L48. The challenges in assessing Takayasu arteritis

Standardised clinical assessments are central to progress in complex multi-system disease. Clinical improvement in small vessel systemic vasculitis (SVV) has come through more effective drug regimes adapted to disease severity. Methods to quantify disease activity, disease extent and damage, plus functional impairment have been developed and validated. These measurements have played a major role in the development of successful national/international networks which in SVV have provided sufficient patient numbers for RCT’s with secure statistical analysis. The first priority in new vasculitis is assessment of disease activity. Birmingham Vasculitis Activity Score (BVAS), developed as a comprehensive index of active involvement across 10 organ-related systems, has major uses in clinical trials and in standard practice. The BVAS score at presentation provides a quantitative measure of disease severity which can indicate long-term prognosis and direct choice of therapy. High BVAS scores predict increased early mortality and reduced long-term survival. Cumulative development of scars from disease and therapy add to this. Measurement of the Vasculitis Damage Score (VDI) shows that scars develop early, even as activity is brought under control. Damage has a poor prognosis, with both total VDI score and the number of involved organs as risk factors for fatality. This supports the need for aggressive initial treatment to rapidly limit inflammation and scar development before switching to milder maintenance therapy. The challenge now is to adapt these tools to fit large vessel vasculitis like Takayasu aorto-arteritis (TA) which appears more common in Asia then Europe/US. In TA, the restricted large vessel involvement leads to a focal pattern of cardiovascular disease differing markedly from diffuse SV. Absence of the widespread tissue infarcts associated with SVV limits systemic illness in TA, while large vessel occlusion may be associated with development of collaterals and presents late, with established scars. The management of TA is a decade behind SVV with no real evidence base for therapy in the absence of validated assessments. The numbers of patients in India stimulated the Indian Vasculitis group (IRAVAS) to develop appropriate assessments.

Disease extent

Initial consensus agreed an inclusive organ-based list of the main clinical features. The resultant disease-extent index (DEI.Tak) was used to analyse the disease pattern in two main Indian centres [1] and has since been used to characterise Turkish cases [2]. DEI.Tak has real value as a database in individual clinics and as an epidemiologic tool – but is not an activity index and it was important to develop one.

Disease activity

Analysis of serial DEI.Tak assessments from a single large clinic series allowed the selection of a set of items reflecting recent active disease to form a clinical activity score. The resultant Indian Takayasu Activity Score (ITAS2010) focuses on CVS items, with special emphasis on bruits, pulse loss, and claudication. It has been extensively validated and reproducibility in scoring live patients was excellent, with better inter-rater variability than for physicians global. Serial assessments showed that ITAS both reflects response to therapy and detects flares. All items scored in less than 5% of cases were omitted, so the slimmed down final ITAS2010 format contains 43 items in six organ-based systems [3]. It is convenient for physicians in the clinic and useful in therapy trials [4]. It remains unclear whether control of clinical evidence of activity is sufficient to prevent progression in a relapsing scarring disease like TA. When PGA is used to judge disease activity, it reflects acute phase response as well as clinical features. We therefore developed a further combined index, ITAS.A, to additionally include acute phase values (ESR or CRP) assigned a score of 0 to 3 – and this provides new information. When assessing response to therapy in one large patient series, ITAS.2010 indicated satisfactory suppression of clinical disease activity at 6/12 [3]. However, the combined ITAS.A score, despite showing an early response, indicated continued disease activity. This pattern was confirmed at a second centre using a different immunosuppressive plus steroid regime [5]. The incomplete response to active induction therapy with persistent disease activity despite clinical improvement noted in ITAS.A was seen in two centres. This observation is consistent with the high relapse rate in TA noted on steroid withdrawal [6], the slow clearance of hot areas in PET scans,
and the evidence of active inflammation in biopsies from clinically inactive disease [7]. The apparent incomplete response to therapy despite clinical improvement has major implications for therapy. Persistent activity would predict development of damage and indeed significantly elevated TADS scores were documented. Further prospective studies are needed to examine whether this continues and to define the relationship of damage accumulation to the degree of initial activity and to the incomplete response.

Damage

Damage is a common feature of TA. Arterial stenosis is often the presentation and may require vascular interventions. The Takayasu Damage Score (TADS), containing 42 items in seven systems, was derived to capture this aspect by scoring only DEI.Tak features present for at least 6/12. TADS scores from one large cohort followed over two decades showed the increase in damage/scars over time related to disease duration and to features of poor outcome such as pulse loss [8]. One third of cases in that cohort underwent vascular interventions and 18% died during follow-up. TADS scores in fatal disease were higher than in non-fatal cases (7.4 vs 4.8). This shows that recording damage in TA captures clinically-relevant outcomes, including pulse loss, long-term stent patency and mortality. Extensive studies are now required to delineate the type and duration of therapy needed to block scar development in TA. This will also require detailed studies of the correlation between different imaging modalities and clinical assessments [9].

The worldwide challenge in treating TA is to provide an evidence-base for therapies. Standardised quantitative assessment adds strength to epidemiological studies and clinical practice but it is an essential part of clinical trial development, enabling the “treat to target” approach. We need to quantify the effects on disease activity and damage of both current recommended procedures and new therapies. IRAVAS work has established a sound basis for setting up prospective randomised controlled trials which will require collaborations between all specialties seeing TA. International integration of interested groups, particularly across Asia where the condition is more frequent, would greatly facilitate planning the series of RCT’s needed to bring the evidence-base for TA to the same standard as for SVV. Consistent use of standardised tools to assess long-term response to therapy should improve overall success rates in individual clinics.

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References


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L49. Percutaneous interventions in Takayasu arteritis

A large proportion of Takayasu arteritis (TA) patients require invasive procedures to restore patency of stenosed/occluded vessels or to repair aneurysmal disease; this may be due to presentation in an advanced state of vascular disease, or due to failure of medical therapy to prevent progression of disease [1,2]. Vascular surgery (VS) has traditionally been the way to salvage these problems, and several published case series from around the world support its effectiveness [1,3–8]; commonly performed procedures include bypass surgery in various anatomic locations, aortic valve replacement and aneurysm repair. However, VS in TA has limitations: the associated morbidity and mortality is not inconceivable; a significant proportion of patients require revision surgery to deal with graft occlusion, anastomotic aneurysms, or progression of