Takayasu's arteritis: Operative results and influence of disease activity

Charles E. Fields, MD,[a] Thomas C. Bower, MD,[a] Leslie T. Cooper, MD,[b] Tanya Hoskin, MS,[c] Audra A. Noel, MD,[a] Jean M. Panneton, MD,[a] Timothy M. Sullivan, MD,[a] Peter Gloviczki, MD,[a] and **Kenneth J. Cherry, Jr, MD,[d]** *Rochester, Minn; and Charlottesville, Va*

Objectives: **To determine the short- and long-term outcomes of patients treated operatively for Takayasu's arteritis and the effect of disease activity on results.**

Methods: **Forty-two (17%) of the 251 patients enrolled in our Takayasu's arteritis registry between 1975 and 2002 required operation for symptomatic disease. Data were obtained from the registry, patient records, phone correspondence, and written surveys.**

Results: **There were 38 females and 4 males with a median age of 29 years (range, 12 to 56 years), and 32 (76%) were white. Sixty operations were performed for symptomatic disease. The mean duration of symptoms before operation was 5.6 months (range, 0 to 25 months). Thirteen (31%) patients had active disease and underwent operation for acute presentation or failure of medical management. Thirty-nine patients (93%) had operation for occlusive disease. Twenty-two (52%) patients had involvement of both the great and abdominal aortic branch vessels; 10 (24%) had great vessel disease alone; 9 (21%) had involvement of abdominal arteries; and 1 (2%) had coronary artery disease. There was no operative death, myocardial infarction, major stroke, or renal failure. Three patients had early graft thrombosis, two had a minor stroke, and two developed hyperperfusion syndrome. The median follow-up was 6.7 years (range, 1 month to 19.3 years). Eleven (26%) patients required 15 graft revisions; five of the patients had active disease at the time of initial operation. All early revisions (<1 year) were in patients with active disease. By Kaplan-Meier analysis, freedom from revision at 5 and 10 years was 100% in patients with quiescent disease not requiring steroids (group I, n = 5, 12%), 95% and 81% in patients whose disease was quiescent on steroids (group II, n = 24, 57%), 57% in patients with active disease on steroids (group III, n = 7, 17%), and 33% in patients with active disease and no long-term steroids (group IV, n = 6, 14%) ($P < .006$). The rate of revision or progression of disease at another site in 5 years was 0% in group 1, 10% in group 2, 57% in group 3, and 67% in group 4 ($P < .001$) The differences were even more pronounced when an analysis was done on the basis of disease activity alone, irrespective of steroid use. During the follow-up period, 3 of 39 great vessel, 2 of 18 mesenteric/renal, and 1 of 9 aortofemoropopliteal reconstructions occluded. The predicted mortality for patients was 4% at both 5 and 10 years (95% CI) respectively (confidence interval [CI], 0% to 11%) and 10 (CI, 0% to 14%) years, respectively.**

Conclusions: **The minority of patients with Takayasu's arteritis require operation. In our predominantly white female patient population, occlusive symptoms were the most common indication for operation. Operation for these selected patients was safe, with no operative mortality, myocardial infarction, major stroke, or renal failure. Patients with active disease requiring operation are more likely to require revision or develop progressive symptomatic disease at another site. Long-term survival is excellent, regardless of disease activity at the time of operation. (J Vasc Surg 2006;43:64-71.)**

Takayasu's arteritis is a nonspecific inflammatory disease most famously described in 1908 by Mikito Takayasu, an ophthalmologist in Japan.[1] The inflammatory process primarily affects large arteries such as the aorta and its branches. The entity includes both occlusive and aneurysmal disease, the type of which varies by geographic location. Occlusive disease is more prevalent in Japan, the United States, and Europe, whereas aneurysmal disease is more common in India, Thailand, Mexico, and Africa.[2] The prevalence is higher in women, and the median age of onset varies from 25 years in Asia and the United States to 41 years in Europe.[3,4]

If untreated, patients will die from cerebral hemorrhage, renal failure, heart failure, myocardial infarction, cerebral thrombosis, or aneurysm rupture. To date, no standard therapy is applicable to all patients. Most patients respond to medical therapy, but complications from the disease may necessitate surgery in a poorly documented minority of patients. Previous reports have shown that operations can be performed safely. The durability of the reconstructions has varied, however, with some authors reporting a high incidence of restenosis or pseudoaneurysm.[4-12] Although clinicians have long felt that disease activity affects outcomes, evidence-based documentation of that effect on operation has been lacking. In the absence of a uniform diagnosis of disease activity, authors have often used steroid usage as

From the Divisions of Vascular Surgery,[a] and Vascular Medicine,[b] and the Section of Biostatistics,[c] Mayo Clinic and Foundation; and the Division of Vascular Surgery, University of Virginia.[d]

Competition of interest: none.

Presented at 58th Annual Meeting or the Society for Vascular Surgery, Anareim, California, June 3-6, 2004.

Reprint requests: Kenneth J. Cherry, Jr, MD, University of Virginia, Division of Vascular Surgery, Charlottesville, VA (e-mail: KJC5KH@hscmail.mcc.virginia.edu).

CME article

0741-5214/$32.00

doi:10.1016/j.jvs.2005.10.010

Table I. The 1990 criteria for the classification of Takayasu arteritis*

1. Development of symptoms or findings related to Takayasu arteritis at age ≤40 years
2. Development and worsening of fatigue and discomfort in muscles of one or more extremities while in use, especially the upper extremities
3. Decreased pulsation of one or both brachial arteries
4. Difference of >10 mm Hg in systolic blood pressure between arms
5. Bruit audible on auscultation over one or both subclavian arteries or abdominal aorta
6. Arteriographic narrowing or occlusion of the entire aorta, its primary branches, or large arteries in the proximal upper or lower extremities, not due to arteriosclerosis, fibromuscular dysplasia, or similar causes; changes usually focal or segmental

*For purposes of classification, a patient shall be said to have Takayasu arteritis if at least three of these six criteria are present. The presence of any three or more criteria yields a sensitivity of 90.5% and a specificity of 97.8%.

that determinant and have not been able to show differences between their patient subsets.

Further, few reports define the number of patients with Takayasu's arteritis needing repair. The purpose of this study was to investigate the short- and long-term results of patients treated operatively for Takayasu's arteritis and the effect of disease status on their outcomes.

PATIENTS AND METHODS

The clinic records of all patients with Takayasu's arteritis who required operation for symptomatic disease between January 1, 1975, and November 30, 2002, at the Mayo Clinic in Rochester, Minn, were abstracted from a Takayasu's arteritis registry. Some of these patients have been previously reported.[8,12] Demographic data, comorbid medical conditions, history and physical findings, diagnostic and laboratory test results, operative records, pathology reports, postoperative complications, graft patency, and mortality were recorded. Complete follow-up was defined as data obtained ≤12 months of the end point of the study.

Diagnosis of Takayasu's arteritis was made by using American College of Rheumatology criteria, which combines three or more clinical features or arteriographic findings (Table I).[13] All patients underwent thoracic and abdominal aortography, with selected runoff views, to define the location and extent of the disease. Pathologic criteria of Takayasu's arteritis included arterial wall infiltration by lymphocytes, epithelioid cells, or giant cells; destruction of medial elastic fibers, or replacement of medial smooth muscle cells with fibrosis. Active disease was defined by two or more of the following: clinical, pathologic, laboratory, or operative criteria. These included systemic features such as fevers, myalgias, or arthralgias; active inflammation on pathologic specimen (eg, lymphoplasmacytic infiltrate, giant cells) taken from diseased arteries; elevation of serum markers such as erythrocyte sedimentation rate (ESR) or C-reactive protein; or acute inflammation of the artery and surrounding soft tissues at the time of operation. The mainstay of medical management was corticosteroids (1 mg/kg), with the addition of other agents as dictated by disease activity and clinical response to the steroids. Steroids were continued for at least 3 months. A taper-in dose was considered in patients who had clinical and laboratory response to treatment.

Operations were done in patients who failed medical therapy. This included those with acute symptoms with an unrelenting clinical course or chronic symptoms despite maximum medical therapy. All reconstructions or revisions were done by open technique. No patient was treated with angioplasty or stenting. All graft anastomoses were performed to noninflamed areas of the target artery whenever practicable. Graft patency was defined by the results of the last imaging study, which included duplex ultrasonography in 59%, arteriography in 23%, magnetic resonance imaging (MRI) in 12%, and computed tomography (CT) in 6%. Ten patients with aortoiliac reconstructions were assessed by clinical examination alone and were not included in analysis of patency.

Revision was defined as any operation performed to maintain or re-establish patency of a vascular reconstruction. *Early revision* was defined as occurring <1 year of the initial operation. *Progression of disease* was defined as the development of a symptomatic arterial stenosis or occlusion in an area that previously had been uninvolved by arteriography and that required another operative reconstruction. Progression of disease was determined by a variety of diagnostic imaging, but primarily arteriography and MRA. Surveillance intervals varied over the study. In the last 5 years of the study, duplex scans were done within 3 to 6 months of operation, 6 months later, and then annually thereafter. Imaging was done for any patient with recurrent or new symptoms.

Life-table analyses were done by the Kaplan-Meier method to determine survival, freedom from revision, and freedom from revision or progression of disease. These outcomes were assessed by steroid use alone, by steroid use and disease activity, and by disease activity alone, regardless of steroid use.

We further subdivided the analysis into four groups: group I included patients with quiescent disease no longer on steroids; group II included patients with quiescent disease on long-term steroids; group III was defined as patients with active disease on steroids; and group IV were those patients with acute active disease not previously on steroids. A significant difference in outcome was denoted by $P < .05$. The study was approved by the Institutional Review Board of the Mayo Foundation.

RESULTS

Demographics, diagnosis, and operation. From January 1, 1975, to November 3, 2002, 42 (17%) of 251 patients in our registry required 60 operations for symptomatic Takayasu's arteritis. Reconstructions were performed to 116 arteries. There were 38 females and 4 males with a median age of 29 years (mean, 32; range, 12 to 56 years); 32 were

Table II. Presenting signs and symptoms of patients with Takayasu's arteritis requiring operation

*Sign or symptom**	*n*	*%*
Extremity Symptoms		
Upper extremity exertional fatigue	1	19
Lower extremity claudication	5	9
Renal Symptoms		
Hypertension	7	12
Renal failure	1	2
Neurologic		
Dizziness	7	12
Visual disturbance	5	9
Global ischemia	5	9
Headache	3	5
Stroke	1	2
Systemic/constitutional symptoms	5	9
Congestive failure	3	5

*Some patients had more than one symptom or sign.

white (76%), 6 were Hispanic (14%), and 4 were Asian (10%).

The clinical presentation is outlined in Table II. The most common symptoms were either cerebrovascular or exercise-induced limb ischemia; both symptom complexes occurred in 16 patients each (38% for each group). Renovascular hypertension or renal insufficiency occurred in 8 patients (19%); constitutional symptoms such as fever, malaise, or fatigue occurred in 5 (9%); and cardiac symptoms occurred in 3 (7%). Atherosclerotic risk factors included hypertension (52%), smoking (38%), hyperlipidemia (14%), and diabetes mellitus (7%).

Pathologic specimens were available in 35 of 42 patients undergoing operation. These were diagnostic of Takayasu's arteritis with giant cells and lymphocytic infiltration in 22 and the remaining 13 had pathology consistent with Takayasu's arteritis, with fibrosis and medial degeneration. The ESR was also evaluated as a marker of disease and had a sensitivity of 36% and specificity of 83% compared with pathologic specimens. All 13 patients with active disease were identified by pathologic specimens, clinical factors, and surgical criteria. Nine of these had an elevated ESR. Seven others with inactive disease were on long-term steroid therapy and did not have pathology specimens available for review. These patients were classified by using clinical presentation, surgical criteria, and the ESR.

Preoperative cardiac testing included clinical history and electrocardiography in 15 patients, dobutamine echocardiography or sestamibi scans in 10 patients, cardiac catheterization in 9, and echocardiography with electrocardiography in 8.

Occlusive disease occurred in 39 patients (93%). The other three had aortic aneurysms (one infrarenal, one thoracic, and one ascending aorta). Twenty-two patients (52%) had involvement of both the aortic arch and abdominal aortic branch vessels; 10 (24%) had great vessel disease alone; 9 (21%) had involvement of the abdominal arteries; and 1 patient (4%) had coronary artery disease. One of the patients with isolated great vessel disease also had pulmonary artery involvement. In addition, three patients had aortic valve replacement at the time of reconstruction. Five patients had reconstructions of the aorta or branch vessels in different territories, all at the same operation (Fig 1).

Quiescent disease was present in 29 patients (69%). Active disease was present in 13 patients (31%), of which six not previously on steroid therapy presented with acute, fulminant, life-threatening symptoms. Three had crescendo transient ischemic attacks or global hypoperfusion, two had congestive heart failure, and one had congestive failure and acute renal failure. Intravenous steroid therapy was initiated in all of these patients perioperatively.

Great vessel reconstructions were performed for patients with global hypoperfusion, transient ischemic attack, or stroke. Ascending aorta and valve reconstructions were performed for those with congestive heart failure, aneurysm, or valve pathology. Renal reconstructions were performed in patients with worsening renal function or hypertension refractory to medical management. Aortoiliac reconstructions were done in patients with incapacitating claudication. Mesenteric reconstructions were performed in symptomatic patients (abdominal pain, weight loss) or, rarely, at the time of renal reconstruction in the few patients who had critical disease in both beds.

Overall, the mean duration of symptoms before operation was 5.6 months (range, 0 to 25 months). The median follow-up was 6.7 years (range, 1 month to 19.3 years). Follow-up was complete in 79% of patients who lived within the United States and in 71% of international patients.

Early outcome. There were no operative or in-hospital deaths. No patient sustained a myocardial infarction, major stroke, or renal failure. Fifteen major postoperative complications occurred in 11 patients (Table III), of which three had in-hospital carotid graft occlusions, and another patient had a renal vein graft stenosis. All four grafts were successfully revised. Two patients developed minor strokes. One of the minor stroke patients was asymptomatic but had a small area of infarction noted on a head CT scan. Two other patients had cerebral hyperperfusion syndrome and required intensive care but had no seizures or focal neurologic deficits and had only small areas of intracranial hemorrhage. One of these also had abdominal compartment syndrome. This problem developed in a young woman whose great vessels, renal arteries, and entire thoracic abdominal aorta were involved. A drawing of her reconstruction is shown in Fig 1. She had no non-reconstructed vascular bed to compensate for the major hemodynamic changes resultant from her operation. She required a large amount of fluid intraoperatively. The four patients with either minor stroke or hyperperfusion syndrome had full recovery before hospital dismissal. Mean length of stay was 11 days, but varied by procedure.

Late outcome. Only one death occurred during follow-up, and this was related to a motor vehicle accident. The survival rate at 1 year was 100% and was 97% at both 5 and 10 years (Fig 2). There was no survival benefit related to the use of steroids (Fig 3).

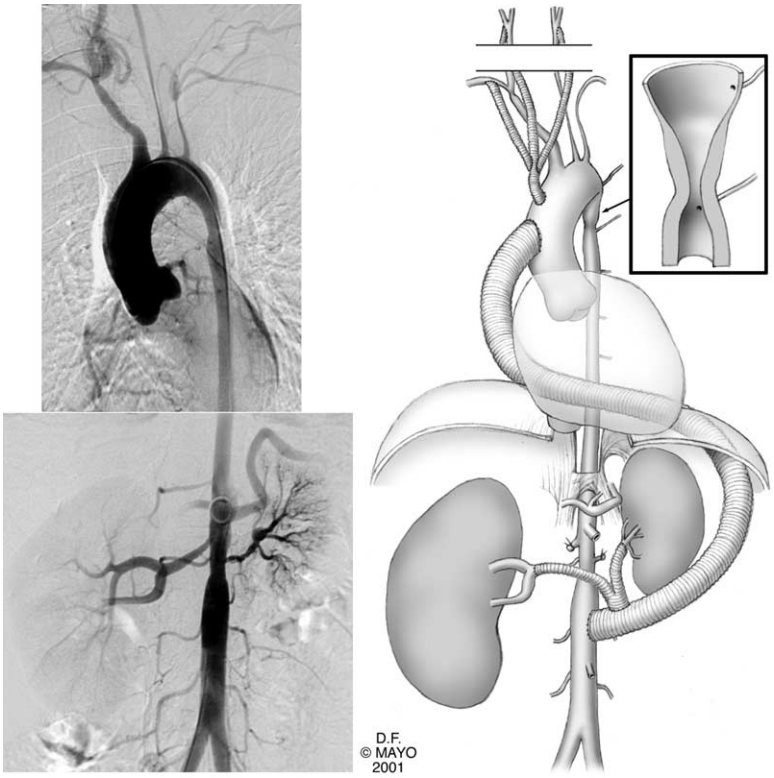

Fig 1. Complex reconstruction performed in a patient with combined great vessel, thoracic aorta, and renal occlusive disease. *Arrows* at areas of revascularization. (Reprinted with permission of the Mayo Foundation.)

Table III. Early operative morbidity of Takayasu's arteritis patients

Complications	*n*
Major complications	
Graft failure	5
Occlusion	4
Stenosis	1
Minor stroke	2
Hyperperfusion syndrome	2
Ureter transection	1
Abdominal compartment syndrome	1
Bilateral vocal cord paralysis	1
Bilateral chylothorax	1
Intestinal ischemia	1
Hemothorax	1
Pancreatitis	1
Major wound infections	1
Minor complications	
Minor wound infection	3
Lymphocele	1

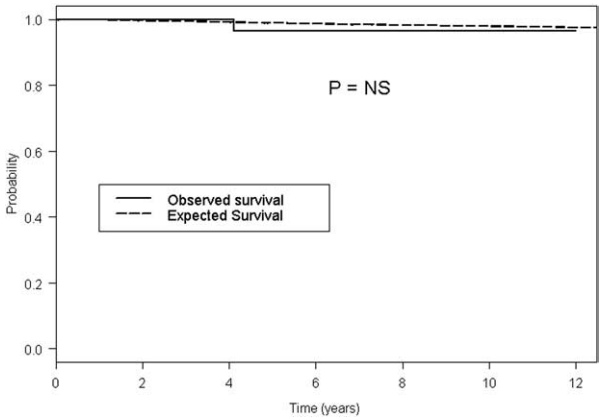

Fig 2. Observed survival among Takayasu's arteritis patients requiring operation compared with the expected survival of the general United States white population based on census data.

Pregnancy. Sixteen patients delivered healthy children by vaginal delivery after their operation for occlusive disease. One patient has a small thoracic aneurysm that has not required surgical repair. Two other patients with aneurysms became pregnant but had elective abortions on the recommendation of their referring physician before undergoing repair. Twelve patients had great vessel involvement alone, three had renal or mesenteric disease, and one had great vessel and iliac involvement. Thirteen of 16 patients were taking long-term steroids, and three had been recently prescribed steroids at operation. The number of patients taking steroids at time of delivery was unknown, however.

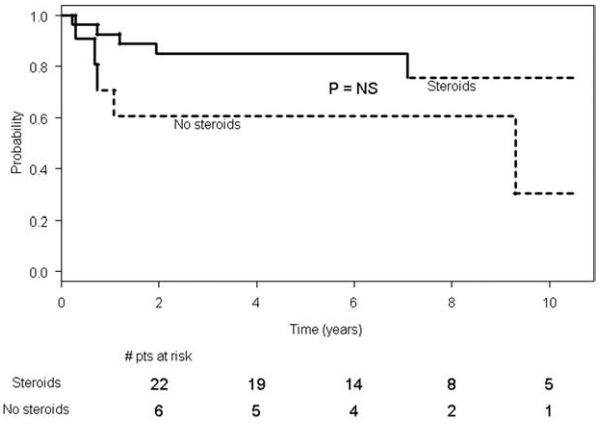

Fig 3. Freedom from revision based on the presence or absence of steroid use at the time of operation.

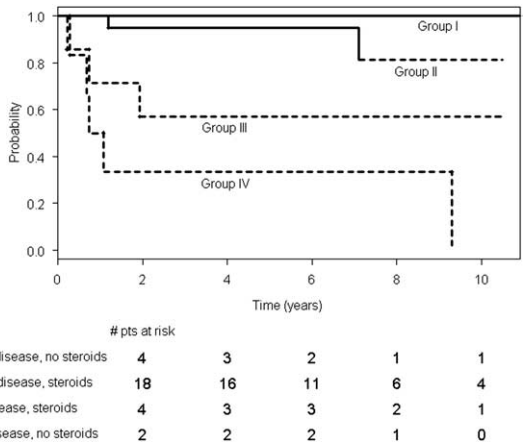

Fig 4. Freedom from revision on the basis of steroid use and disease activity. Group I vs group II ($P = .49$), I vs III ($P = .14$), I vs IV ($P = .03$), II vs III ($P = .045$), II vs IV ($P = .0002$), III vs IV ($P = .17$)

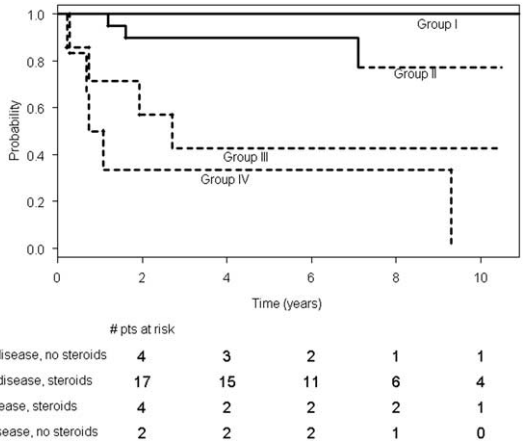

Fig 5. Freedom from revision or progression on the basis of steroid use and disease activity. Group I vs II ($P = .40$), I vs III ($P = .09$), I vs IV ($P = .03$), II vs III ($P = .02$), II vs IV ($P = .0005$), III vs IV ($P = .29$).

Late graft patency, graft revision, and progression of disease. The graft patency in 32 patients (76%) was confirmed by duplex ultrasound, MRI, CT, or arteriography. All 42 patients had clinical evidence of patency that included absence of symptoms, palpable pulses, equal extremity blood pressure measurement, normal ankle-brachial indices, improvement or stability of renal function, and absence of neurologic deficits.

Eleven patients (26%) required 15 graft revisions. Ten were done <1 year, and the other five were done later. All 10 early revisions (<1 year) and three of five late revisions were in patients with active disease at the initial operation. Three of 39 great vessel reconstructions, 2 of 18 mesenteric/renal, and 1 of 9 aortofemoropopliteal reconstructions occluded during the follow-up period.

Three patients (7%) had progressive disease requiring operation at another arterial site. One had a mesenteric reconstruction followed by an upper extremity reconstruction and subsequently an aortoiliac reconstruction. Another had a carotid reconstruction followed by a subclavian reconstruction. The third patient had an aortic valve replacement with great vessel reconstruction followed by a left renal bypass and then a right renal bypass.

Kaplan-Meier analysis was used to determine the effect of steroid use, steroid use and disease activity, and activity alone on the need for graft revision or progression of disease. When all 42 patients were analyzed only by the presence or absence of long-term steroid therapy, with no regard to disease activity, no differences in freedom from revision or disease progression were noted. However, when analyzed with respect to steroid use and disease activity, there were significant differences (Figs 4 and 5). Freedom from revision at 5 and 10 years was 100% in patients with quiescent disease not requiring steroids (group I, n = 5), 95% and 81% in patients whose disease was quiescent on steroids (group II, n = 24), 57% at both 5 and 10 years in patients with active disease on steroids (group III, n = 7), and 33% at both 5 and 10 years in patients with active disease not on long-term steroids (group IV, n = 6) ($P < .006$) (Fig 6). The freedom from graft revision or progression of disease at another site that required operation was 100% in group I, 90% in group II, 43% in group III, and 33% in group IV ($P < .001$) (Fig 7). The differences were even more pronounced when disease activity alone, irrespective of steroid use, was used for the analysis (Figs 8 and 9).

DISCUSSION

Takayasu's arteritis is a rare but potentially fatal disease if left untreated. The disease is most common in Japan. In the United States, it is estimated to occur in only 2.6 cases per million people per year based on a population study from Olmsted County, Minnesota.[14] There is little in the literature to tell us what percentage of patients with the disease will require operation. The National Institutes of Health reported operative interventions in 38% of 60 pa-

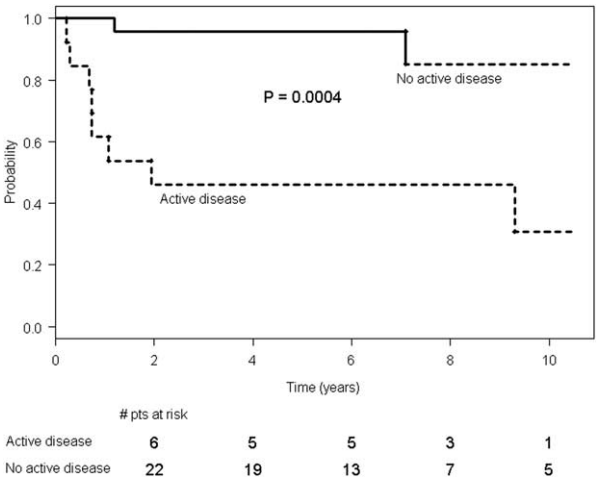

Fig 6. Freedom from revision on the basis of disease activity.

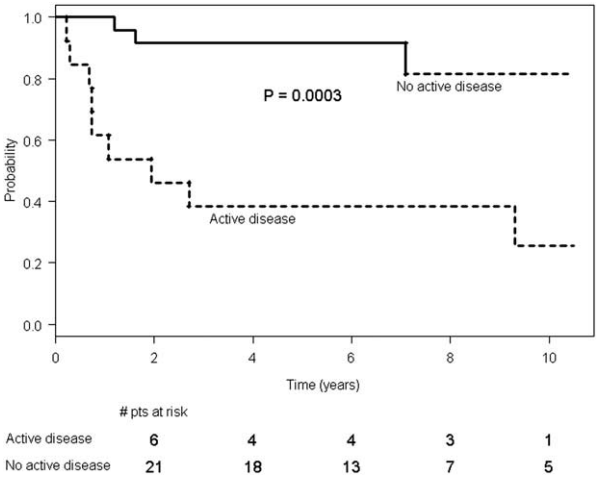

Fig 7. Freedom from revision or progression on the basis of disease activity.

tients treated. The actual denominator in this group may be higher because the patient cohort was selected only from patients referred for vasculitis clinical trials and 25% of them were lost to follow-up.[4] Ishikawa et al[15] operated on 12% of their patients. Of the 251 patients entered in our registry, which captures all patients at the Mayo Clinic with the diagnosis of Takayasu's arteritis, 17% needed operation. Therefore, based on Ishikawa's study and our own, we believe that <20% of patients with Takayasu's arteritis require operation.

Most reports define patient outcome after operation by early mortality and morbidity, survival, or graft-patency and graft-related complications.[5-7, 9-11] Operation for Takayasu's arteritis, even in multiple vascular territories, was safe in these patients. Similar findings have been reported by Weaver et al[16]for the treatment of patients with renovascular disease. Operative mortality can certainly be affected by whether the problem treated is occlusive or aneurysmal disease. Robbs et al,[7] from South Africa, reported an operative mortality of 3% to 4% in their patients with Takayasu's arteritis, most of whom had aneurysms. The mortality was related to patients with ruptured aneurysms. A similar mortality rate was noted by Kieffer et al[17] for patients with renovascular disease and Takayasu's arteritis. In that series, 87% of the 24 patients operated on had combined aortic and renal reconstruction and 71% had both renal and mesenteric reconstruction. One patient (4%) died in the immediate postoperative period from myocardial and intestinal infarction. This patient had aortic, visceral, and renal disease, but only the aortic and renal arteries were reconstructed. We did not use endovascular techniques in the patients in our series owing to the panmural involvement of the artery in the disease process. Additionally, reports of endovascular therapy for Takayasu's are anecdotal.

The major complication rate in our series was low. No patients had a major stroke, myocardial infarction, renal failure, or pseudoaneurysm. The most common complications were cerebrovascular, and this reflects our patient population, most of whom had great vessel disease, either alone or with abdominal aortic branch vessel disease. Fortunately, no patients had a major stroke, and the patients with minor stroke recovered before hospital discharge. Hyperperfusion syndrome, noted in two patients, is a risk for patients with extensive great vessel involvement. In four patients, early graft occlusions occurred during a time when we were not routinely using intraoperative duplex scans to access the technical outcome of the reconstruction.

Another important outcome in our study was the safety of pregnancy in women of childbearing age. Female patients frequently ask about the safety of pregnancy. Traditional teaching has suggested that these patients may have a higher risk of complications during the gestational period that can affect both the mother and fetus. Two patients in our series with aneurysmal disease became pregnant but had elective abortions on the recommendation of their local physician before referral to our institution. Sixteen other patients had safe vaginal deliveries after their operations for occlusive disease. One of these patients had a small thoracic aneurysm that has not been treated to date. In contrast, a study from India showed that among 24 pregnant women with Takayasu's arteritis, there were five intrauterine fetal deaths and two abortions. The mothers did not seek prenatal or perinatal care until late in the pregnancy.[18]

The most significant findings from our study were the impact of disease activity on survival, the need for graft revision, and the progression of disease at a remote site. Our long-term survival is excellent up to 10 years and was not affected by disease activity or the use of steroids. Similar survival was noted by Weaver et al.[16]

Complex analyses have been reported by the Japanese in an effort to predict long-term prognosis. Ishikawa et al[15] proposed a cumbersome staging system based on a modification of the Akaike information criterion. We did not use this staging system in our study because of its unwieldy nature and because few of our patients had retinopathy,

aortic valve regurgitation, or arterial aneurysms; therefore, it was not useful for our analysis. We found serum markers of less value than operative findings, clinical presentation, course of disease, and arteriographic findings. There was also poor correlation between serum markers in our patients and their pathologic findings. With erythrocyte sedimentation rate specifically, the sensitivity of the test was 36% and specificity 83% based on comparison with the pathologic specimen.

It may be argued that our 10-year length of follow-up is too short to determine the mortality rate. Miyata et al[5] reported 12 hospital deaths and an additional 31 late deaths in a series of 106 patients treated operatively for Takayasu's disease. Their mean follow-up was 19.8 years, and the mean survival rate at 20 years was 73.5%. The most common cause of death in that series was congestive heart failure. These authors believe that long-term follow-up of >20 years is mandatory to make any statistical conclusions about the impact of surgical therapy on the natural history of disease. In contrast to our patients, anastomotic aneurysms were found in 13.8% of their patients at the 20-year follow-up.[5] No false aneurysms occurred in our series, and we believe that the incidence of false aneurysms can be reduced by constructing anastomoses beyond inflamed areas.

It has been a clinical impression for years that the results of operation are impacted by disease activity at the time of surgery. We have been able to provide clinical evidence of this by grouping our patients with respect to both their medication needs and clinical status.

Other authors have relied on steroid use as the sole determinant of disease activity. We found no difference in the rate of graft revision or on progression of symptomatic disease at another site when we analyzed our patients in this fashion (Fig 3). To equate steroid use alone as a marker of disease activity in these patients is inherently inaccurate. For example, our "best risk" patients —those with quiescent disease no longer requiring steroids—would be lumped with our "worst" patients—those who had active disease presenting acutely and not yet on steroids. Similarly, the groups of patients with active or quiescent disease on steroids would have been analyzed as a single cohort.

Our best outcomes, when analyzed according to the need for graft revision, occurred in patients with quiescent disease on no steroids. Freedom from graft revision at 5 and 10 years was 100% in this group. Those who had quiescent disease on steroids had a slightly worse outcome, with freedom from graft revision 95% at 5 years and 81% at 10 years. The worst outcomes were noted in patients with active disease, especially those with acute presentations not previously on glucocorticoid therapy (Figs 4-7).

Finally, when we analyzed the rate of graft revision or progression of disease based on activity alone, irrespective of steroid use, the differences in graft revision or progression of disease were even more pronounced. Patients with active disease did significantly worse than those with quiescent disease. Some have argued that most patients have an initial insult from the disease and they have little chance of late symptomatic recurrence, but our findings dispute that supposition.[16]

The interpretation of our results may have several limitations:

First, the operations were done over a long period of time, during which medical treatment changed and the routine use of imaging studies for assessment of graft patency varied.

Second, the definition of active vs quiescent disease is difficult and not uniform in the current literature. Our definition of active disease, however, was very stringent and included a combination of clinical, pathologic, or laboratory findings. We believe this definition provides a better assessment of the acuity of illness than the American College of Rheumatology criteria used to define active disease.[13] Our patients with active disease had to have two or more of the following: systemic symptoms, evidence of acute inflammation in the target artery and surrounding tissues, pathologic evidence of active inflammation in the arterial wall, or elevated serum markers.

Third, follow-up was complete in approximately 80% of our patients who resided in the United States. Although this represented most of our group, it is possible that we did not capture some asymptomatic graft stenoses or occlusions, which could skew the results in our analysis. The follow-up in our study is similar to that reported recently by Weaver et al,[16] but it is not as long as that reported in the Japanese literature.[5,15] It is possible that longer follow-up would have uncovered other late graft-related problems such as false aneurysms. Additionally, since Takayasu's arteritis is rare and the experience at any single center is limited, it is difficult to accumulate larger numbers of patients in a short time frame to increase the predictive value of our life-table analyses.

Finally, the results of our study may primarily be applicable to patients with occlusive disease, which represented 93% of our group.

CONCLUSION

Few patients with Takayasu's arteritis require operation. In our predominantly white female population, occlusive symptoms were the most common indication for operation. Operations for these problems can be performed safely in selected patients. Long-term survival is excellent, regardless of disease activity at the time of operation. However, disease activity significantly increased the likelihood of graft revision or the progression of symptomatic disease at another site. These findings support the need for long-term monitoring of vascular reconstructions in patients with Takayasu's arteritis, especially in patients with active disease at the time of initial operation.

AUTHOR CONTRIBUTIONS

Conception and design: KJC
Analysis and interpretation: KJC, TCB, CEF, LTC, AAN, PG

Data collection: CEF, KJC, TCB, LTC
Writing the article: CEF, TCB, KJC, LTC
Critical revision of the article: CEF, KJC, TCB
Final approval of the article: KJC, TCB, LEF, LTC, AAN, PG
Statistical analysis: CEF
Overall responsibility: KJC

REFERENCES

1. Numano F. Introductory remarks for this special issue on Takayasu arteritis. Heart Vessels Suppl 1992;7:3-5.
2. Desiron Q, Zeaiter R. Takayasu's arteritis. Acta Chir Belg 2000;100:1-6.
3. Koide, K. Takayasu arteritis in Japan. Heart Vessels Suppl 1992;7:48-54.
4. Kerr GS, Hallahan CW, Giordano J, Leavitt RY, Fauci AS, Rottem M, et al. Takayasu arteritis. Ann Intern Med 1994;120:919-29.
5. Miyata, T, Sato O, Koyama H, Shigematsu H, Tada Y. Long-term survival after surgical treatment of patients with Takayasu's arteritis. Circulation 2003;108:1474-80.
6. Lagneau P, Michel JB, Vuong PN. Surgical treatment of Takayasu's disease. Ann Surg 1987;205:157-66.
7. Robbs JV, Abdool-Carrim AT, Kadwa AM. Arterial reconstruction for non-specific arteritis (Takayasu's disease): medium to long-term results. Eur J Vasc Surg 1994;8:401-7.
8. Cherry KJ Jr, McCullough JL, Hallett JW Jr, Pairolero PC, Gloviczki P. Technical principles of direct innominate artery revascularization: a comparison of endarterectomy and bypass grafts. J Vasc Surg 1989;9: 718-23.
9. Weaver FA, Yellin AE. Surgical treatment of Takayasu arteritis. Heart Vessels Suppl 1992;7:154-8.
10. Giordano JM, Leavitt RY, Hoffman G Fauci AS. Experience with surgical treatment of Takayasu's disease. Surgery 1991;109:252-8.
11. Tada Y, Sato O, Ohshima A, Miyata T, Shindo S. Surgical treatment of Takayasu arteritis. Heart Vessels Suppl 1992;7:159-67.
12. Rhodes JM, Cherry KJ Jr, Clark RC, Panneton JM, Bower TC, Gloviczki P, et al. Aortic-origin reconstruction of the great vessels: risk factors of early and late complications. J Vasc Surg 2000;31:260-9.
13. Arend WP, Michel BA, Bloch DA, Hunder GG, Calbrese LH, Edworthy SM, et al. The American College of Rheumatology 1990 criteria for the classification of Takayasu's arteritis. Arthritis Rheum 1990;33: 1129-34.
14. Hall S, Barr W, Lie JT, Stanson AW, Kazmier FJ, Hunder GG. Takayasu arteritis. A study of 32 North American patients. Medicine (Baltimore) 1985;64:89-99.
15. Ishikawa K, Maetani S. Peripheral arterial and aortic diseases: long-term outcome for 120 Japanese patients with Takayasu's disease: clinical and statistical analyses of related prognostic factors. Circulation 1994;90, 1855-60.
16. Weaver FA, Kumar SR, Yellin AE, Anderson S, Hood DB, Rowe VL, et al. Renal revascularization in Takayasu arteritis-induced renal artery stenosis. J Vasc Surg 2004;39:749-57.
17. Kieffer E, Piquois A, Bertal A, Bletry O, Godeau P. Reconstructive surgery of the renal arteries in Takayasu's disease. Ann Vasc Surg 1990;4:156-65.
18. Sharma BK, Jain S, Vasishta K. Outcome of pregnancy in Takayasu arteritis. Int J Cardiol. 2000;75 Suppl 1:S159-62.

Submitted Jun 21, 2004; accepted Oct 3, 2005.

DISCUSSION

Dr Lars Svensson (Cleveland, Ohio). Dr White, Dr Ouriel, ladies and gentlemen: I congratulate Dr Fields and his Mayo Clinic colleagues on an excellent study and well-written manuscript on a 27-year experience. Our experience has been similar at the Cleveland Clinic with 105 patients followed by my colleague, Dr Gary Hoffman; however, 50 have undergone surgery, which perhaps, is a reflection of our referral patterns.

I have three questions about the diagnosis, medical therapy, and bypass graft types you used. You refer to the 1990 preoperative criteria for the diagnosis in your manuscript and your table. Do you not think that these are too liberal? Any patient with a subclavian or innominate artery stenosis could technically qualify, making it hard to differentiate former TB patients, young female heavy smokers, or as we have seen in about a half a dozen patients, patients with silicone breast prostheses. TB may account for the increased diagnosis of Takayasu's type aneurysms in the countries of Africa, India, and Russia.

You divided patients partly by steroid use, but how did you categorize patients who were on and off steroids? Did you use C-reactive protein levels for both treatment, timing of surgery and prognostication? It appears that patients with CRP levels below 1 mg/dL have an excellent long-term outcome, but those with 1 mg or higher had frequent events and close long-term follow-up is required in these patients.

We learned in the 1980s that saphenous vein grafts were unsuitable for bypasses and that Dacron polyester grafts were preferable in these types of patients. Can you comment on your experience, what you currently use for grafts, and how many of your patients that failed had saphenous vein bypasses?

I thank the Society for the invitation to comment on this excellent study.

Dr Charles Fields. To address the first point, the American College of Rheumatology criteria for diagnosis of Takayasu's disease are basically clinical criteria, which inherently, as Dr Svensson has suggested, can miscategorize patients. However, we accounted for this by also looking at the pathologic slides of these patients that underwent operation. And although the ACR criteria does not include review of pathology as part of the criteria, we feel that patients with three of the six symptoms described by the ACR criteria, as well as findings on pathology, definitely had Takayasu's arteritis.

In reference to patients with tuberculosis or with silicone breast implants or other possibly etiologies of Takayasu's arteritis, we agree wholeheartedly that the Takayasu's arteritis that is seen in places such as India or South Africa may be of a different variant, since these patients tend to have aneurysmal disease. We did not have any patients in our series that had had silicone breast implants, and we only had two patients that had had a history of positive PPD in the past. So these are excellent points.

As far as patients who had been on or off steroids during the course of our review, we have basically clinical medical management criteria that we use at Mayo Clinic that consist primarily of corticosteroid use as first-line therapy. This is usually dosed at 1 mg/kg for all of these patients, and then we taper the steroid dose accordingly as the symptoms subside. We did not have any patients in this series that were classified originally as the on-steroid group that were able to come off steroids at some point during the study period. However, we did have patients that weren't on steroids initially in our active disease group, and they received pulses of steroids at the time of operation. So we did try to give them some steroid coverage, but it wasn't as chronic as the other active or chronic disease patients.

As far as measuring the levels of C-reactive protein, we actually did a sensitivity and specificity analysis of sed rate compared to our pathologic specimens. And as several authors have found, the data was not very good as far as using serum markers for a determinant of disease. However, as far as C-reactive protein is concerned, only a minority of our patients had that level measured, as we tend to use sed rate as our marker.

And finally, as far as type of graft, we had one patient who had had aortorenal grafts constructed with saphenous vein, which later became aneurysmal. Most of the other patients in this series had Dacron graft reconstructions.