving steroid or immunosuppressant therapy at the time of operation, and 35% were maintained on therapy long term. Nevertheless, graft failure was uncommon and as likely to occur in patients receiving therapy as those not receiving medical therapy. Our findings are consistent with two reports from

the National Institutes of Health, which documented the durability of vascular reconstructions performed to treat symptomatic TA.[17,18] However, in both reports the specifics of the postoperative medical therapy are not provided.

The natural history most consistent with the foregoing observations is that segmental injury to the aorta and its branches from TA is a one-time insult of unknown cause. This ultimately results in fibrous obliteration and stenosis, and at times superimposed atherosclerosis of the affected arterial segments. In this context the primary and greatest benefit of medical therapy is to limit the arterial inflammation in involved segments, particularly early in the disease. How much benefit this provides over time and whether it justifies the long-term use of immunosuppressant and corticosteroid therapy is unknown. Furthermore, the absence of reliable biochemical markers, such as ESR, C-reactive protein, and von Willebrand factor, to determine the acuity of the inflammatory process[19] means that the indications for medical therapy are inexact and empirically based on patient symptoms and elevated inflammatory markers. However, medical therapy does not eliminate, should not delay, and cannot be used in place of renal revascularization in the patient with TARAS complicated by malignant hypertension, renal dysfunction, or cardiac decompensation.

With these assumptions in mind, renal revascularization was performed in patients with TARAS, and provided 1, 3, and 5-year patency rates similar to those reported by others for TARAS and approaching those reported for fibromuscular dysplasia[20] and atherosclerosis.[21] Concomitant aortic reconstruction or suprarenal location for inflow was often necessary to avoid an infrarenal aorta with extensive TA involvement. Mesenteric revascularization was rarely required in the absence of clinical symptoms of mesenteric ischemia. The type of renal bypass graft used did not appear to influence the results, because late failures occurred with both autogenous and prosthetic grafts.

Previous studies of surgical revascularization for TA have documented graft failures secondary to inflammatory involvement at anastomoses. Consequently, we altered our operative technique in the mid-1980s so that all anastomoses are placed in macroscopically normal aorta or renal artery segments, or, in the absence of that possibility, segments with minimal TA involvement. For location of the aortic anastomosis a preoperative contrast-enhanced CT scan can be helpful in identifying which aortic segment has the least mural thickening from TA. On occasion, because of diffuse mural abdominal aortic involvement, optimal aortic inflow requires concomitant aortic reconstruction or a suprarenal or thoracic aortic anastomosis. In addition, placing the distal anastomosis in normal renal artery may require extensive dissection of the segmental branches of the kidney, branch reconstruction, and ex vivo techniques. Since adoption of the above surgical approach we have not observed progression of TA to cause graft failure in any patient with TARAS or in patients with TA with failed extrarenal reconstructions.[3] Rather, the pathologic features of explanted failed grafts are typical of the intimal hyperplasia found in failed vascular reconstructions performed to treat atherosclerotic occlusive disease. Furthermore, unlike the experience of Miyata et al,[22] who reported an 8.5% incidence of anastomotic aneurysm in 103 patients with surgically treated TA, anastomotic aneurysms did not occur in our patients. However, those authors reported that 25% of TA lesions they treated were aneurysms, compared with only 7% in our series. They also documented that aneurysmal TA is an independent predictor for the development of an anastomotic aneurysm.

The decision to proceed with revascularization was predicated on the angiographic findings of an occluded or stenotic (>60%) renal artery from TARAS in a patient with hypertension. Associated renal or cardiac dysfunction was also considered when making the decision to proceed with revascularization. Functional tests such as renal vein renin assays or captopril renography were not routinely used to determine the appropriateness of revascularization. Nephrectomy was performed only for kidneys that at operative exploration had nonreconstructible renal anatomy. As Oskin et al[23] documented, minimal kidney size or lack of visualization of a distal renal artery or nephrogram at preoperative angiography were not predictive of nonreconstructible renal anatomy.

After revascularization a significant improvement in BP control and reduction in medication requirements was achieved. It is well-recognized that renovascular hypertension is responsible for a greater degree of target organ damage than is essential hypertension.[24] Consequently, when successful renal revascularization provides substantial benefit in BP control, it should be expected to limit target organ damage as well.[25] The magnitude and duration of this benefit is unknown, because previous reports of either endovascular or open surgical techniques to treat TARAS have restricted outcome analyses to hypertension control only.[10,12,15]

In our series, revascularization to treat TARAS resulted in successful retrieval of renal function, consistent with what has been demonstrated by Dean et al[26] in atherosclerotic renal artery disease. A documented increase in estimated GFR, lowering of mean SCr, and withdrawal of two patients from hemodialysis occurred after renal revascularization. The importance of improvement or stabilization of renal function on survival is evident when one considers that two of the three patients who died during the course of this study had failed renal interventions, which ultimately resulted in the need for hemodialysis. The effect of an initially successful revascularization on subsequent renal function and patient survival has been demonstrated by Hansen et al[27] for atherosclerotic renal artery disease.

The most dramatic and immediate responses to renal revascularization occurred in patients with severe cardiac dysfunction. Refractory, uncontrolled heart failure, which was present in 16% of the patients reported by Keiffer et al[14] and 7% in our series, responded immediately to successful revascularization, and never recurred. This is similar to the dramatic results of renal revascularization for "flash" pulmonary edema and cardiovascular collapse due to renal artery stenosis. Given the unique effects of angiotensin II

on the myocardium and the development and maintenance of LVH and dysfunction,[28] these dramatic responses are not entirely unexpected. However, the subtler finding of echocardiographic evidence of LVH regression was unexpected. LVH regression after successful revascularization to treat TARAS has not been previously reported, but LVH regression has been reported in patients with atherosclerotic renal artery disease treated medically[29] or with renal revascularization.[25] Our findings require further prospective validation, because echocardiographic data were collected over more than two decades, and the technology and diagnostic criteria have evolved considerably. These findings and the prevalence of echocardiographic abnormalities in this patient population have prompted us to perform echocardiography routinely in the initial evaluation of TARAS.

The specific effect of TARAS on survival has not been reported, because most studies concerning patients with TA have focused on brachiocephalic involvement. However, it is well known that severe hypertension is an independent predictor of premature death and major adverse events in patients with TA,[2,30,31] with 5-year survival rates less than 60%.[30] Ishikawa[31] demonstrated that the presence of severe hypertension alone reduces the 10-year event-free survival from 97% to 59%. This is in a patient population consisting predominantly of women of childbearing age, whose life expectancy should be 68 to 70 years.[32] In addition, renal dysfunction[33] and LVH[34] both independently increase the risk for cardiovascular events and death from all causes. Survival in today's era of more sophisticated medical management of hypertension has not been reported for TARAS. This precludes a direct comparison of survival between patients managed with revascularization versus those medically managed. However, the actuarial survival rates of 96% at 5 years and 80% at 10 years reported in this series strongly suggest that the response of BP and of renal and cardiac function to renal revascularization positively influenced survival.

In conclusion, TARAS is an often unrecognized clinical entity that can result in life-threatening hypertensive and cardiovascular events. Surgical revascularization with use of bypass grafts or endovascular intervention for early stenotic, nonocclusive TARAS provides demonstrable improvements in BP, and renal and cardiac function. The documented salutary clinical response on BP, and renal and cardiac function after successful intervention positively influenced survival. This positive global response establishes renal revascularization as a successful and durable intervention for TARAS and a benchmark to which other therapies should be compared.

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DISCUSSION

Dr Linda Reilly (San Francisco, Calif). Thank you, Mr Chairman, members, and guests. I would like to thank the Society for inviting me to discuss this paper, and I would like to thank the authors for providing me a copy of the paper in a timely manner. I would also like to thank them for the second version of the paper, and I'd like to thank them for the third version of the paper. Of course, I am just teasing a little bit, because my usual state of being way behind protected me from doing anything with any of the first two versions of the paper. As my sister, with whom I am sharing a room, will tell you, I was doing this last night.

The authors have reported their results managing 27 patients with renal artery stenosis related to Takaysu's arteritis. I have a few questions for the authors regarding study design, data, and their conclusions.

You included in your study group eight patients who underwent prior renal artery treatment that had failed, including three who had undergone previous aortorenal bypass. Other than the obvious benefit of having more patients in the report, why include this group of people? The fact that they have already failed treatment may actually bias your results. In light of that, can you tell us if the subsequent six graft stenoses or occlusions correlated with the prior treatment failure, or not?

Approximately half of your patients were on steroids at the time of the intervention for their Takaysu's-induced renal artery stenosis. Did the subsequent six graft failures correlate with steroid use at the time of your intervention, or not?

Because these patients were accumulated over a long time interval, I assume that this is a retrospective study. So how many of these patients actually had creatinine clearance measurements? Also, how many underwent transthoracic echocardiography to establish the presence or absence of left ventricular hypertrophy and its resolution?

I am also intrigued by the observation that two patients developed left ventricular hypertrophy during follow-up. I wonder if you have some comments on why that happened.

You report that both duplex ultrasound and MRA were used for postoperative surveillance, but to the best of my recollection neither of these modalities was available during the first several years of your study, which began in 1977. Were you able to use any surveillance modalities during that early time frame? If not, does the lack of a surveillance instrument in the early part of the study have any implication for your identification of end points, particularly graft stenosis or occlusion?

You suggest that an endoluminal approach to Takaysu's-induced renal artery stenosis might be appropriate in early circumstances, when the pathologic process is limited and somewhat reversible. Could you characterize the stage for us in some manner that would allow others to recognize it? Do you have information about the interval between the onset of Takaysu's disease in your patients, or as a surrogate perhaps the point of diagnosis of Takaysu's in your patients, and the point at which you intervene for the renal artery stenosis? This might possibly be used to guide others in determining when endoluminal treatment might be worth considering.

Based on the treatment outcomes, you conclude that surgical renal revascularization is the primary intervention for patients with Takaysu's-related renal artery stenosis. Your results are certainly quite laudable, and I don't disagree with your view about the role of operative renal revascularization in this condition. However, I am not sure that your data can actually prove that point, particularly in view of the lack of a comparison group of patients managed with endoluminal techniques. It is important to realize that this group of 27 patients was accumulated over 26 years, or 1 patient per year. During that time both operative renal artery reconstruction and endoluminal reconstruction have evolved. Furthermore, since many of the renal arteries treated in this series were occluded, I think it amounted to approximately one third, the endoluminal approach was likely not really an option for many of these patients. So I would come to a different conclusion. I would conclude that the exact role of each treatment approach remains to be defined, with the debate centering on the areas of durability versus reduced risk.

Again, I would like to thank the Society for the opportunity to discuss the paper.

Dr Fred A. Weaver. Thank you, Dr Reilly. Hopefully I captured all of those questions.

As far as the patients who had previously thrombosed aortorenal bypasses, these were all procedures done at an outside insti-

tution, not at our own. The fact that they had a failed aortorenal bypass did not correlate with any subsequent failure or stenoses in our own group. There was no relation to the use of steroids or lack of steroids or immunosuppression and graft failure. Our own bias with regard to steroids and immunosuppressants is that it is a modality to slow the disease progression. As we mention in the article, our concept of the natural history of this disease is that it is a one-time event, in which segments of the aorta are affected. They then go on to develop an inflammatory process that over the course of time develops into lesions and then occlusive lesions. There may be superimposed atherosclerosis, as well, in the late stages of the disease. But the disease is not one that over time involves new segments previously not affected by the initial event. Consequently, steroids and immunsuppressants are used to manage the ongoing inflammatory response in those affected segments. Since we attempt, as mentioned in the article, to place all of our anastomoses in uninvolved aorta, aortic graft, and/or the distal renal artery, the immunosuppressive management may have little or no effect on the vascular reconstructions. That also explains why we had so many branch renal artery reconstructions, because, in order to find normal renal artery, dissection beyond the main renal artery was common.

All of the creatinine clearance was an estimated GFR based on height, weight, and serum creatinine at the time of preoperative evaluation and follow-up.

We had data on 21 patients with echocardiography and subsequent echo follow-up, and that's where the regression data come from. It is admittedly a soft finding, and we mention this in the article, because the techniques of echocardiography, as well as diagnostic criteria, have evolved considerably over the time of this study.

With regard to follow-up, it is true that duplex or MRA modalities were not available. Any surveillance was performed based on clinical findings and angiography. There was one patient operated on in 1977, another patient in the early 1980s, and the remaining patients were from the mid-1980s and on, when duplex ultrasound scanning as well as early MRA were available at our institution.

With regard to the role of endovascular therapy, I think the one patient who we used who primarily was treated in this manner is a good example of how it should be employed. This patient had a febrile prodromal viral-type illness, and then about 2 years later began to develop evidence of renal artery stenosis as well as infrarenal aortic stenosis. It was at that time that she had intervention in one renal artery, and then subsequently 1 year later in the other renal artery, and throughout that period of time was maintained on steroids initially, and then methotrexate and cytoxan immunosuppression subsequently. That patient has not developed restenosis, and we have follow-up on her of 8 years. I fully expect that over the course of time she most likely will require formal surgical revascularization as the process continues in her renal arteries. There is also no data in the literature at all on the use of stents and whether in fact they might help in the outcome of endovascular therapy.

I would agree that our data are not a straightforward comparison, and given the infrequency of this disease and the rarity of reports, not only in the United States but in the world in general, comparison prospective studies are not going to happen. We have substantial experience in other vascular beds in Takaysu's, and we have found that surgical reconstruction works in our hands much better than endovascular interventions, which we have used in other beds as well.

I would like to thank Dr Reilly for the questions, and would be happy to answer any other questions you might have.

Dr Louis Messina (San Francisco, Calif). Fred, I would like to compliment you and your colleagues on another really excellent publication in patients with Takaysu's arteritis. I have two questions for you.

One, Takayasu's is a clinical diagnosis, and so I was wondering how many of your patients had arch or pulmonary artery involvement, or how is it that you reach the diagnosis? As you know, histologically they show giant cell infiltration, which makes it difficult to distinguish from arteritis, so I would just appreciate more information in that regard.

And then you did show an illustration of a patient who clearly had visceral disease. Did any of your patients have symptomatic visceral disease or disease that you thought required treatment? How many did you treat, and in what way did you treat them?

Dr Weaver. With regard to the visceral artery disease, I would say about a third of patients had concomitant visceral artery disease of at least either the celiac or SMA. Our approach to revascularization has been that, if they have no clinical symptoms, for example, weight loss, abdominal pain, and so on and so forth, and in the operating room they have a pulse in the small bowel mesentery, we do not perform a prophylactic revascularization. On the other hand, in those patients who do have visceral disease and are symptomatic, we obviously will perform a revascularization. We did that in one patient. A second patient had to be taken back to the operating room and an aorta-SMA bypass performed, because she developed mesenteric ischemia postoperatively. I will say, I violated one of my premises in the operating room in the sense that her SMA pulse after revascularization really was not so strong as it should have been. I should have done it at the initial operation.

With regard to the diagnosis, you are absolutely right. It is a clinical diagnosis, and we relied on the American College of Rheumatology criteria. Predominantly, patients are female. They are young. In our group, about half of them had brachiocephalic disease. We had two patients with pulmonary artery disease, and we had 13 patients or so for whom we had actual biopsy specimens demonstrating an inflammatory arteritis. But, as you have well said, it is a very nonspecific finding, and you cannot base the diagnosis on histologic findings at operation.

Dr Ronald Dalman (Palo Alto, Calif). Fred, how did you manage the oversewn aneurysm in the thoracic aorta?

Dr Weaver. We basically cross-clamped proximal, put our graft in, just opened up that thrombosed aneurysm, left it in place, oversewed distally, and then put the grafts in.

Dr Dennis Baker (Los Angeles, Calif). Do you have a standardized approach to decide whether you are going to use saphenous vein or prosthetic for your bypass, because I see you have a mix of the two?

Dr Weaver. That's a good question. There are no data in the literature as to which is preferable, prosthetic or saphenous vein. I am beginning to move to the point where I think a prosthetic graft may be a better choice, as long as it is a short-segment graft. I think

suprarenal grafts with long segments of prosthetic probably will not behave as well. I am a little reticent to do that if I have good saphenous vein available.

Dr Charles Andersen (Tacoma, Wash). I question medical treatment, surgical treatment, and the timing between the two. Do you feel it is important to have the inflammatory component of the disease under somewhat of a controlled state prior to surgical intervention, and likewise in the postoperative course, to prevent restenosis do you feel it is important to keep that inflammatory component under control?

Dr Weaver. Well, the short answer is no, because the clinical estimation of the inflammatory process is very inexact. You cannot rely on ESR. In fact, in our earlier study back in the 1980s we compared biopsy specimens with ESR, and found no correlation between the amount of inflammatory process on the biopsy specimens and the degree of ESR. So we do not make any attempt to bring the ESR down with immunosuppression to less than 20 or so. All that does is delay a necessary operation.

With regard to postoperative treatment, as I mentioned, we make every effort, and it is actually absolutely essential for the patency of these grafts to sew into proximal and distal vessels that are uninvolved. Consequently the immunosuppression and steroids are not used to prevent graft failure. It was not recurrent Takaysu's arteritis in the two patients in whom we had histologic specimens to review; the pathologic finding was intimal hyperplasia. The long-term steroid use is to prevent the progression of the disease in other segments that may have TA involvement, such as the brachiocephalic and visceral vessels.