

Longterm Outcomes of Renal Artery Involvement in Takayasu Arteritis

Seokchan Hong, Byeongzu Ghang, Yong-Gil Kim, Chang-Keun Lee, and Bin Yoo

ABSTRACT. *Objective.* Takayasu arteritis (TA) involving the renal artery can result in hypertension (HTN), renal dysfunction, and premature death. The aim of this study was to investigate the longterm outcomes and factors that predict outcomes in patients with TA with renal artery stenosis.

Methods. The medical records of patients diagnosed with TA between January 1997 and December 2014 were reviewed retrospectively. Renal artery involvement was based on computed tomography and/or angiography findings. Poor outcome was defined as refractory HTN, chronic renal insufficiency, or death.

Results. Of the 62 TA patients with renal artery involvement, 11 (17.7%) underwent renal artery revascularization. Younger age, male sex, and more severe stenosis (> 70%) were associated with vascular intervention. After a median followup of 90.6 months, 11 (17.7%) of the 62 patients had refractory HTN and 6 (9.7%) had chronic renal insufficiency. Renal insufficiency [5/15 (33.3%) vs 3/47 (6.4%), $p = 0.016$] and bilateral involvement [12/15 (80.0%) vs 23/47 (48.9%), $p = 0.041$] were significantly more frequent in patients with poor than good outcomes. Multivariate Cox analysis revealed that renal insufficiency at presentation (HR 13.778, 95% CI 3.530–53.786, $p < 0.001$) and bilateral renal artery involvement (HR 5.053, 95% CI 1.179–21.661, $p = 0.029$) were significant risk factors for poor outcomes at followup, but performance of revascularization procedure was not (HR 0.663, 95% CI 0.176–2.498, $p = 0.543$).

Conclusion. Bilateral lesions and renal functional impairment at presentation, but not implementation of revascularization procedures, were significant factors for outcomes in TA patients with renal artery involvement. (First Release February 15 2017; J Rheumatol 2017;44:466–72; doi:10.3899/jrheum.160974)

Key Indexing Terms:

TAKAYASU ARTERITIS RENAL ARTERY HYPERTENSION REVASCULARIZATION

Takayasu arteritis (TA) is a chronic, large vessel vasculitis that primarily affects the aorta and its main branches, including the renal artery^{1,2}. TA typically occurs in young women, resulting in substantial morbidity and mortality related to involvement of the major vessels^{1,2,3}. Chronic inflammation in the vessel wall can lead to stenosis or occlusion, eventually causing tissue ischemia and organ damage. Up to 60% of patients with TA have renal artery

involvement, often resulting in refractory hypertension (HTN) and impaired renal function^{4,5,6}.

Revascularization procedures, including balloon angioplasty with or without stenting, are often used for the treatment of steno-occlusive lesions^{6,7,8}. However, previous studies on vascular interventions in patients with TA have shown inconsistent results, ranging from a high risk of restenosis to good longterm efficacy and patency, although open revascularization resulted in superior patency rates compared with endovascular intervention^{4,6,9,10,11}. Further, relatively little is known about longterm clinical outcomes, such as chronic renal insufficiency and death, in TA patients with renal artery stenosis. Moreover, previous studies included only patients who underwent vascular intervention^{5,9,10,11}. Therefore, outcomes in patients with TA-associated renal artery stenosis have not been evaluated independent of revascularization procedures. Further, it should be considered that stenotic lesions in TA may be resolved after treatment with immunosuppressants, even without vascular intervention^{12,13,14}.

Therefore, our study analyzed longterm outcomes and clinical variables associated with poor outcomes (e.g., refractory HTN, chronic renal insufficiency, or death) in all patients with TA-associated renal artery involvement,

From the Division of Rheumatology, Department of Internal Medicine, University of Ulsan College of Medicine, Asan Medical Center, Seoul, Korea.

S. Hong, MD, PhD, Division of Rheumatology, Department of Internal Medicine, University of Ulsan College of Medicine, Asan Medical Center; B. Ghang, MD, Division of Rheumatology, Department of Internal Medicine, University of Ulsan College of Medicine, Asan Medical Center; Y.G. Kim, MD, PhD, Division of Rheumatology, Department of Internal Medicine, University of Ulsan College of Medicine, Asan Medical Center; C.K. Lee, MD, PhD, Division of Rheumatology, Department of Internal Medicine, University of Ulsan College of Medicine, Asan Medical Center; B. Yoo, MD, PhD, Division of Rheumatology, Department of Internal Medicine, University of Ulsan College of Medicine, Asan Medical Center.

Address correspondence to Dr. B. Yoo, Division of Rheumatology, University of Ulsan College of Medicine, Asan Medical Center, 88, Olympic-ro, 43-gil, Songpa-gu, Seoul 05505, Korea.

E-mail: byoo@amc.seoul.kr

Accepted for publication December 21, 2016.

Personal non-commercial use only. The Journal of Rheumatology Copyright © 2017. All rights reserved.

regardless of whether they underwent revascularization procedures.

MATERIALS AND METHODS

The medical records of patients who were diagnosed with TA at a tertiary referral hospital in Seoul, South Korea, between January 1997 and December 2014 were retrospectively reviewed. All patients fulfilled the 1990 revised American College of Rheumatology criteria for the classification of TA¹⁵, except age of onset < 40 years because delayed diagnosis of TA was common. Patients were excluded from the analysis if imaging evaluation of renal artery involvement was not available. All patients underwent an aortic computed tomography (CT) scan and/or conventional angiography at the time of TA diagnosis. Clinical features, including vascular manifestations (e.g., limb claudication, decreased pulse, asymmetric blood pressure, and vascular bruit), were recorded, as were laboratory findings such as erythrocyte sedimentation rate (ESR), C-reactive protein, and creatinine concentrations. Estimated glomerular filtration rate (eGFR) was calculated using the chronic kidney disease epidemiology collaboration equation¹⁶. Renal insufficiency was defined as an eGFR < 60 ml/min. The performance of revascularization procedures, including percutaneous renal artery stenting, was also assessed. Poor outcomes at followup were defined as chronic renal insufficiency, refractory HTN, and/or death. Refractory HTN was defined as blood pressure > 140/90 mm Hg, despite use of maximal doses of at least 2 antihypertensive drugs. The severity of renal artery stenosis in each patient was categorized as < 50%, 50%–70%, or > 70%.

Continuous variables were compared using the Student t test and categorical variables by Fisher's exact test. Variables expressed as median with interquartile range (IQR) range were compared by the Mann-Whitney U test. Potential risk factors for poor outcomes were evaluated by univariate analysis, and those factors with p values < 0.20 were included in a multivariable Cox regression analysis with a stepwise elimination process. Results were expressed as HR with 95% CI. All statistical analyses were performed using SPSS software (version 21.0; SPSS Inc.), with a p value < 0.05 considered statistically significant.

This study was approved by the Institutional Review Board of the Asan Medical Center, Seoul, South Korea (IRB No.: 2016-0547).

RESULTS

Clinical characteristics of the study subjects. In total, 246 patients with TA were identified between 1997 and 2014, and all patients were classified according to the angiographic classification, which is based on the distribution of major vessel involvement of TA¹⁷. Type V (117 patients, 47.6%) was the most common pattern, and the other types were as follows: Type I (62, 25.2%), Type IIa (21, 8.5%), Type IIb (29, 11.8%), Type III (9, 3.7%), and Type IV (8, 3.3%). Among the total patients, 62 (25.2%) were identified as having renal artery involvement. The clinical characteristics of these patients at the time of diagnosis are shown in Table 1. Mean age was 39.6 ± 14.5 years, and 53 patients (85.5%) were women. At initial presentation, their mean creatinine concentration was 0.83 ± 0.21 mg/dl, and 8 (12.9%) showed impairment of renal function. Symptoms of vascular insufficiency such as claudication, decreased pulse, and asymmetric blood pressure were documented in 22 (35.5%), 50 (80.6%), and 52 patients (83.9%), respectively. Severe stenosis, defined as > 70% stenosis, was found in 26 patients (41.9%). Of the 62 patients, 11 (17.7%) with renal artery involvement underwent revascularization procedures,

including percutaneous angioplasty alone (n = 6), with a stent (n = 3), or with open surgery (n = 2).

The clinical characteristics of patients who did or did not undergo revascularization procedures are shown in Table 1. Patients who underwent vascular intervention were younger (28.2 ± 10.1 yrs vs 42.1 ± 14.2 yrs, $p = 0.003$) and were more likely men [5/11 (45.5%) vs 4/51 (7.8%), $p = 0.006$]. Although serum creatinine concentrations were slightly higher in patients who did compared to those who did not undergo revascularization, eGFR values and the percentage of patients with renal function impairment did not differ significantly. The proportion of patients with HTN and/or diabetes mellitus was similar in the revascularization and non-revascularization groups. Severe stenosis of the renal artery was significantly more frequent in patients with than without vascular intervention [11/11 (100.0%) vs 15/51 (29.4%), $p < 0.001$]. Treatment with calcium-channel blockers [10/11 (90.9%) vs 28/51 (54.9%), $p = 0.039$] and aspirin [9/11 (81.8%) vs 22/51 (43.1%), $p = 0.020$] was significantly more frequent in revascularized than in non-revascularized patients. However, treatments with immunosuppressants, including corticosteroid, and warfarin were similar in the 2 groups at baseline, which was before or shortly after vascular intervention.

Clinical outcomes of TA patients with renal artery involvement. Median followup duration after diagnosis of TA was 90.6 months (IQR 45.7–143.9 mos). Of the total 62 patients, 11 (17.7%) developed refractory HTN despite treatment with antihypertensive drugs and 6 (9.7%) developed chronic renal insufficiency. Of the 6 patients with chronic renal insufficiency, eGFR values were $40.13 (\pm 8.45)$ ml/min, but none of them need permanent dialysis. Followup duration was significantly longer in patients with than without revascularization (124.9 mos, IQR 94.1–160.5 mos vs 85.9 mos, IQR 37.6–137.7 mos, $p = 0.037$; Table 2). During followup, 2 patients died, both of heart failure. However, the development of refractory HTN, chronic renal insufficiency, or death did not differ between groups of patients regardless of vascular intervention. In addition, outcomes did not differ significantly in patients treated with angioplasty alone (n = 6) and with angioplasty followed by stent insertion (n = 3; Table 3). When comparing outcomes before intervention to those at the end of followup in patients who underwent vascular intervention, there was no significant difference, including the frequency of refractory HTN and chronic renal insufficiency (data not shown).

Followup images (median 80.7 mos, IQR 49.6–153.3 mos) were available for 9 of the 11 patients with revascularization procedures. Good primary patency in the revascularized vessels was observed in 6/9 patients (66.7%), but restenosis was detected in 3 patients, including 1 patient who required open surgery for revascularization. Interestingly, all these patients (n = 3) who developed restenosis had undergone angioplasty with stent insertion. We did not,

Table 1. Baseline characteristics of the 62 Takayasu arteritis patients with renal artery involvement. Values are n (%) or mean ± SD unless otherwise specified.

Characteristics	Total, n = 62	Without Revascularization, n = 51	With Revascularization, n = 11	p
Age at diagnosis, yrs	39.6 ± 14.5	42.1 ± 14.2	28.2 ± 10.1	0.003
Age > 35 yrs	35 (56.5)	33 (64.7)	2 (18.2)	0.007
Male/female, n	9/53	4/47	5/6	0.006
Delay in diagnosis, > 1 yr	31 (50.0)	23 (45.1)	8 (72.7)	0.096
ESR, mm/h	34.92 ± 30.75	35.18 ± 31.74	33.73 ± 26.99	0.889
CRP, mg/dl	1.16 ± 2.26	1.25 ± 2.43	0.72 ± 1.02	0.506
Creatinine, mg/dl	0.83 ± 0.21	0.80 ± 0.18	0.95 ± 0.31	0.037
Estimated GFR, ml/min	100.11 ± 37.46	100.00 ± 36.96	100.62 ± 41.57	0.961
Renal function impairment	8 (12.9)	7 (13.7)	1 (9.1)	1.000
HTN	44 (71.0)	34 (66.7)	10 (90.9)	0.152
Refractory HTN	6 (9.7)	5 (9.8)	1 (9.1)	1.000
Diabetes	3 (4.8)	3 (5.9)	0 (0.0)	1.000
Dyslipidemia	9 (14.5)	8 (15.7)	1 (9.1)	1.000
Limb claudication	22 (35.5)	21 (41.2)	1 (9.1)	0.079
Decreased pulse	50 (80.6)	42 (82.4)	8 (72.7)	0.432
Asymmetric blood pressure	52 (83.9)	44 (86.3)	8 (72.7)	0.363
Vascular bruit	19 (30.6)	14 (27.5)	5 (45.5)	0.288
Bilateral involvement	35 (56.5)	27 (52.9)	8 (72.7)	0.321
Severity of stenosis				
< 50%	24 (38.7)	24 (47.1)	0 (0.0)	
50%–70%	12 (19.4)	12 (23.5)	0 (0.0)	
> 70%	26 (41.9)	15 (29.4)	11 (100.0)	< 0.001
Classification ¹⁷				
Type III	1 (1.6)	0	1	
Type IV	4 (6.5)	0	4	
Type V	57 (91.9)	51	6	< 0.001
Antihypertensive drug				
Any	44 (71.0)	34 (66.7)	10 (90.9)	0.152
ACE inhibitor or ARB	17 (27.4)	15 (29.4)	2 (18.2)	0.712
B blocker	17 (27.4)	14 (27.5)	3 (27.3)	1.000
CCB	38 (61.3)	28 (54.9)	10 (90.9)	0.039
Numbers	1.18 ± 0.97	1.1 ± 1.0	1.5 ± 0.8	0.298
Antiplatelet drug				
Any	38 (61.3)	29 (56.9)	9 (81.8)	0.178
Aspirin	31 (50.0)	22 (43.1)	9 (81.8)	0.020
Cholesterol-lowering drug	34 (54.8)	30 (58.8)	4 (36.4)	0.200
Warfarin	12 (19.4)	11 (21.6)	1 (9.1)	0.675
Corticosteroid	28 (45.2)	23 (45.1)	5 (45.5)	1.000
Immunosuppressant	31 (50.0)	27 (52.9)	4 (36.4)	0.319
Revascularization	11 (17.7)	34 (66.7)	10 (90.9)	0.152
Angioplasty	9 (14.5)	15 (29.4)	2 (18.2)	0.712
Surgery	2 (3.2)	14 (27.5)	3 (27.3)	1.000

Significant data are in bold face. ESR: erythrocyte sedimentation rate; CRP: C-reactive protein; GFR: glomerular filtration rate; HTN: hypertension; ACE: angiotensin-converting enzyme; ARB: angiotensin receptor blocker; CCB: calcium channel blocker.

Table 2. Outcomes of Takayasu arteritis patients with and without revascularization. P values were generated by the Mann-Whitney U test or the chi-square test, as appropriate. Values are n (%) unless otherwise specified.

Variables	Without Revascularization, n = 51	With Revascularization, n = 11	p
Followup duration, mo, median (IQR)	85.9 (37.6–137.7)	124.9 (94.1–160.5)	0.037
Refractory HTN [†]	8 (15.7)	3 (27.3)	0.394
Chronic renal insufficiency [‡]	6 (11.8)	0 (0.0)	0.580
Death [§]	1 (2.0)	1 (9.1)	0.326

Significant data are in bold face. [†] Refractory HTN was defined as blood pressure > 140/90 mm Hg, despite use of maximal doses of at least 2 antihypertensive drugs. [‡] Defined as an estimated glomerular filtration rate < 60 ml/min. [§] Causes of death: heart failure (n = 2). IQR: interquartile range; HTN: hypertension.

Table 3. Outcomes of patients with Takayasu arteritis who underwent angioplasty with and without stent insertion. P values were generated by the Mann-Whitney U test or the chi-square test, as appropriate. Values are n (%) unless otherwise specified.

Variables	Without Stent Insertion, n = 6	With Stent Insertion, n = 3	p
Followup duration, mos, median (IQR)	118.9 (94.1–134.5)	101.6 (92.9–192.1)	1.000
Refractory HTN [†]	1 (16.7)	2 (66.7)	0.226
Chronic renal insufficiency [‡]	0 (0.0)	0 (0.0)	0.580
Death [§]	0 (0.0)	1 (33.3)	0.333

[†] Refractory HTN was defined as blood pressure > 140/90 mm Hg, despite use of maximal doses of at least 2 antihypertensive drugs. [‡] Defined as an estimated glomerular filtration rate < 60 ml/min. [§] Cause of death: heart failure (n = 1). IQR: interquartile range; HTN: hypertension.

however, detect significant difference in primary patency rate between patients with open surgery and those with endovascular intervention, although there was a trend toward reduction in risk of restenosis after open surgical intervention (p = 0.541; Appendix 1).

Factors related to poor outcome in TA patients with renal artery involvement. Finally, we performed analysis to identify factors associated with longterm outcome in TA-associated renal artery stenosis. Patients were divided into 2 groups: those with poor outcome (refractory HTN, chronic renal insufficiency, or death at last followup) and those with better outcome (Table 4). Factors associated with poor outcomes were identified by comparing the baseline characteristics of patients with and without poor outcomes. Univariate analysis showed no significant differences in baseline clinical characteristics, such as age and sex, between the 2 groups. However, renal insufficiency and HTN at diagnosis were more common in patients with than without poor outcomes. Bilateral involvement [12/15 (80.0%) vs 23/47 (48.9%), p = 0.041] and use of antihypertensive drugs, including β blockers and calcium channel blockers, were significantly more frequent in patients with poor than with favorable outcomes. Multivariate analysis using Cox proportional hazards models was performed to determine which baseline clinical variables, including vascular intervention, were independent significant factors for poor outcome in TA with renal artery involvement. Potential factors such as HTN at presentation and use of antihypertensive drugs were excluded during the backward stepwise process. Further, revascularization procedure was not significantly associated with longterm outcome in patients with renal artery stenosis. However, renal insufficiency at presentation (HR 13.778, 95% CI 3.530–53.786, p < 0.001) and bilateral involvement (HR 5.053, 95% CI 1.179–21.661, p = 0.029) were significantly associated with an increased risk of poor outcome at the last followup visit (Table 5). Kaplan-Meier analysis showed that patients with renal dysfunction at initial presentation had a significantly higher probability of having poor outcomes at followup (p < 0.001; Figure 1).

DISCUSSION

Renal artery involvement, which is observed in some patients with TA, can lead to renal impairment and refractory renovascular HTN. Our present study was designed to identify clinical factors related to longterm outcomes in patients with renal stenosis of TA. Interestingly, vascular intervention was not associated with outcomes. Revascularization procedures, however, were performed more frequently in patients with severe stenosis, and thus need to be taken into consideration in the interpretation of the results. Rather, severe disease at presentation, manifested by renal function impairment and bilateral involvement, was significantly and independently associated with poor outcome.

Renal artery stenosis or occlusion is one of the major manifestations of vascular involvement in TA. The development of renovascular HTN is induced by various signals associated with reduced renal perfusion. These signals include the activation of the renin–angiotensin system, oxidative stress, and sympathoadrenergic responses¹⁸. Sustained reduction in perfusion leads to ischemia and renal function disturbance, and may result in premature death. Given that TA-associated renal artery stenosis can often result in refractory HTN and renal failure, awareness of a possible risk factor for poor outcomes could be important in the clinical setting (Table 4 and Table 5). Relative to unilateral stenosis, bilateral renal artery stenosis was associated with a higher incidence of cardiovascular complications, including congestive heart failure¹⁹. Indeed, 2 deaths during our present study were caused by congestive heart failure and both patients had bilateral renal artery stenosis. Because arterial stenosis in TA is frequently bilateral, it is noteworthy that bilateral renal artery stenosis was significantly associated with poor outcome (Table 5).

Several methods have been attempted to relieve vascular stenosis, in particular atherosclerotic renal artery stenosis^{20,21,22}. To date, however, revascularization procedures in patients with atherosclerotic renovascular disease have not had any benefits in controlling HTN, or on renal function, heart failure, or mortality^{23,24}. Further, although

Table 4. Univariate analyses of factors associated with poor outcomes (chronic renal insufficiency, refractory HTN, and/or death) in patients with Takayasu arteritis. Values are n (%) unless otherwise specified.

Variables	Patients without Poor Outcome*, n = 47	Patients with Poor Outcome*, n = 15	p
Age > 35 yrs	26 (55.3)	9 (60)	0.750
Male/female, n	7/40	2/13	1.000
Delay in diagnosis, > 1 yr	22 (46.8)	9 (60)	0.554
Elevated ESR at presentation [†]	28 (59.6)	9 (60)	0.977
Elevated CRP at presentation [‡]	15 (31.9)	2 (13.3)	0.314
Renal insufficiency at presentation [§]	3 (6.4)	5 (33.3)	0.016
HTN at presentation	30 (63.8)	14 (93.3)	0.047
Diabetes at presentation	2 (4.3)	1 (6.7)	1.000
Dyslipidemia at presentation	6 (12.8)	3 (20.0)	0.674
Limb claudication	15 (31.9)	7 (46.7)	0.359
Decreased pulse	35 (74.5)	15 (100.0)	0.029
Asymmetric blood pressure	39 (83.0)	13 (86.7)	1.000
Vascular bruit	14 (29.8)	5 (33.3)	1.000
Bilateral involvement	23 (48.9)	12 (80.0)	0.041
Severity > 70%	17 (36.2)	9 (60.0)	0.137
Antihypertensive drug			
Any	30 (63.8)	14 (93.3)	0.047
ACE inhibitor or ARB	10 (21.3)	7 (46.7)	0.094
B blocker	9 (19.1)	8 (53.3)	0.018
Calcium-channel blocker	24 (51.1)	14 (93.3)	0.005
Antiplatelet drug			
Any	29 (61.7)	9 (60.0)	1.000
Aspirin	22 (46.8)	9 (60.0)	0.554
Cholesterol-lowering drug	26 (55.3)	8 (53.3)	1.000
Warfarin	8 (17.0)	4 (26.7)	0.461
Corticosteroid	31 (66.0)	7 (46.7)	0.363
Immunosuppressant	30 (63.8)	6 (40.0)	0.228
Revascularization	7 (14.9)	4 (26.7)	0.437

Significant data are in bold face. * Poor outcome was defined as the composite of chronic renal insufficiency, refractory HTN, and/or death. [†] Defined as ESR > 9 mm/h in men, > 20 mm/h in women. [‡] Defined as CRP > 0.6 mg/dl. [§] Defined as an estimated glomerular filtration rate < 60 ml/min. HTN: hypertension; ESR: erythrocyte sedimentation rate; CRP: C-reactive protein; ACE: angiotensin-converting enzyme; ARB: angiotensin receptor blocker.

Table 5. Multivariate analysis of clinical factors predictive of poor outcome in patients with Takayasu arteritis with renal artery involvement.

Variables	HR	95% CI	p
Renal impairment at presentation*	13.778	3.530–53.786	< 0.001
Bilateral involvement	5.053	1.179–21.661	0.029
Revascularization	0.663	0.176–2.498	0.543

Significant data are in bold face. * Defined as an estimated glomerular filtration rate < 60 ml/min.

revascularization procedures, including percutaneous transluminal angioplasty, have often been performed in patients with TA-associated renal artery stenosis, their effects on longterm clinical outcomes remain unknown in TA. Vascular intervention has been suggested for patients with refractory HTN caused by renal artery stenosis^{25,26}. Indeed, surgical revascularization for TA-related renal artery stenosis showed beneficial effects on the clinical outcomes, including control of blood pressure^{11,27}. However, proper indications for revascularization procedures remain unclear because little is known

about the prognosis of TA patients with renal artery stenosis who do not undergo vascular intervention. Interestingly, in our present study, we found that revascularization was not a significant independent factor affecting longterm outcome (Table 5). Additional controlled studies are required to determine the effects of more intensive treatment, including vascular intervention and/or immunosuppressive therapy, in particular in patients with bilateral renal artery involvement.

Renal artery revascularization procedures include endovascular intervention and surgical bypass. In previous

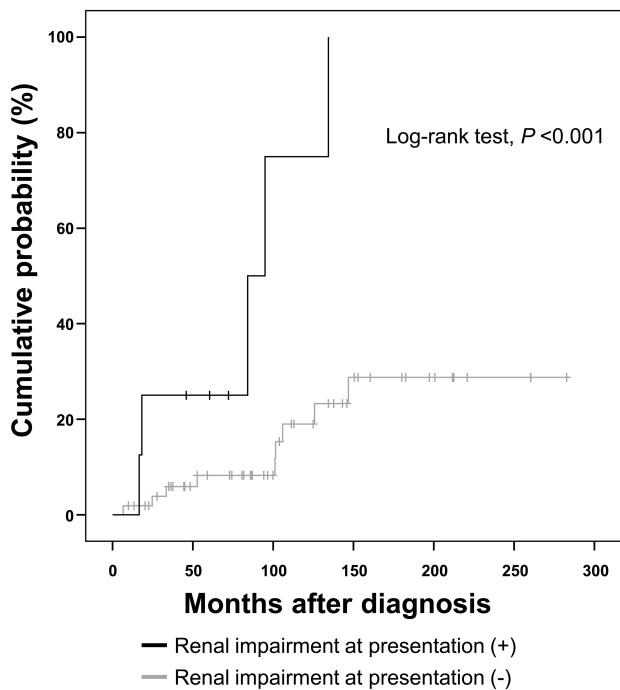


Figure 1. Cumulative probability of the development of poor outcomes in Takayasu arteritis-associated renal artery stenosis according to renal impairment at presentation ($p < 0.001$).

retrospective analyses, surgical procedures showed better results in the risk of restenosis compared with endovascular interventions^{11,28}. However, other studies have shown that endovascular treatments were generally effective in controlling HTN with good 5-year patency rates ranging from 67% to 79%^{5,6,7}. Moreover, patients with TA treated with angioplasty were found to have a significantly lower rate of restenosis in stenotic lesions than those treated with stent placement, indicating differences in endovascular management^{9,10}. Our present study showed no significant differences in poor outcome rates between angioplasty and stent insertion. Because stent implantation resulted in lower restenosis rates in patients with atherosclerotic renal artery stenosis²⁹, further studies are required to determine the optimal revascularization method for patients with TA-related renal artery stenosis.

Because active vascular inflammation could be associated with a higher rate of complications after revascularization, administration of immunosuppressive drugs appears to be helpful in the treatment of TA-related vascular stenosis^{27,28,30}. In our present study, however, the risk of poor outcome was not related to inflammatory status (e.g., elevated ESR) or use of immunosuppressants. About half of the patients in our present study cohort had a delayed diagnosis (> 1 yr), and thus were older (> 35 yrs; Table 1). These findings suggest that chronic vascular lesions observed in patients with delayed diagnosis are less responsive to immunosuppressive agents.

Our present study had several limitations. Because this study was retrospective in design and without a control group, treatment strategies were not randomized. Indeed, revascularization procedures were more frequently performed in patients with more severe disease, defined as the degree of renal artery stenosis. Thus, we cannot fully exclude the possibility that the effects of vascular intervention were underestimated by differences in severity. Second, the numbers of patients in our present study were small, particularly of those undergoing revascularization. Therefore, it was difficult to be certain about the effectiveness of the specific procedures in TA.

Our current study showed that revascularization procedures were more frequently performed in more severe stenosis of the renal artery. Bilateral lesions and renal functional impairment at presentation were significantly predictive of poor outcomes. These findings suggest that TA patients with bilateral stenosis and renal dysfunction at initial presentation may require more intensive management including revascularization procedures.

REFERENCES

1. Johnston SL, Lock RJ, Gompels MM. Takayasu arteritis: a review. *J Clin Pathol* 2002;55:481-6.
2. Kerr GS, Hallahan CW, Giordano J, Leavitt RY, Fauci AS, Rottem M, et al. Takayasu arteritis. *Ann Intern Med* 1994;120:919-29.
3. Ishikawa K, Maetani S. Long-term outcome for 120 Japanese patients with Takayasu's disease. Clinical and statistical analyses of related prognostic factors. *Circulation* 1994;90:1855-60.
4. Maksimowicz-McKinnon K, Clark TM, Hoffman GS. Limitations of therapy and a guarded prognosis in an American cohort of Takayasu arteritis patients. *Arthritis Rheum* 2007;56:1000-9.
5. 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.
6. Sharma S, Gupta A. Visceral artery interventions in Takayasu's arteritis. *Semin Intervent Radiol* 2009;26:233-44.
7. Tyagi S, Verma PK, Gambhir DS, Kaul UA, Saha R, Arora R. Early and long-term results of subclavian angioplasty in aortoarteritis (Takayasu disease): comparison with atherosclerosis. *Cardiovasc Intervent Radiol* 1998;21:219-24.
8. Sharma BK, Jain S, Bali HK, Jain A, Kumari S. A follow-up study of balloon angioplasty and de-novo stenting in Takayasu arteritis. *Int J Cardiol* 2000;75 Suppl 1:S147-52.
9. Peng M, Ji W, Jiang X, Dong H, Zou Y, Song L, et al. Selective stent placement versus balloon angioplasty for renovascular hypertension caused by Takayasu arteritis: Two-year results. *Int J Cardiol* 2016;205:117-23.
10. Park HS, Do YS, Park KB, Kim DK, Choo SW, Shin SW, et al. Long term results of endovascular treatment in renal arterial stenosis from Takayasu arteritis: angioplasty versus stent placement. *Eur J Radiol* 2013;82:1913-8.
11. Ham SW, Kumar SR, Wang BR, Rowe VL, Weaver FA. Late outcomes of endovascular and open revascularization for nonatherosclerotic renal artery disease. *Arch Surg* 2010;145:832-9.
12. Hall S, Barr W, Lie JT, Stanson AW, Kazmier FJ, Hunder GG. Takayasu arteritis. A study of 32 North American patients. *Medicine* 1985;64:89-99.
13. Fukudome Y, Abe I, Onaka U, Fujii K, Ohya Y, Fukuhara M, et al. Regression of carotid wall thickening after corticosteroid therapy in Takayasu's arteritis evaluated by B-mode ultrasonography: report of 2 cases. *J Rheumatol* 1998;25:2029-32.

14. Iga K, Gohma I, Hori K. Regression of the left main trunk lesion by steroid administration in Takayasu's aortitis. *Chest* 1991;99:508-10.
15. Arend WP, Michel BA, Bloch DA, Hunder GG, Calabrese LH, Edworthy SM, et al. The American College of Rheumatology 1990 criteria for the classification of Takayasu arteritis. *Arthritis Rheum* 1990;33:1129-34.
16. Levey AS, Stevens LA, Schmid CH, Zhang YL, Castro AF 3rd, Feldman HI, et al; CKD-EPI (Chronic Kidney Disease Epidemiology Collaboration). A new equation to estimate glomerular filtration rate. *Ann Intern Med* 2009;150:604-12.
17. Hata A, Noda M, Moriwaki R, Numano F. Angiographic findings of Takayasu arteritis: new classification. *Int J Cardiol* 1996;54 Suppl:S155-63.
18. Textor SC, Lerman L. Renovascular hypertension and ischemic nephropathy. *Am J Hypertens* 2010;23:1159-69.
19. Bloch MJ, Trost DW, Pickering TG, Sos TA, August P. Prevention of recurrent pulmonary edema in patients with bilateral renovascular disease through renal artery stent placement. *Am J Hypertens* 1999;12:1-7.
20. Bax L, Woittiez AJ, Kouwenberg HJ, Mali WP, Buskens E, Beek FJ, et al. Stent placement in patients with atherosclerotic renal artery stenosis and impaired renal function: a randomized trial. *Ann Intern Med* 2009;150:840-8, W150-1.
21. Cooper CJ, Murphy TP, Cutlip DE, Jamerson K, Henrich W, Reid DM, et al; CORAL Investigators. Stenting and medical therapy for atherosclerotic renal-artery stenosis. *N Engl J Med* 2014;370:13-22.
22. ASTRAL Investigators, Wheatley K, Ives N, Gray R, Kalra PA, Moss JG, et al. Revascularization versus medical therapy for renal-artery stenosis. *N Engl J Med* 2009;361:1953-62.
23. Jenks S, Yeoh SE, Conway BR. Balloon angioplasty, with and without stenting, versus medical therapy for hypertensive patients with renal artery stenosis. *Cochrane Database Syst Rev* 2014;12:CD002944.
24. Riaz IB, Husnain M, Riaz H, Asawaer M, Bilal J, Pandit A, et al. Meta-analysis of revascularization versus medical therapy for atherosclerotic renal artery stenosis. *Am J Cardiol* 2014;114:1116-23.
25. Perera AH, Mason JC, Wolfe JH. Takayasu arteritis: criteria for surgical intervention should not be ignored. *Int J Vasc Med* 2013;2013:618910.
26. Chaudhry MA, Latif F. Takayasu's arteritis and its role in causing renal artery stenosis. *Am J Med Sci* 2013;346:314-8.
27. Perera AH, Youngstein T, Gibbs RG, Jackson JE, Wolfe JH, Mason JC. Optimizing the outcome of vascular intervention for Takayasu arteritis. *Br J Surg* 2014;101:43-50.
28. Saadoun D, Lambert M, Mirault T, Resche-Rigon M, Koskas F, Cluzel P, et al. Retrospective analysis of surgery versus endovascular intervention in Takayasu arteritis: a multicenter experience. *Circulation* 2012;125:813-9.
29. Leertouwer TC, Gussenhoven EJ, Bosch JL, van Jaarsveld BC, van Dijk LC, Deinum J, et al. Stent placement for renal arterial stenosis: where do we stand? A meta-analysis. *Radiology* 2000;216:78-85.
30. Park MC, Lee SW, Park YB, Lee SK, Choi D, Shim WH. Post-interventional immunosuppressive treatment and vascular restenosis in Takayasu's arteritis. *Rheumatology* 2006;45:600-5.

APPENDIX 1. Kaplan-Meier analysis for comparison of primary patency between surgical intervention and endovascular intervention ($p = 0.541$).

