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EDITORIAL

# Emerging Concepts in the Evaluation and Management of Takayasu Arteritis:New Wine in an Old Bottle

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Takayasu arteritis is an enigmatic granulomatous large vessel vasculitis more common in the Indian scenario than in the West. Takayasu arteritis associates with impaired quality of life and also increases the risk of dying.[1] Takayasu arteritis can present to virtually any medical or surgical specialty. In this editorial, we overview emerging concepts in the evaluation and management of Takayasu arteritis.

The 1990 American College of Rheumatology (ACR) classification criteria have been used for Takayasu arteritis for the past three decades. The limitations of these criteria were the use of a comparator group of patients with other forms of vasculitis rather than those diseases involving large vessels (akin to Takayasu arteritis).[2] Also, these criteria lacked sensitivity in other populations (albeit they were specific).[2] Collaborative efforts over the past decade have harnessed the clinical picture of thousands of patients with vasculitis worldwide under the Diagnostic and Classification Criteria for Vasculitis (DCVAS) study.[2, 3] These efforts have resulted in the development of newer criteria for Takayasu arteritis from the ACR and European Alliance of Associations for Rheumatology (EULAR), based on statistical analysis of clinical features of Takayasu arteritis when compared with other diseases associated with similar large vessel involvement (including Giant Cell Arteritis, the other form of large vessel vasculitis). These criteria were presented at the annual meeting of the ACR in 2021 and are eagerly awaited to be published, likely within this year.[3] Assessing disease activity in Takayasu arteritis is difficult. The traditional inflammatory markers erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) have poor correlation with active disease. A seminal study from the National Institutes of Health, United States of America, included patients with Takayasu arteritis who had been taken up for vascular surgical procedures. Such procedures are generally undertaken when the disease is clinically inactive, for fear of complications and death if vascular interventions are performed during active disease. This study revealed that > 40% with clinically inactive disease based on peripheral blood inflammatory markers had ongoing inflammatory activity in the large vessels evident on histopathology.[4] Newer inflammatory markers such as pentraxin-3 have been subsequently evaluated for disease activity of Takayasu arteritis, but results have been inconsistent.[5] 18-fluoro deoxyglucose (18-FDG) positron emission tomography computerized tomography (PET-CT) enables in-vivo visualization of metabolic activity in the body, including in the large vessels. Such vascular uptake of 18-FDG can indicate active large vessel vasculitis.[6] With the increasing availability of PET-CT in India (which shall hopefully reduce costs over time), it is to be expected that this modality shall be progressively used in future clinical practice for assessing disease activity in Takayasu arteritis. Two points need to be kept in mind while interpreting PET-CT reports for Takayasu arteritis. First, PET-CT identifies a subgroup of Takayasu arteritis with active large vessel vasculitis where the CRP might be normal.[7] Thus, the information regarding disease activity of Takayasu arteritis available from PET-CT is complementary to that provided by CRP.[7] Second, patients on glucocorticoid therapy (for greater than three days) might have diminished vascular uptake on PET-CT despite active disease.[6] Thus, the diagnostic role of PET-CT for disease activity in Takayasu arteritis is best when the patient has not been previously treated with

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corticosteroids. Management of disease activity in Takayasu arteritis is challenging. Takayasu arteritis shows good initial response to corticosteroid therapy.[8] However, when corticosteroids are tapered, the disease tends to relapse.[8] Immunosuppressive disease-modifying anti-rheumatic drugs (DMARDs) are commonly used to maintain clinical remission in Takayasu arteritis.[9] However, there are no successful clinical trials of DMARDs in Takayasu arteritis, whether it be conventional, biological or targeted synthetic DMARDs.[9] Conventional DMARDs like methotrexate, azathioprine and mycophenolate mofetil or biological DMARDs such as anti-tumor necrosis factor alpha agents or the interleukin-6 receptor blocker tocilizumab are used in clinical practice for managing Takayasu arteritis based on observational data.[9] While these drugs are effective for maintaining clinical remission in a majority of Takayasu arteritis, angiographic disease often progresses despite DMARD therapy.[9] Recent literature has implicated T helper 17.1 lymphocytes (which express the drug efflux protein p-glycoprotein, thereby imparting the property of corticosteroid resistance) and programmed cell death 1 expressing Th17 lymphocytes (which secrete transforming growth factor beta - the key cytokine involved in fibrosis) in Takayasu arteritis.[10] In-vitro experimental data suggests that combining tacrolimus (which is a conventional DMARD with the additional property of blocking p-glycoprotein) with tadalafil (which exerts anti-fibrotic properties by virtue of antagonizing intracellular pathways downstream to transforming growth factor beta) might be effective in Takayasu arteritis.[10] Apart from conducting well-designed, adequately-powered clinical trials of DMARDs in Takayasu arteritis (possibly involving multiple countries), this strategy of combining immunosuppressive drugs along with anti-fibrotic drugs should be further researched in Takayasu arteritis.[10]

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There are no conflicts of interest.

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