Takayasu's Arteritis: Vascular Interventions and Outcomes

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ABSTRACT. ***Objective.*** To provide an analysis of outcomes of vascular interventions in 20 patients with Takayasu's arteritis (TA) who received care at the Cleveland Clinic Foundation between 1979 and 2001.

Methods. We performed a retrospective chart review. The primary outcome measure of our review was patency of vessels as assessed by repeat invasive angiography or magnetic resonance angiography. The secondary outcome measures included periprocedural complications, morbidity, and mortality. Interventions included bypass grafts, patch angioplasty, endarterectomy, percutaneous transluminal angioplasty (PTA), or stent placement.

Results. Sixty-two revascularization procedures were performed in 20 patients. Followup evaluations were available for 52 procedures. Eleven of 31 bypass grafts restenosed or occluded between one day to 168 months after surgery. Three of 7 PTA and 5 of 7 stents restenosed or became occluded after 1–72 months and 2–45 months of followup, respectively. There were no deaths associated with revascularization procedures.

Conclusion. Despite providing short term benefit, endovascular revascularization procedures are associated with a high failure rate in patients with TA. (J Rheumatol 2004;31:102–6)

Key Indexing Terms:
TAKAYASU'S ARTERITIS VASCULAR INTERVENTION
BYPASS ANGIOPLASTY STENTS

The successful treatment of Takayasu's arteritis (TA) is limited by both imperfect medical and surgical therapies. Inflammatory aspects of TA are treated with corticosteroids and, in selected patients, other immunosuppressive agents. The goals of treatment are arrest of progression of existing lesions and prevention of new lesions. Established lesions, however, are not usually reversed by medical therapy[1,2].

As most patients present after fixed vascular injuries have occurred, it is common for patients who have critical stenoses and ischemia, or enlarging aneurysms, to undergo attempts at revascularization to avoid further morbidity or mortality. Procedures for patients with TA include graft bypass, endarterectomy, patch angioplasty, percutaneous transluminal angioplasty (PTA), and more recently placement of vascular stents.

Indications for revascularization procedures include hypertension in the setting of renal artery stenosis; extremity ischemia limiting routine activities of daily living; cerebral ischemia and/or critical (> 70%) symptomatic stenosis of cerebral vessels[2]; moderate (grade II, New York Heart Association) aortic regurgitation; cardiac ischemia in the setting of proven coronary artery stenosis; severe aortic coarctation; or progressive aneurysmal enlargement and dissecting aneurysm.

Because TA is a rare disease and single-center cohorts tend to be small, limited data are available about the success of attempts to correct or stabilize vascular anatomic lesions. Nevertheless, good results (both short and longterm) have been reported with bypass grafts. While excellent short term outcomes have been described with PTA and stent placement, longterm maintenance of vessel patency is less well defined.

The Cleveland Clinic Foundation (CCF) is a tertiary care center that tends to attract patients with severe and unusual cardiovascular diseases. Consequently, we considered that valuable information would result from an analysis of this center's experience in providing vascular interventions for TA.

MATERIALS AND METHODS

We conducted a retrospective review of 20 patients with TA who underwent revascularization procedures between 1979 and 2001. Interventions were performed during periods of apparent disease remission. Disease was considered active if new onset or worsening of 2 or more of the following occurred: systemic features, such as fever and musculoskeletal symptoms (no other cause identified); elevated erythrocyte sedimentation rate (ESR) or C-reactive protein (CRP); features of vascular ischemia or inflammation, such as claudication, diminished or absent pulse, bruit, vascular pain, or asymetric blood pressure in either upper and/or lower limbs; or change in angiographic features on invasive or magnetic resonance (MR) studies.

Primary outcome measure. Post-procedure patency of vessels as evaluated by invasive angiography or MR angiography.

Secondary outcomes. Procedure-related morbidity and mortality.

Exclusion criteria. All revascularization procedures that were performed on coronary arteries in patients ≥ 35 years old were excluded from this

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analysis. Beyond this age we felt that significant overlap might occur between atherosclerosis and TA affecting coronary artery disease, thus confounding the ability to distinguish these 2 conditions.

RESULTS

Between 1979 and 2001, 20 patients with TA underwent a total of 62 revascularization procedures: 38 bypass grafts; 7 patch angioplasties ± endarterectomy; 2 endarterectomies; 7 stent implantations; and 8 PTA procedures. Followup was available in 31, 6, 1, 7, and 7 procedures, respectively, for a total of 52 procedures. Indications for revascularization are presented in Table 1. Patients included 19 women and one man. Two patients were Kuwaiti and 18 were Caucasian. Age at diagnosis ranged from 5 to 47 (mean 32.7) years. Age at first revascularization procedure ranged from 5 to 49 (mean 33.9) years.

Thirty-eight bypass graft procedures were performed compared to 24 endovascular procedures (Table 2). Restenosis, occlusion, or need for revascularization occurred in 11 of 31 (35.0%) bypass grafts (median followup 11 months; range one day to 168 months). Stenosis or occlusion of grafts did not appear to show a predilection for any particular vessel, although the small number of procedures per individual anatomic site did not lend itself to statistical analysis. Thrombosis in all of 3 coronary artery bypass-grafted vessels occurred in one patient less than 24 h after the operation.

Patch angioplasty, with or without associated endarterectomy, led to unsatisfactory results in 4 of 6 procedures (median followup 8 months; range 2–120 months). Three grafts occluded in one patient, and one other patient developed a pseudoaneurysm for which reoperation with patch angioplasty was required 120 months after the initial intervention. Followup 54 months later showed recurrence of a small (≤ 1 cm) pseudoaneurysm.

Endarterectomy as the sole procedure was performed in 2 patients (one celiac artery and one right common carotid artery). Although one patient was lost to followup, restenosis has not occurred after a period of 96 months in the other patient. Restenosis or occlusion occurred in 3 of 7 PTA procedures (median followup 13 months; range 5 weeks to 72 months) and in 5 out of 7 stent procedures (median followup 11 months; range 2–45 months). In one patient, PTA of the superior mesenteric artery (SMA) was complicated by dissection of the SMA and by a long but nonobstructive dissection of the aorta from the level of the celiac artery to the renal arteries. A 50% post-PTA residual stenosis remained in one patient. It did not progress by 13 months' followup.

Deaths were not associated with any of the revascularization procedures.

Table 1. Indications for revascularization.

Indication	Procedures, n
Angina	13
Extremity claudication	14
Transient ischemic attack (s)	11
Bowel ischemia/infarction	10
Stroke	3
Amaurosis fugax	1
Hypertension from renal artery stenosis	5
Prophylactic bypass*	4
Pseudoaneurysm**	1
Total	62

* Revascularization procedures performed in 3 patients with extensive cervicocranial vessel involvement. Extent of disease: Patient 1: proximal left subclavian, right vertebral, bilateral internal carotid, left external carotid stenoses; Patient 2: bilateral subclavian, bilateral carotid stenoses; Patient 3: bilateral stenosis of common carotid, internal carotid, subclavian arteries. ** Formation of a 4 × 7 cm pseudoaneurysm at the site of a saphenous vein graft patch angioplasty performed 10 years earlier.

DISCUSSION

During the period under review, only 20 TA patients underwent interventions for relief of stenotic or occlusive lesions. Our observations are limited by the relatively small number of patients in this retrospective series. However, the CCF is

Table 2. Results.

Procedure	n	Available for Followup	Restenosis, Occlusions, Need for Revascularization	Time to Outcome, mo	Complications*
Bypass grafts	38	31	11	Mean 26.2 Median 11	1 (one patient)
Patch angioplasty ± endarterectomy	7	6	4	Mean 34.5 Median 8	2,3 (same patient)
Endarterectomy	2	1	0	96 mo followup	—
PTA	8	7	3	Mean 28 Median 13	4 (one patient) 5 (one patient)
Stents	7	7	5	Mean 15.4 Median 11	—
Total procedures, n	62	52	23		

* 1. Graft thrombosis within 24 h of surgical intervention. 2. Pseudoaneurysm requiring reoperation 120 mo later. 3. Small pseudoaneurysm at distal graft (≅ 1 cm). 4. Dissection of superior mesenteric artery and of aorta from level of celiac to renal arteries. 5. 50% residual stenosis post-PTA. However, no further progression of stenosis over 13 mo followup. PTA: percutaneous transluminal angioplasty.

Table 3. Selected studies of bypass grafting in TA.

Author	Patients/Procedures, n	Material	Followup, yrs	Restenosis/Occlusion, %	Thrombosis, %	Perioperative Mortality*, %
Kerr[2] (1970-1990)	23/50	Synthetic 39 Autologous 11	Median 5.3 Range 0.5–20	24	4	0
Weaver[1] (1963-1989)	10/13	Synthetic 8 Autologous 5	Median 6.25 Range 0.5–15.4	31	15 (2pts) 1 pt: successful thrombectomy	0
Pajari[3] (1960-1984)	18/36	Synthetic 14 Autologous 22	Median 4.8 Range 0.1–14	31		7 (2/29)
Lagneau[4] (1976-1984)	31/52	Synthetic 38 Autologous 14	Mean 3 years ± 7 months	8		0
Teoh[5]	11/18	Synthetic 9 Autologous 9	Median 0.6 Range 0.1–6.7	5 (1 occlusion at 6 yrs)	10 (2 early thrombosis)	0

* The perioperative period is defined as the time from admission for surgery to hospital discharge. Although no deaths occurred during the perioperative period, one patient died 2 months post-operation as a result of graft infection.

Table 4. Outcomes of selected trials of percutaneous revascularization procedures in TA.

Author	Patients, n	Lesions Available for Followup, n	Followup, mo	Patency Rate, n (%)	Method for Patency Assessment
Tyagi[23]	54	PTA Renal: 52	Mean 14.2	7/52 (86.5)	Angiography
Sharma[21]	20	PTA 12 / Stent 16 Aorta 5 / 5 Renal 4 / 2 Subclav 3 / 3 Coronary 0 / 1 Carotid 0 / 5	Median 6 Range 4–10	PTA 12/12 (100) Stent 14/16 (88)	Angiography 15 Other ** 13
Rao[24]	16	PTA Aorta (thoracic and abdominal): 16	Mean 21.4 Range 2–52	10/16 (67.3)	Angiography (only if symptoms occurred): 5 ABI 14
Sharma[25]	56	PTA Renal 77	Mean 23 Range 4-84	62/77 (81)	Angiography: 35 BP, ΔRx: 42
Fava[27]	20	PTA Renal 12 Abd aorta 3 Iliac 5	All patients: 60	Renal 4/12 (33) Abdominal aorta 1/3 Iliac 3/5 (60)	Unspecified
Sakaida[26]	4	Stents 14 Subclavian 6 Common carotid 8	Mean 12	10/11 (91)	Symptoms

** Symptoms, blood pressure, pulses, Doppler, requirement for increased number of anti-hypertensive drugs. ABI: ankle-brachial index with Doppler ultrasound; BP: blood pressure; ΔRx: medication requirement; PTA: percutaneous transluminal angioplasty.

a tertiary care referral center, and significantly larger TA-vascular intervention cohorts are uncommon (Tables 3, 4). In spite of these limitations, our study suggests that vessel patency is best achieved with bypass grafts, whereas patch angioplasty and percutaneous endovascular procedures (stents in particular) have a great risk of restenosis or occlusion. This observation is of importance when considering which revascularization procedure is best suited for a patient with TA and ischemic symptoms. About one-third (35%) of bypass grafts restenosed, occluded, or required another revascularization procedure, a finding comparable to that from other studies (Table 3)[1-6]. This estimate, however, represents a higher rate of restenosis than that found in atherosclerosis. For example, Fitzgibbon, *et al* describe the results of angiographic followup of 5065 coronary bypass grafts[7]. Vein graft patency was 81% and 75% at one and 5 years, respectively. An 85–90% graft patency rate at 5 years can be expected following aortofemoral bypass grafting for atherosclerotic lesions[8]; similarly, excellent results can be achieved following surgical revascularization for atherosclerotic renal artery disease[9]. Why this apparent trend towards a higher graft failure rate in TA occurs is uncertain, but reports by Hall, *et al*[10] and Pajari, *et al*[3] suggest that overt or covert inflammation at the time of surgery is associated with a higher incidence of graft failure. Kerr, *et al*[2] found that over 40% of biopsy specimens obtained at the time of bypass revealed features of inflammation in patients thought to be in remission by clinical, laboratory, and angiographic variables. Similarly, in our review, all patients were considered to be in remission at the time vascular procedures were performed. Although we did not have available tissue samples from revascularized vessels, persistent inflammation at the site of graft anastomosis may have been responsible for at least some of the grafts later undergoing restenosis.

The role of endarterectomy and patch angioplasty in TA is unsettled. Some authors have reported positive results[11-13], while others have not[3,14]. Because TA may involve the entire thickness of the vessel wall[15], one would not expect endarterectomy to have a high rate of success. Endarterectomy is adequate for removal of plaque in atherosclerotic vessels. However, the performance of endarterectomy in TA may not lead to achieving an appropriate plane of cleavage to enable sustained patency.

In our cohort, PTA and stent procedures have had encouraging short term outcomes. However, longterm followup has been disappointing. This may at first seem surprising, especially when comparing outcomes to those achieved in atherosclerosis. Differences might be explained by several factors unique to TA.

In TA, chronically diseased vessels are typically fibrotic and often noncompliant, which may result in incomplete dilatation. It is known from trials in atherosclerosis that failure to achieve optimal dilatation is associated with a higher risk of restenosis[16]. In addition, in TA, the noncompliant nature of the vessel wall often requires higher balloon inflation pressures and repeated inflation of the balloon may be required to obtain satisfactory results[17]. This may expose the vessel wall to increased risk of injury. Persistent inflammation in the TA vessel at the time of dilatation/stenting may lead to enhanced myointimal proliferation. And finally, stenotic lesions in TA are characteristically long compared to the short and segmental lesions of atherosclerosis. Higher rates of restenosis correlate with the length of lesions in both atherosclerosis and TA. Conversely, best results of PTA in TA have been obtained in short, focal lesions[18-21].

Our results with percutaneous endovascular revascularization procedures, especially with stent implantation, differ from the positive outcomes reported by others (Table 4)[22,23]. Different vessel characteristics (e.g., anatomic site, length of lesions, severity of lesions) may account for different outcomes. For instance, Tyagi, *et al*[24] showed that for renal artery lesions, which are usually short, excellent longterm outcomes may be achieved. Varying degrees of inflammation at the time of intervention, and differences in endovascular technique and in modalities of assessing vessel patency might also influence perceived outcomes. Angiography or MR imaging and MR angiography were used to assess post-procedure vessel patency in our patients. Others have relied on clinical evaluation, changing requirements of antihypertensive drugs, or duplex ultrasonography to detect restenosis, while reserving more direct means of vessel visualization for only symptomatic patients (Table 4)[25-27]. Longer duration of followup may also contribute to our less satisfying results. Whereas good outcomes are achieved on short term followup[22,23], in some cases, a longer period of observation may lead to different conclusions[28] (Table 4). Our patients were followed for a mean period of over a year.

In summary, experience acquired over the last 21 years at the CCF shows that revascularization procedures in TA (surgical or percutaneous) are safe, and associated with low morbidity and mortality. Good short term outcomes are obtained regardless of the revascularization approach. The best longterm outcomes, as defined by vessel patency, are achieved by open surgical approaches with bypass grafts. Patch angioplasty and endarterectomy were associated with a higher failure rate. Despite providing short term benefit, endovascular revascularization procedures adapted for atherosclerotic disease, stents in particular, are associated with a higher failure rate in patients with TA.

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