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 SV. 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


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 inconsiderable; a significant proportion of patients require revision surgery to deal with graft occlusion, anastomotic aneurysms, or progression of
disease; treatment of lesions in multiple vascular territories (which is frequently required) necessitates either extensive VS or acceptance of incomplete revascularization and its consequences [1,9,10].

Percutaneous interventions (PI) are an attractive alternative to VS, their less invasive nature conferring lower procedural risks; other inherent advantages of PI include ability to treat multiple vascular territories through a single access site, and ease of repeatability through the same access site should restenosis occur. The worldwide experience with PI in TA is not as extensive as for VS. Early TA PI experience in the late 20th century was confined to balloon angioplasty and emanated mainly from Asian countries: five studies [11–15] collectively treating 254 lesions reported 89-100% initial success and minimal morbidity; the restenosis rates were 13 to 23% at 1–3-year follow-up. Use of stents during PI in TA followed a few years later; stents are an important adjunct to balloon angioplasty in TA when vessel recoil or dissection occurs, but have been used electively as well: three series [16–18] each treating 12 to 21 lesions, showed high immediate success rates with minimal procedural complications; restenosis occurred at follow-up in 20% of lesions in each of the studies. The low restenosis rates obtained after balloon angioplasty or stenting in the above studies have not been reproduced in other studies from different parts of the world where restenosis rates ranging from 51% to 78% were observed after PI in TA, significantly higher than that seen after VS in the same studies [1,2,9,19–21]. Consequently, the European League Against Rheumatism (EULAR) currently recommends VS as the treatment of choice for vascular lesions in TA, and cautions that though balloon angioplasty and stenting may be appropriate for some patients, PI is associated with higher restenosis rates than VS [22].

The relative rarity of TA, small numbers of patients in most TA case series, and wide variation in treatment strategies have retarded elucidation of the best way to treat vascular lesions in TA; this is especially true of PI which is a relatively new modality. However, there are three areas where significant progress is occurring:

The first area of progress is improved understanding of the influence of persisting disease activity on treatment outcomes, and developing new ways to effectively control disease activity. Persisting disease activity in TA can compromise VS outcomes, and also lead to progression of disease, both of which may necessitate additional VS procedures [4,19,23–25]. Absence of disease activity is associated with low restenosis rates after PI: Lee et al. [26] performed PI restricted to patients in the chronic inactive stage of TA, and obtained a restenosis rate of 31%; Min et al. [27] attribute the 17% restenosis rate they obtained after PI in 58 lesions to rigorous control of disease activity prior to PI. Conventional medical treatment for TA is far from effective, and relapses remain common despite use of adjunctive immunosuppressants along with corticosteroids [1]; life-long global vascular surveillance is therefore mandatory [23,28]. New therapies such as tocilizumab may hold the key to solving the problem of controlling disease activity in TA [29]; recent experience from our center suggests that monthly tocilizumab infusions can halt the restenotic process, at least in the short-term, in TA patients with recurrent restenosis after PI.

The second area in which significant recent progress has occurred is in equipment and techniques used during PI in TA. Recanalizing occluded lesions in TA is particularly challenging, and each vessel needs different strategies; subclavian artery and aortic occlusions typically require a bi-directional approach using femoral and radial/brachial artery accesses, and a combination of hydrophilic and stiff guidewires; occluded renal arteries are best dealt with using contemporary equipment and techniques used to recanalize atherosclerotic coronary arteries. Dilating resistant lesions is another challenge in TA PI; balloon dilatation at high pressures using compliant balloons or use of cutting balloons may cause arterial rupture or dissection; conversely, inadequate lesion dilatation makes for sub-optimal PI outcomes; at our center we have largely overcome this problem by using undersized non-compliant balloons at pressures up to 30 atmospheres and staged dilatation of resistant lesions. Covered stents may reduce restenosis after PI in TA [30]; at our center we found that covered stents used to resolve arterial rupture during PI in TA restenosed infrequently, and this lead us to use them electively in aorto-ostial lesions; restenosis was seen at follow-up at the stent-edge in 2 of 16 lesions treated with covered stents.

The third area of progress is in dealing with restenosis after PI in TA. Balloon angioplasty usually suffices to treat post-PI restenotic lesions, and this is usually simpler to perform than the original PI; such procedures have high early success rates and low related risk [26]. At our center we repeat PI (balloon angioplasty) in recurrently restenosing lesions till sustained success is obtained; most restenotic lesions require only one or two PI procedures before sustained success is obtained, but a few may need more: this usually happens in patients with persisting disease activity despite conventional medical therapy, or in non-compliant patients. The strategy of repeated PIs has paid dividends: in 659 lesions (most were stented) when follow-up was obtained after the first PI, 53% had restenosis; however after repeated PIs and subsequent follow-up, restenosis remained in only 13%; yielding an overall success rate of 87%; in this cohort the average number of PIs per lesion was 1.43, and ranged from 1 to 7. PI in TA should thus be viewed as a potentially multi-session treatment and patients should be counseled accordingly at the start; the key ingredients to a successful final outcome are control of disease activity, use of appropriate PI equipment and technique and, above all, persistence.
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References


L50. The future of international clinical trials in vasculitis

Introduction

Great progress has been made in the past 20 years in the treatment of various forms of vasculitis. This progress has been the direct result of the vasculitis clinical research community working collaboratively to successfully complete multi-centered randomized clinical trials (RCTs). These trials include seminal studies defining the evolving standard of care for various forms of vasculitis, especially ANCA-associated vasculitis [1–8] but also key studies in giant cell arteritis [9–12],