Mid-Term Results of Surgical and Endovascular Treatments in Takayasu's Arteritis

Takayasu Arteritinde Cerrahi ve Endovasküler Tedavilerin Orta Dönem Sonuçları

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ABSTRACT Objective: Takayasu's arteritis (TA) is first described by a Japanese ophthalmologist, Mikito Takayasu, in 1908. It is a disease of unknown etiology, primarily affecting aorta and its branches. We present mid-term results of 20 patients who underwent surgery or endovascular intervention due to TA. **Material and Methods:** Between January 2003 and January 2013, 20 patients with TA underwent surgery or endovascular intervention in our clinic. Their symptoms and findings were upper extremity ischemia (n=10), upper extremity hypertension (n=7), lower extremity claudication (n=5), subclavian steal (n=5), syncope (n=2), vertebro-basillary insufficiency (n=2), and visual disturbances (n=1). Of 20 patients, 13 underwent surgery, 6 underwent endovascular intervention, and 1 underwent a hybrid approach. **Results:** Restenosis was observed in 6 patients. Aneurysm occurred at right distal anastomotic site of the aorto-bifemoral graft in 1 patient who underwent surgery due to atypical coarctation of the aorta. Transient ischemic attack occurred in 1 patient on 48th day after endovascular intervention to the left carotid artery. There was no mortality in our series. **Conclusion:** Both surgical and endovascular approaches are commonly used techniques in TA. Restenosis rates of these interventions are similar. Treatment depends on the on the characteristics of the lesion, and the experience of the surgeon.

Key Words: Takayasu's arteritis; surgery; endovascular techniques

ÖZET Amaç: Takayasu arteriti (TA) ilk olarak 1908 yılında Japon göz hekimi Mikito Takayasu tarafından tanımlanan, etyolojisi bilinmeyen, aorta ve dallarını tutarak semptom veren bir hastalıktır. TA nedeniyle cerrahi veya endovasküler girişim uygulanan 20 hastanın orta dönem sonuçlarını sunmayı amaçladık. **Gereç ve Yöntemler:** Ocak 2003-Ocak 2011 tarihleri arasında TA tanılı toplam 20 hastaya kliniğimizde cerrahi veya endovasküler girişim uygulandı. Başlıca semptom ve bulgular üst ekstremite iskemisi (n=10), üst ekstremitede hipertansiyon (n=7), alt ekstremitede kladikasyo (n=5), subklavian çalma (n=5), senkop (n=2), vertebrobaziller yetmezlik (n=2) ve görme bozukluğu (n=1) idi. Yirmi hastanın 13'üne cerrahi, 6'sına endovasküler girişim, 1 hastaya ise hibrid yaklaşım uygulandı. **Bulgular:** Toplam 6 hastada restenoz izlendi. Atipik aort koarktasyonu nedeniyle aorto-bifemoral bypass uygulan 1 hastanın sağ distal anastomoz bölgesinde anevrizma gelişti. Sol internal karotisine endovasküler girişim uygulanan 1 hastada, işlemden 48 gün sonra geçici iskemik atak izlendi. Olgularımızın takip sürecinde mortalite izlenmedi. **Sonuç:** TA'da hem cerrahi hem de endovasküler yaklaşımlar sıklıkla kullanılmaktadır. Her ikisinde de izlenen restenoz oranları benzerdir. Bu bağlamda hangi tedavi modalitesinin seçileceği, lezyonun özelliğine ve cerrahın tecrübesine bağlıdır.

Anahtar Kelimeler: Takayasu arteriti; cerrahi; endovasküler prosedürler

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Takayasu's arteritis (TA) is first described by a Japanese ophthalmologist, Mikito Takayasu, in 1908. It is a disease of unknown etiology primarily affecting the aorta and its branches.[1] Vessel inflammation

leads to wall thickening, fibrosis, stenosis, and thrombus formation. Incidence, distribution, and presentation of TA vary geographically, and these discrepancies affect the treatment and prognosis of the patients. Although there is no pathognomonic histopathologic finding, TA is classified as a giant cell vasculitis. Middle aortic syndrome, young female arteritis, nonspecific aortoarteritis, pulseless disease, and aortic arch syndrome are the other commonly used names of TA, based upon the clinical findings.

Diagnosis is associated with a high suspicion due to rarity of the disease. TA must be kept in mind by the surgeons, because it can manifest as arterial occlusions, stenosis, or aneurysms. A detailed physical examination must be done in the light of complaints of the patient. When the vessels involved are considered, histolopathological diagnosis is usually impractical, and limited to the cases undergoing revascularization procedures. Doppler ultrasound is a useful non-invasive procedure for the assessment of vessel wall inflammation. Angiography remains the gold standard for the diagnosis. Erythrocyte sedimentation rate (ESR) is a useful parameter for follow-up (not for diagnosis) to determine acute exacerbations of the disease, and the effectiveness of treatment.

Absence of pathognomonic and objective findings challenged surgeons to develop adopted diagnostic criteria. Ishikawa first published the criteria of TA in 1988, and several modifications of this description were reported in thereafter. *"Sharma's Criteria for TA"* is currently the most commonly used diagnostic criteria for TA (Table 1).[2]

TABLE 1: Sharma's criteria for Takayasu's arteritis.

Three major criteria	
Left mid subclavian artery lesion	The most severe stenosis or occlusion present in the mid-portion, from the point 1 cm proximal to the vertebral artery orifice up to that 3 cm distal to the orifice determined by angiography
Right mid subclavian artery lesion	The most severe stenosis or occlusion present in the mid-portion, from the right vertebral artery orifice to the point 3 cm distal to orifice determined by angiography
Characteristic signs and symptoms for at least one month duration	These include limb claudication, pulselessness or pulse differences in limbs, an unobtainable or a significant blood pressure difference (>10 mmHg systolic blood pressure difference in limb), fever, neck pain, transient amaurosis, blurred vision, syncope, dyspnea or palpitations.
Ten minor criteria	
High ESR	Unexplained persistent high ESR >20 mm/h (Westergren) at diagnosis or presence of the evidence in patients history
Carotid artery tenderness	Unilateral or bilateral tenderness of common arteries on palpation. Neck muscle tenderness is unacceptable
Hypertension	Persistent blood pressure >140/90 mmHg brachial or >160/90 mmHg popliteal
Aortic regurgitation or anuloaortic ectasia	Aortic regurgitation by auscultation or Doppler echocardiography or angiography; or anuloaortic ectasia by angiography or two-dimensional echocardiography
Pulmonary artery lesion	Lobar or segmental arterial occlusion or equivalent determined by angiography or perfusion scintigraphy, or presence of stenosis, aneurysm, luminal irregularity or any combination in pulmonary trunk or in unilateral or bilateral pulmonary arteries determined by angiography
Left mid common carotid lesion	Presence of the most severe stenosis or occlusion in the mid-portion of 5 cm in length from the point 2 cm distal to its orifice determined by angiography
Distal brachiocephalic trunk lesion	Presence of the most stenosis or occlusion in the distal third determined by angiography
Descending thoracic aorta lesion	Narrowing, dilatation or aneurysm, luminal irregularity or any combination determined by angiography: tortuosity alone is unacceptable
Abdominal aorta lesion	Narrowing, dilatation or aneurysm, luminal irregularity or aneurysm combination
Coronary artery lesion	Documented on angiography below the age of 30 years in the absence of risk factors like hyperlipidemia or diabetes mellitus
Presence of two major or one major and two minor criteria or four minor criteria suggests a high probability of Takayasu's arteritis	

ESR: Erythrocyte sedimentation rate.

Treatment strategy is chosen according to the segment of the arterial structure involved. Therefore, a classification that gives anatomic and angiographic data about the patient is important. There are several classifications such as Ueno, Nasu, and Tokyo. Comparison of these classifications are shown in Table 2.[2]

Vascular inflammation leads arterial stenosis in TA, and this may require surgical or endovascular interventions. Increased experience enabled most of the vascular surgery centers to be able to perform both surgery and endovascular approaches. The treatment option to be used is determined by the surgeon, according to the vascular lesion of the patient.

In this paper, we aimed to present mid-term results of our 20 patients who underwent surgery or endovascular intervention due to TA.

TABLE 2: Comparison of classifications for Takayasu's arteritis.

Ueno Classification	
Type I	Disease of the aortic arch and its branches
Type II	Disease confined to the descending thoracic and abdominal aorta
Type III	Combination of type I and II
Type IV	Any of the above features with pulmonary artery involvement
Nasu Classification	
Type I	Disease limited to vessels originating from the aortic arch
Type II	Also involves aortic root and arch
Type III	Localized to subdiaphragmatic area
Type IV	Entire aorta and its branches
Tokyo International Conference on Takayasu's Arteritis Classification*	
Type I	Aortic arch branches alone
Type IIa	Ascending aorta, arch and branches
Type IIb	IIa + descending thoracic aorta
Type III	Descending thoracic aorta and abdominal aorta/branches
Type IV	Abdominal aorta/branches
Type V	Entire aorta and branches

* Modification of any with C (+) for coronary and P (+) for pulmonary artery involvement.

MATERIAL AND METHODS

Between January 2003 and January 2013, 20 patients with TA underwent surgery or endovascular intervention in our clinic. All patients were females, and their mean age was 31.2 ± 13.6 years. Their symptoms and findings were upper extremity ischemia (n=10), upper extremity hypertension (n=7), lower extremity claudication (n=5), subclavian steal (n=5), syncope (n=2), vertebro-basillary insufficiency (n=2), and visual disturbances (n=1).

TA was diagnosed according to the Sharma's criteria (Table 1). Patients with active systemic disease, as manifested by symptoms such as fever, musculoskeletal pains, or increased ESR, received an immunosuppressive therapy before surgery. Surgical treatment was performed after the ESR had been normalized.

All patients underwent diagnostic angiography prior to surgery or endovascular intervention. Patients were classified according to Ueno classification. Twelve patients were Type-1, 5 patients were Type-2, 2 patients were Type-3, and 1 patient was Type-4. Distribution of arterial involvements and types are detailed in Table 3.

Of 20 patients, 13 underwent surgery, 6 underwent endovascular intervention, and 1 underwent a hybrid approach. The list of performed interventions are detailed in Table 4.

TABLE 3: Distribution of the arterial involvements.

Type	Patients (n)	Involved Arteries	Patients (n)
I	12	Left subclavian artery	6
		Right subclavian artery	2
		Left carotid artery	2
		Right carotid artery	1
		Right vertebral artery	1
II	5	Abdominal aorta	4
		Descending aorta	1
III	2	Descending aorta + right subclaivan artery	1
		Descending aorta + left vertebral artery	1
IV	1	Left subclavian + main pulmonary artery	1

The statistical analysis of the data was performed using the Statistical Package for the Social Sciences (SPSS Inc., Chicago, Illinois, USA) version 13.0 software program. Continuous variables were expressed as arithmetical mean ± standard deviation (SD), and categorical variables were expressed as frequency (n).

RESULTS

Female dominance in our patient population was consistent with the literature.[3] We did not observe any visceral or renal artery involvement in our

TABLE 4: The interventions performed.

Involved arteries	Patients (n)	Intervention	n
Left subclavian artery	6	Axillo-axillary bypass	5
		Carotico-subclavian bypass	1
Right subclavian artery	2	Axillo-axillary bypass	1
		Carotico-axillary bypass	1
Left carotid artery	2	Balloon angioplasty and stent	2
Right carotid artery	1	Balloon angioplasty and stent	1
Right vertebral artery	1	Balloon angioplasty and stent	1
Abdominal aorta	4	Aorto-bifemoral bypass	2
		Aorto-aortic bypass	1
		Axillo-bifemoral bypass	1
Descending aorta	1	Tube graft interposition	1
Descending aorta + right subclavian artery	1	Tube graft interposition + Balloon angioplasty and stent	1
Descending aorta + left vertebral artery	1	Balloon angioplasty and stent	1
Left subclavian + main pulmonary artery	1	Balloon angioplasty and stent	1

cases. Only 3 patients had double arterial involvement, and a hybrid approach was performed to one of these patients who had descending aorta and right subclavian artery lesions. She had coarctation of the descending aorta, and severe stenosis in right subclavian artery. Coarctation was corrected with polytetrafluroethylene graft interposition (Figure 1), whereas balloon angioplasty and stenting were performed to right subclavian artery. Remaining 2 patients with double arterial involvement were treated by endovascular intervention. There were 4 patients with atypical coarctation of abdominal aorta. Aorto-bifemoral (Figure 2), aorto-aortic, and axillo-bifemoral bypasses were performed in 2, 1, and 1 patients, respectively. All of carotid and vertebral artery lesions were treated by balloon angioplasty and stenting. Axillo-axillary bypass was performed in 6 patients due to total occlusion of the subclavian artery. Proximal anastomosis to carotid artery was made in 2 patients with subclavian artery occlusion, since contralateral axillary arteries had stenosis that did not require any surgical or endovascular interventions.

Medical therapy administered at the time of the intervention consisted of corticosteroids in 19 of the 20 (95%) and immunosuppressants in 11 (55%) patients, including methotrexate (n:7), mycophenolate mofetil (n:2), and azathioprine (n:2). Only 1 patient used methotrexate without corticosteroids, however the remaining 10 patients used immunosuppressants combined with corticosteroids. In addition, all patients received low-dose aspirin (100 mg/day). Patients who underwent balloon angioplasty and stenting also used clopidogrel (75 mg/day).

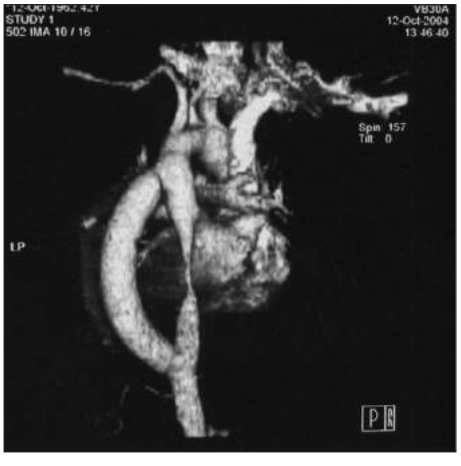

FIGURE 1: Aortic tube graft interposition in coarctation of descending aorta.

Procedure-related complications were classified as early (<30 days) and late (>30 days) and, are listed in Table 5. Graft thrombosis was seen in 1 of axillo-axillary bypass patients. Her proximal anastomosis incision was re-opened, and a thrombectomy was performed via graft. Restenosis was observed in 6 patients. An aneurysm occurred on right distal anastomotic site of the aorto-bifemoral graft in 1 patient

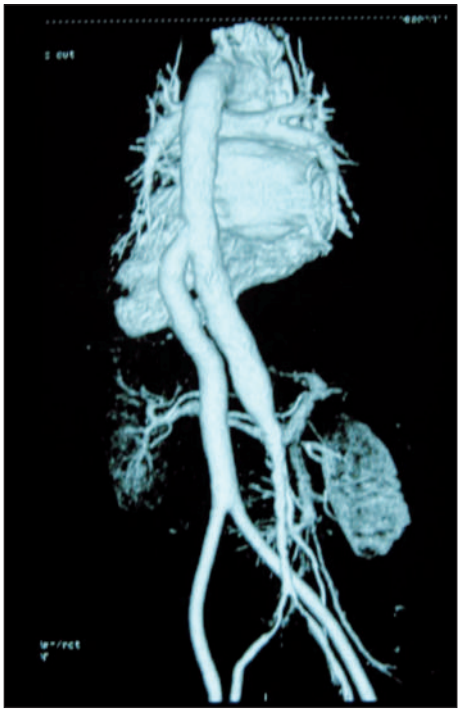

FIGURE 2: Aorto-bifemoral bypass in coarctation of abdominal aorta.

who underwent surgery due to an atypical coarctation of aorta. Subcutaneous infection occurred in this patient after aneurysm repair; however a graft infection did not develop. Postoperative bleeding revision was performed in 2 patients after axillo-axillary bypass and aorto-bifemoral bypass. Transient ischemic attack occurred in 1 patient 48 days after the endovascular intervention to the left carotid artery. There was no mortality in our series.

DISCUSSION

TA is a chronic vasculitis of unknown etiology which may lead to arterial occlusion as well as development of aneurysm. Aneurysmal development shows geographic diversity, and it is particularly unusual in United States, in contrast to series from South Africa and Japan that report incidences as 70% and 32%, respectively.[4] Aneurysm formation is most commonly seen in aorta, and the rupture risk is lower than the typical nonvasculitic aneurysms.[5] The pathology is a "panarteritis" with intimal fibrous thickening and vessel wall destruction producing irregularity, stenosis or even total occlusion. The clinical expression of the disease consists of a systemic non-vascular phase followed by a chronic phase characterized by vascular disorders; however, this classic presentation may be true in only minority of the cases. The symptoms of the patients usually depend on the nature, degree and location of the arterial involvement. These patients usually present with upper extremity hypertension and lower extremity claudication. However, they may be asymptomatic despite a major arterial involvement, and the diagnosis of the arterial occlusion requires a high index of suspicion.

Ischemia of the upper extremities is the most common presentation, and the left subclavian artery is the most frequently involved vessel with some series reporting as many as 90% of the patients having such a lesion.[6] This involvement may manifest as diminished pulse (73%) or even upper extremity claudication (52%).[7] Angiographic evidence from a series reported by Yamato et al. demonstrated that almost 80% of left subclavian lesions were proximal to the origin of the vertebral artery. This may cause vertebro-basillary insufficiency symptoms, and syncope.[8]

TABLE 5: Complications after surgical and endovascular interventions in 20 patients.

	Early (<30 days)		Late (>30 days)		
	Surgery	Endovascular	Surgery	Endovascular	Total
Thrombosis	1	-	-	-	1
Restenosis	-	1	3	2	6
Aneurysm	-	-	1	-	1
Bleeding	2	-	-	-	2
Infection	1	-	-	-	1
Stroke	-	-	-	1	1
Death	-	-	-	-	-

Coronary arteritis is not common, but if occurs, tends to affect the ostia. Pulmonary artery involvement is about 50% in angiographic studies, and may lead to pulmonary hypertension. However, this usually does not present with any initial finding.[9] We had 1 patient with main pulmonary artery involvement. Although the pulmonary artery pressure was in the normal ranges, there was severe stenosis on the angiography, and balloon angioplasty and stenting was performed.

Corticosteroids are the mainstay of the treatment, but steroid-unresponsive patients may receive cytotoxic drugs, and these agents are required in about half of the patients.[10] It is now accepted that approximately half of the patients treated with steroids will respond. This lack of universal success and the side effects associated with corticosteroid use have led to a search for a more effective treatment. An early report of methotrexate suggested that it was a clinically useful, and well tolerated drug. A follow up study of 16 steroid-unresponsive patients treated with methotrexate and steroids demonstrated remission in 81%.[11]

Although hypertension is a common finding reported more in than 70% of the patients in some series, it may be difficult to determine due to subclavian artery involvement.[12,13] Therefore, arterial pressure of the lower extremities should also be measured. Management of hypertension and the prevention and treatment of thrombosis are the other important medical issues. Management of hypertension can be particularly difficult, and worsened by the use of steroids with their fluid retaining side effects. The use of angiotensin converting enzyme inhibitors requires careful monitoring in view of the frequency of renal artery stenosis. Anti-aggregant and anti-coagulant regimens should also be handled with care to prevent and treat thrombosis formation. In postoperative period, we used both aspirin (100 mg/day) and clopidogrel (75 mg/day).

Microscopically, the vasculitis may be divided into an acute florid inflammatory phase, and a healed fibrotic phase. In the acute phase, a vasa vasoritis is seen in the adventitia. The media is infiltrated by lymphocytes and occasional giant cells with neovascularisation. Mucopolysaccharides, smooth muscle cells, and fibroblasts thicken the intima. In the chronic phase, there is fibrosis with destruction of the elastic tissue.[14] Similar histopathological findings are also seen in giant cell arteritis; therefore, biopsy results may not differentiate these two vasculitides. One of our patients' histopathologic specimen is shown in Figure 3, but there is no specific finding. This is why we also preferred clinical and angiographical parameters rather than histopathological findings to diagnose TA.

Ishikawa found that the ESR was elevated in 29 of 54 patients studied, with an equal distribution in the four disease categories.[15] Higher values were seen in the younger patients, declining with age, perhaps representing the natural history of the disease. Hall and Buchbinder found an elevated ESR in three quarters of 32 cases, and reported that it showed an excellent correlation with the treatment effect.[16] Both surgical and endovascular interventions are recommended after completion of acute phase treatment with corticosteroids and/or cytotoxic drugs. Therefore, we postponed the interventions, and placed the patients on immunosuppressive treatment until they were in remission. Although it is not always reliable, ESR can be used to screen the disease activity during this time period.

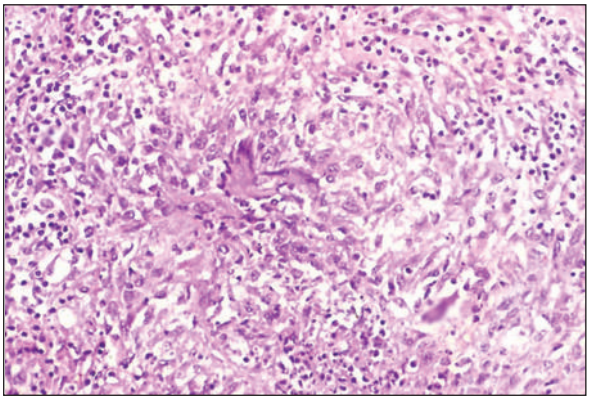

FIGURE 3: Histopathological specimen showing unspecific findings. Stained with hematoxylin & eosin, and magnified approximately x20.

CONCLUSION

TA should be considered as a possible cause of arterial stenosis, especially in young female patients. Symptomatic improvement can be expected after surgical or endovascular intervention. Choice of treatment depends on the characteristics of the lesion and the experience of the surgeon. During acute exacerbation of the disease, surgical intervention should be avoided if possible, and immunosuppressive treatment should be instituted to control the acute phase of the disease.

Conflict of Interest

Authors declared no conflict of interest or financial support.

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