




# Takayasu's Arteritis

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**ABSTRACT**

Takayasu's arteritis (TA) is a chronic inflammatory arteritis that commonly affects aorta and its branches. The exact etiology of TA remains unknown, but many researchers believed that it is autoimmune in nature. Eventhough TA is categorized as a rare disease, the prevalence rate is 2.6 per million annually, and its complications can be life-threatening. Early diagnosis and treatment may prevent the irreversible damage in the affected vessels and improve treatment outcome. This review article provides a brief summary of etiopathogenesis, clinical diagnosis, and treatment options for TA.

**Keywords:** Takayasu's arteritis, autoimmune, inflammatory arteritis, vasculitis

**ABSTRAK**

*Takayasu's arteritis* (TA) adalah suatu penyakit inflamasi arteri kronik yang biasanya mempengaruhi aorta dan cabang-cabangnya. Penyebab pasti penyakit ini belum diketahui, tetapi banyak peneliti percaya bahwa TA merupakan suatu penyakit autoimun. Walaupun TA merupakan kategori penyakit yang jarang – prevalensinya 2,6 kasus per juta orang setiap tahun, dan komplikasi TA dapat sangat membahayakan. Diagnosis dan pengobatan awal dapat mencegah kerusakan permanen pembuluh darah yang terkena dan dapat memperbaiki hasil pengobatan. **Angelina Febrina. Arteritis Takayasu.**

**Kata kunci:** Arteritis Takayasu, autoimun, inflamasi arteri, vaskulitis

## INTRODUCTION

Takayasu's arteritis (TA) was firstly announced scientifically by a Japanese ophthalmologist, Mikito Takayasu, in 1908. He reported a case of a young female patient with a retinal neovascularization, described as "wreathlike arteriovenous anastomoses around the papillae", and the absence of upper-extremity pulses.[1,2] More recently, in 1990 American College of Rheumatology defined Takayasu's arteritis as "an idiopathic inflammatory disease of the large elastic arteries occurring in the young and resulting in occlusive or ectatic changes mainly in the aorta and its immediate branches as well as the pulmonary artery and its branches".[3] Due to these reasons, Takayasu's arteritis is also known as pulseless disease, occlusive thromboarthropathy, aortic arch syndrome.

## INCIDENCE AND EPIDEMIOLOGY

TA is an uncommon vasculitis that can be found world-wide, the annual incidence is ~2.6 cases per million with its highest rates seen in Japan, Southeast Asia, India, and South America.[2,4] TA mostly affects young women in their second or third decade of life with female-to-male ratio 8:1.[5]

## ETIOLOGY AND PATHOGENESIS

Despite decades of extensive researches, the exact etiopathogenesis remains unknown.[4,5] Several authors mentioned autoimmune and genetic predisposition as the mechanisms behind TA.[1,6] However, a theory has been developed as a general understanding that an unknown stimulus triggers 65kDa heat-shock protein in the aortic tissue, induces the major histocompatibility class 1 chain-related A (MICA) on the vascular cells, and finally results in acute inflammation.[5,7] Another hypothesis stated that there may be a possible link between *Mycobacterium tuberculosis* and TA due to the high incidence of the disease in the previously affected TB patients.[8,9]

TA mainly involves medium- and large-sized arteries. Aorta, classically the aortic arch, and its branches and pulmonary arteries are commonly involved. TA is a form of panarteritis with irregular thickening of the lumen, that leads to stenotic lesions (>90% of patients), occlusion, dilatation, and aneurysms.[5,10] The most commonly affected arteries in TA cases are subclavian artery, common carotid artery, and abdominal aorta.[11]

## CLINICAL FEATURES

The course of the disease begins with the "pre-pulseless" phase, usually lasts for weeks to months, and is presented with claudication and non-specific systemic features, such as fever, fatigue, malaise, arthralgia, anorexia, weight loss, night sweats, and vision changes.[2,5] As the disease progresses, lesions in the arteries develop, causing stenosis and eventually may lead to diminished or absent pulse (84-96%) associated with limb claudication and blood pressure discrepancies (>10mmHg) between arms, vascular bruits (80-94%), hypertension (33-83%), retinopathy (37%), aortic regurgitation (20-24%), neurologic features, and pulmonary artery involvements.[2,12]

Although TA is believed to be an auto-

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**Table 1.** ACR diagnostic criteria of Takayasu's arteritis in 1990

| Criteria | Definition |
|---|---|
| Age of disease onset ≤40 years | Development of symptoms or findings related to TA at age ≤40 years |
| Claudication of extremities | Development and worsening of fatigue and discomfort in muscles of 1 or more extremit(ies) while in use, especially the upper extremities |
| Decreased brachial artery pulse | Decreased pulsation of 1 or both brachial arteries |
| Blood pressure difference >10 mmHg | Difference of >10 mmHg in systolic blood pressure between arms |
| Bruit over subclavian arteries or aorta | Bruit audible on auscultation over 1 or both subclavian arteries or abdominal aorta |
| Arteriogram abnormality | Arteriographic narrowing or occlusion of the entire aorta, its primary branches, or large arteries in the proximal upper or lower extremities, not caused by arteriosclerosis, fibromuscular dysplasia, or similar causes; changes usually focal or segmental |

**Table 2.** The angiographic classification of Takayasu's arteritis, Takayasu conference 1994

| Type | Vessel Involvement |
|---|---|
| Type I | Branches from the aortic arch |
| Type IIa | Ascending aorta, aortic arch and its branches |
| Type IIb | Ascending aorta, aortic arch and its branches, thoracic descending aorta |
| Type III | Thoracic descending aorta, abdominal aorta, and/or renal arteries |
| Type IV | Abdominal aorta and/or renal arteries |
| Type V | Combined features of type IIb and IV |

immune disease, there are no specific autoantibodies or other serologic markers that can be associated with this disease.[6,13] However, acute phase reactants, like C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR), are frequently elevated and anemia is usually detected.[4,5,8]

## DIAGNOSIS AND DIFFERENTIAL DIAGNOSIS

The American College of Rheumatology (ACR) defined specific diagnostic criteria of TA in 1990. A diagnosis of Takayasu arteritis requires that at least 3 of the 6 criteria are met (Table 1).[3]

Ultrasonography is a basic non-invasive technique to assess the vessel's lesions. Findings in TA may include wall thickening "macaroni sign", luminal narrowing or stenosis, luminal dilatation and aneurysms, occlusions, and decreased pulsality.[14] Angiography remains the gold standard in establishing diagnosis by identifying the arterial lesions.[12,15] Classification of TA based on the angiographic findings has been proposed in the 1994 (Table 2) to assess patients' characteristics in details based on the involved vessels.[2] Other techniques such as CT angiography and MR angiography,[18] F-Fluorodeoxyglucose positron emission tomography (F-FDG PET) imaging, contrast-enchanced MRI (*Magnetic Resonance Imaging*), and IVUS (*Intravascular Ultrasound*) may aid the diagnosis of TA and monitor disease progressions.[4,8,11,13,15]

Differential diagnosis of TA include other causes of large vessel vasculitis, such as giant cell arteritis, Kawasaki disease, systemic lupus erythematosus, or certain congenital condition that may mimic TA presentations, such as Marfan syndrome or coarctation of the aorta.

## TREATMENT

The goal therapy in TA is to reduce the ongoing systemic and vascular inflammation and to prevent irreversible damage of the affected vessels.

### Pharmacologic Therapy

Corticosteroid therapy has been regarded as the standard and the mainstay treatment of TA. High dose oral prednisolone therapy (1 mg/kgBW daily) is usually used up to a maximum dose of 60 mg daily for 1-3 months or until the symptoms or laboratory reports are improved, and then the drug can be tapered and discontinued in 6-12 months.[8,13,16] The initial dose is tapered at a rate of 5 mg every 2 weeks down to 10 mg and thereafter at a rate of 2.5 mg every 2 weeks until withdrawal or to the minimum required dose to control inflammation.[17] Corticosteroid therapy may result in clinical remission in up to 60% of patients; however, it cannot reverse the vascular injury.[13] Most patients given corticosteroid therapy are well-responded, but relapses are common, especially in the drug-tapering period.[16] In steroid-resistant or relapse cases, the additional therapy of conventional immunosuppressants such as methotrexate (0.15-0.3 mg/kgBW weekly, maximum dose of 25 mg weekly) or cyclophosphamide (2 mg/kgBW daily) can be helpful.[5,8] With all the known possible adverse effects with long term steroid use, specific attention must be made.

Despite aggressive treatment with varied immunosuppressant agents, some patients may still develop refractory TA that can be defined by any of the following characteristics: (1) Prednisolone dose >7.5mg daily after 6 months of treatment, despite the administration of conventional immunosuppressant agents; (2) New surgery due to persistent activity of the disease; (3) Frequent attacks (more than 3 times a year); and (4) Death associated with disease activity.[16] Therefore, TNF-α (*Tumor Necrosis Factor-α*) agents (mostly infliximab) may be added to achieve clinical improvements in refractory TA cases.[4,5] In some cases, anti-platelet may benefit to decrease ischemic incidence; while anticoagulant is used in cases with critical thrombotic events.[4]

### Revascularization Therapy

Revascularization techniques in TA can reduce complications and increase long term survival. These techniques can be done either by invasive endovascular interventional approach or by bypass surgery.[16,17] Not all TA patients shall undergo revascularization. It is limited only for patients with progressive aneurismal enlargement with risk of rupture and bleeding, stenotic lesion resulting in severe symptomatic coronary artery disease or cerebrovascular disease, severe aortic regurgitation, severe aortic coarctation, uncontrolled hypertension as consequences of renal artery stenosis, and aortic stenosis leading to critical limb ischemia.[2,13]

Complications like re-stenosis, graft occlusions, and aneurysms formation in the anastomotic site are often seen.[16]




These complications are related to the progressive inflammation of TA. Therefore, revascularization techniques should be done after the ongoing inflammation ceases. Among all the complications, re-stenosis of the previous lesion is the most common. Its rate may reach up to 30% of cases,[13] but antiplatelet treatment before and after endovascular intervention may decrease the likelihood. The commonly used regimens are the loading doses of aspirin and clopidogrel 12 hours before the procedure, and then continue with maintenance dose of aspirin of 100 mg daily indefinitely and clopidogrel of 75 mg daily for 4 weeks after the intervention.[16]

## PROGNOSIS

The prognosis for uncomplicated TA cases is promising. The 5-year survival rate may reach up to 88-90%.[5] However, TA cases with aneurismal rupture and bleeding, cerebrovascular events, and cardiac failure may complicate the disease outcome and lead to mortality.[11,12] Therefore, establishing timely accurate diagnosis and starting early treatment before the complications appear is quite challenging, but they may improve the prognosis.

## CONCLUSION

Takayasu's arteritis is a world-wide rare disease predominantly seen in Asia and mostly affects female patients at age ≤40 years, mainly between the ages of 25-30 years. Because, to date, there is no single marker that can be used to identify the disease accurately, angiography remains the gold standard in establishing the diagnosis of TA. Corticosteroid is the mainstay treatment of TA, but in cases of refractory TA, conventional immunosuppressant agent like methotrexate or cyclosphosphamide is often added. Revascularization techniques may improve long term survival, but due to their associated-risk, these techniques can only be done in patients fitted the specific indications. Prognosis of uncomplicated case of TA is good.

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