Takayasu’s Arteritis in Children: A Developing World Perspective

Christiaan Scott¹, Mignon McCulloch¹, Peter Nourse¹

Abstract

This review summarises recent available literature on Takayasu’s Arteritis, with an emphasis on a developing world perspective.

Key words: Vasculitis, takayasu, arteritis, large vessel, developing countries

Introduction

Takayasu Arteritis (TA) is a large vessel granulomatous vasculitis affecting the Aorta and its main branches. This disease has remained enigmatic since its ocular signs were first described in a young woman, by Japanese ophthalmologist Mikito Takayasu in 1908 [though it has been suggested that the first case was described earlier, in 1835 by another Japanese author, also in a young woman] [1]. Ironically the description by Takayasu himself did not mention involvement of the aorta or great vessels.

The cause of TA is unknown but this disease demonstrates multifactorial aetiology, as it occurs with different clinical features, different infectious associations and with varying degrees rarity in different population groups. This review will consider general aspects of TA and highlight some aspects which are important from a developing world perspective.

Epidemiology

Takayasu Arteritis is a disease of younger people with an increased prevalence in females, though the true incidence and prevalence in children is not known.

While it has been described in all populations, it does appear to occur with increased frequency in persons of Asian, South East Asian and African descent. Studies indicate incidences ranging from 2.6/million in the Olmsted County USA to 0.4 per million in Norwich, United Kingdom [2,3]. Given the nature of the disease, with protean and non-specific symptoms in the absence of end organ damage, these figures are almost certainly an underestimation. This is supported by one post mortem study from Japan, which showed sings of Takayasu in 1 per 3000 autopsies [4]. In our experience TA is also much more prevalent in South African children, yet no formal epidemiological studies have been published in this regard.
Classification and Diagnostic Criteria

Classification and diagnostic criteria for TA have evolved over the years, from the Ishikawa criteria proposed in 1978 to the more recently adopted EULAR/PRINTO/PReS criteria in 2005 (Table 1). The PReS criteria were validated between 2008 and 2010 in a global collaborative effort, which recruited 87 children with TA and measured the sensitivity and specificity of the EULAR/PRINTO/PReS criteria against 1183 children with other vasculitides. The classification criteria performed well with 100% sensitivity, 99.9% specificity and AUC of 99.95% (κ-agreement of 0.99) [5].

Pathophysiology

Inflammation of the aorta and the large vessels in TA is driven by a complex immune response involving components of innate and adaptive immunity. The distribution of vessel involvement in TA can be explained by the fact that different parts of the vascular tree express a different Toll-like Receptor profile, leading to a site specific initiation of the innate immune response [6]. In the case of TA the lesions appear to arise symmetrically in paired components of the large vessels and contiguously in the aorta [7,8]. Heat Shock Proteins are a primitive early warning and protective mechanism for cells exposed to stress and have an important role in folding and managing proteins in the “stressed” cell. The 60kDa HSP in humans and its homologue Mycobacterial 65kDa HSP have been implicated in the initiation of the innate immune response in TA. Patients with TA have an increased expression of 65kDa HSP in aortic tissue as well as T-Cell and IgG response to both human 60kDa HSP and mycobacterial 65kDa HSP compared to healthy controls [9,10]. It has been proposed that a loss of tolerance to HSP is the triggering event, leading to activation of an innate immune response in cytotoxic cells by activation of Toll-like receptors and NLRs (Nucleoside Oligomerisation Domain Like Receptors), leading to the expression MHC class I chain-related A (MIC-A) molecules in ‘stressed’ cells and subsequent recognition of MICA by the NKG2D receptors in NK-Cells and γδ T cells [11]. This leads to perforin induced vascular inflammation. Dendritic cells, which have been shown to be present in the aortic tissue of patients with TA, are activated by TLR and present antigen to T-lymphocytes [9]. This results in oligoclonal expansion of autoreactive T-cells and recruitment of cells to the site of inflammation after up-regulation of adhesion molecules and neovascularization, which leads to proliferation of the vasa vasorum [12]. The Th-1 response results in the formation of giant cells and the recruitment and activation of macrophages via interferon γ [13]. A Th-17 response leads to cytokine release and the recruitment of neutrophils. Cytokines such as IL-6 and IL-8, amongst many others, have been shown to be elevated in the serum of TA patients and there is also evidence of up-regulation of mRNA gene expression of TNF-α and IFN-γ in the PBMC’s such patients [14]. This has led to the use anti-TNF and anti-IL-6 biologics in the treatment of TA.

TB or not TB

In countries such as South Africa and India, where infection with Mycobacterium Tuberculosis is prevalent, the link between evidence of previous TB exposure and Takayasus Arteritis is clearly established. A recent review of the management renovascular hypertension in children with Takayasus Arteritis from Cape Town, South Africa showed that 93.2% (55/59) had a positive Tuberculosis skin test [15].

A previous review from Gauteng South Africa showed a strongly positive mantoux skin test in 27/31 patients (90%). This strongly positive reaction was present in 5% of the control population. Interestingly, 3 patients were receiving treatment for pulmonary TB; 1 had prior therapy for TB and 3 had a family history of TB at the time [16]. A study of 272 adult patients from Cape Town South Africa showed that active pulmonary tuberculosis (demonstration of acid-fast bacilli in sputum, an ulcerating Mantoux test, a highly suggestive chest radiograph

Table 1. EULAR/PRINTO/PReS criteria.

| Classification of childhood TA requires: |
| Typical angiographic abnormalities of the aorta or its main branches and pulmonary arteries (mandatory criterion) |
| **PLUS:** one of the following: |
| 1. Pulse deficit or claudication |
| 2. Blood pressure discrepancy in any limb; |
| 3. Bruits |
| 4. Hypertension |
| 5. Elevated acute phase reactants |

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or acid-fast bacilli in histological material), was diagnosed in 54 patients (20%) [17]. Mexican patients had similar findings with 8/44 patients having had a previous diagnosis of tuberculosis, and 81% a positive PPD skin test. In a study comparing Tb quantiferon gold with Tuberculin Skin Test, 63.9% of TA patients vs. 42.1% healthy controls had a positive TST. However, the quantiferon gold test was positive in similar proportions between TA patients and healthy controls [18].

A number of reviews from countries such as France, Serbia, China and the USA do not report skin test results, which seems to indicate that TB is not considered a major association in these populations.

The role of 65 kDA HSP has been described earlier, which lends credence to the theories about a pathogenic role for TB infection and a subsequent higher prevalence of TA in countries with high TB burden and/or BCG vaccination.

### Clinical Features

The clinical features of TA can be divided into two phases. The first is a period of non-specific systemic inflammation, with low-grade fever, fatigue, malaise, arthralgia, weight loss and night sweats [19]. The diagnosis is seldom made in this phase, before the onset of complications related to vascular insufficiency. The occlusive phase follows and is characterised by the effects of perfusion deficits to specific areas, especially the kidneys, brain and limbs. Renal-vascular hypertension, leading to seizures or cardiac failure is by far the most common mode of presentation of children with TA. It is the most common cause of renal-vascular hypertension in Asian and South African children [20-22]. Ischaemic neurological symptoms such as headache, dizziness or stroke, mesenteric angina, vomiting and limb claudication are less frequent modes of presentation in children. It is usually only after a dramatic presentation with convulsions or cardiac failure, or an incidental finding of hypertension, that features such as absent or diminished peripheral pulses, discrepant limb blood pressure or arterial bruits are appreciated. Posterior Reversible Encephalopathy Syndrome (PRES) is a manifestation of severe hypertension, which has been described in Takayasu Arteritis [22]. Complaints of jaw, neck or arm pain, which are common in adults, rarely occur in children. Aortic root dilatation may lead to congestive cardiac failure [23]. A number of cases of ulcerative colitis associated with TA have been documented, especially in Japan [24-28]. An association with uveitis has been reported in some series from Mexico, USA and South Africa [16,29,30]. Skin manifestations are infrequently reported in children, but skin nodules, erythema nodosum, pyoderma gangrenosum and rashes have been reported in adults [31-33]. There are recent reports of large vessel vasculitis occurring in patients with Blau syndrome [34,35].

### Differential Diagnosis

Fibromuscular dysplasia is frequently difficult to distinguish from TA, and is one of the more prominent causes of renal-vascular hypertension in children, especially in studies from Northern Europe. A recent review also emphasises the difficulty in distinguishing these two conditions [36]. The presence of systemic symptoms, significantly raised inflammatory markers, vessel wall thickening on MRA and abnormalities on PET CT help to confirm the diagnosis. In our experience a strongly positive (frequently ulcerating), tuberculin skin test, which is present in 90% of patients with TA in Cape Town is an additional feature suggesting the diagnosis [15,37].

Renal-vascular stenosis due to other syndromic causes such as Williams Syndrome, Neurofibromatosis Type 1, Marfan’s Syndrome and Ehlers-Danlos Syndrome need to be considered before a diagnosis of TA can be made. In the developing world infectious causes of aortitis such as Treponema Pallidum, Staphylococcus, Shigella and Tuberculosis have to be considered [38-40].

### Investigation for Takayasu’s Arteritis

TA is a challenge to diagnose, as advanced diagnostic modalities are often not available in regions of the world such as Africa and the Indian sub-continent where TA is prevalent. This is further complicated, by the fact that these patients often present late into their illness with advanced disease and organ involvement. The link with Tuberculosis (TB) requires the exclusion of active TB, which presents an additional challenge [41] (table 2). Important clinical features and laboratory markers for the diagnosis of TA are summarised in table 3.

Angiophraphic findings of TA include localised stenosis of vessels at their origin, aneurysms and the presence of ‘skip lesions’ (vessels abnormalities such as stenosis or aneurysm interspersed with areas of normal vessel) [42,43]. A recent
review emphasizes the difficulty in differentiating FMD from TAK in children as a similar distribution of vessel involvement is found in both conditions [36]. In our experience angiographic findings that may distinguish TA from FMD are the presence of saccular aneurysms of the abdominal aorta, found in 31% of patients and undulations of the luminal margins in 86% of patients [37]. Early recognition of vascular inflammation or wall thickening/oedema has become an important therapeutic advance as it may allow diagnosis of TA in the pre-stenotic, potentially reversible phase and there are a number of modalities which can now identify the vessel wall thickness including MR, intravascular ultrasound or PETscans [36,44].

**Radiology**

**Ultrasound:**

Ultrasound is an inexpensive and non-invasive modality, which is particularly useful in poorly resourced areas. Renal artery involvement is common in TA and differential renal sizes as well as evidence of scarring or infarct can be visual-

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### Table 2. Investigations for TB in TA.

<table>
<thead>
<tr>
<th><strong>TB Diagnosis</strong></th>
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<tbody>
<tr>
<td>Skin testing</td>
<td>Evidence of BCG immunisation. Tuberculin skin testing in the form of a Mantoux ulcerating or strongly positive (useful in young children but in teenagers may just show evidence of previous exposure)</td>
</tr>
<tr>
<td>CXR</td>
<td>Evidence of Lymphadenopathy/ signs of active TB infection</td>
</tr>
<tr>
<td>Quantiferon-TB Gold test (QFT)</td>
<td>In vitro assay measuring interferon-gamma response to M. tuberculosis antigens and may be helpful in diagnosing latent TB infection [99]</td>
</tr>
<tr>
<td>Newer PCR testing such as Gene Xpert®</td>
<td>Direct detection of Mycobacterium tuberculosis complex (MTBC) and rifampicin (RIF) resistance using induced sputum or tracheal aspirates (if intubated) has a much higher specificity and sensitivity (&gt;94%) compared to gastric washings/aspirates which can have a yield as low as 10% [100]</td>
</tr>
</tbody>
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### Table 3. Clinical and laboratory examinations in TA.

<table>
<thead>
<tr>
<th><strong>Clinical – Bed-Side</strong></th>
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<tbody>
<tr>
<td>Blood Pressure</td>
<td>4 Limb BP – Differential BP or absent pulses</td>
</tr>
<tr>
<td>Bruits</td>
<td>Abdomen especially renal arteries. Neck vessel regions</td>
</tr>
<tr>
<td>Urine testing</td>
<td>Presence of blood &amp; protein</td>
</tr>
<tr>
<td>Ophthalmology review</td>
<td>Hypertensive retinopathy</td>
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<tr>
<th><strong>Cardiology Testing</strong></th>
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<tbody>
<tr>
<td>ECG</td>
<td>Cardiomegaly with signs of Ventricular strain</td>
</tr>
<tr>
<td>CXR</td>
<td>Cardiomegaly</td>
</tr>
<tr>
<td>Echocardiography</td>
<td>Cardiomegaly with thickened ventricular walls</td>
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<table>
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<tr>
<th><strong>Laboratory Testing</strong></th>
<th></th>
</tr>
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<tbody>
<tr>
<td>Renal function</td>
<td>Urea and Creatinine raised in severe renal failure</td>
</tr>
<tr>
<td>Acute phase reactants</td>
<td>ESR and CRP specifically and additional markers such as platelet count, fibrinogen and ferritin</td>
</tr>
<tr>
<td>Monitoring of the disease activity using newer modalities still need evaluation</td>
<td>Autoantibodies (anti-endothelial anitbodies) as well as newer biomarkers (IL-6, IL-8, IL-18, Matrix metalloproteinase-9 and pentraxin 3) [101]</td>
</tr>
</tbody>
</table>
ised. Doppler examination of the abdominal aorta and renal arteries examining for reduced flow or waveform should be performed. In severe cases of renal stenosis there may be no flow detectable and large collateral vessels may ‘falsely’ provide Doppler signal suggesting vessel flow.

Overall ultrasound circumvents the radiation risk of other imaging modalities, but does have limitations in small vessels especially in young children [37].

Contrast-enhanced carotid artery ultrasound is a newer modality that promises easily reproducible measure of arterial wall inflammation where supra-aortic vessels are involved. It allows direct visualization of parietal vasa vasmorum and neovascularization, therefore providing real-time information about the inflammatory response to treatment [45].

**Angiography:**

**Conventional Angiography:**

The current gold standard for diagnosis and follow-up has been x-ray angiography, which can image the entire aorta and all its main branches thus assisting in anatomical classification. Older angiographic classifications (Pantanowitz) included pulmonary and iliac vessels separately [46] , however the current angiographic classification consists of 6 types with coronary or pulmonary arteries included in the main classification [47].

Angiography has limitations in that it is invasive and requires injection of contrast media. Furthermore, it is unreliable in that it does not identify the early inflammatory phase but only identifies late structural changes in vessels.

One advantage of conventional angiography is that it allows for selective blood sampling from upper and lower inferior vena cava as well as left and right renal veins for renin levels, which may guide therapeutic interventions by identify which kidney is contributing most to the hypertension.

**CT Angiography:**

CT scan imaging has been the mainstay of diagnostic imaging, but of late Magnetic Resonance Angiography is predominantly used in view of reduced radiation exposure. CT and CT angiogram may still be useful in identifying the vessels involved especially for cerebral involvement or in poorly resourced areas. It is important that small children are well sedated and thin slice imaging is used to accurately identify pathology. Contrast administration should be used with caution in cases where there is renal involvement.

**MRI Angiography:**

MRI angiogram is attractive in view of reduced radiation and more accurate imaging. There are concerns that MRI may ‘over-estimate’ the degree of stenosis [48] or show inconsistency in assessment of vessel wall oedema compared to conventional angiography [49] and thus it may be wise not to base intervention on this modality alone.

Newer MRA scoring system of lumen stenosis, wall thickness and wall enhancement moderately correlate with acute phase reactants [50].

**Other Modalities:**

Positron emission tomography (PET) has developed a role in diagnosing vessel wall thickness and a marker of vessel inflammation using an isotope [18F] Fluorodeoxyglucose identifying with a single scan all the vessels affected [51].

The presence or absence of [18F] FDG uptake in the vessel wall has proved to be a reliable guide to disease activity thereby identifying active TA before treatment but also as follow-up in patients receiving immunosuppression. This can be used in combination with CT scan as FDG-PET/CT or MRI (but at extreme financial implications) [52,53].

Nuclear imaging apart from PET scans can be used in a variety of tests, including DMSA scans which can identify grossly differential renal function as a percentage. More specifically, areas of scarring as well as infarcts can be identified. Mag 3 renograms with individualized Glomerular Filtration Rates (GFR) using EDTA are also useful in that the differential renal function and GFR of each kidney can be assessed. Post revascularisation of kidneys, Mag 3 renogram with individualized GFRs is a useful test for follow up to detect changes in renal function.

Finally, as a last resort, where nephrectomy is considered and no nuclear imaging for differential function is available, Intravenous pyelograms(IVP) with all its accompanying radiation risk may be used in poor resource settings.

**Disease Activity Scoring**

There have been positive recent developments in the search for an ideal measuring tool that can reliably assess disease activity and response to treatment in children with TA. The Birmingham Vasculitis index, designed predominantly to
assess disease activity in small vessel vasculitis, has been adapted for children to create the PVAS, though it has not been validated in large numbers of children with TA. The recent development of the ITAS2010 (also adapted from the BVAS) and the ITAS-A (a composite tool incorporating acute phase reactants) have shown promising results in a large Indian cohort of 300 patients but have not been validated in other populations or for children. Quality of life measures have also not been specifically designed or validated in children with TA.

**Medical Treatment**

The aim of immunosuppressive treatment is control of inflammation and prevent further damage to the vessel wall. There are no randomised controlled trials comparing various forms of treatment in TA. Furthermore there is no evidence that steroids alter long term outcome of patients with TA. Because of the overlap in vessel disease (as noted above) between TAK and FMD in children it is imperative to differentiate between these diseases before embarking on immunosuppressive treatment. The benefit of treating ‘burnt out’ Takayasu’s without evidence of inflammation is also questionable. Most patients, seem to go into remission once given steroids and there is a halt in constitutional symptoms and normalization of ESR [54-56]. A generally acceptable regime for children is to give prednisone 2 mg/kg and then to taper to alt day after 1-3 months. [56,57]. Researchers have pointed out that many patients do not stay in remission once prednisone is stopped [58,59] and that slow tapering of prednisone is important.

A beneficial effect was has been shown using cyclophosphamide in steroid resistant disease [60,61]. There is also one study from Turkey showing that induction therapy in children is safe and beneficial [62]. In a recent report from Germany IVI pulsed cyclophosphamide in 10 patients showed a sustained response after 45 months in 80% of patients with steroid resistant or organ threatening TA. Response was measured by PET/CT scan as well as ESR and CRP [63]. Cyclophosphamide is more readily available in developing countries than newer agents and should be used in life threatening Takayasu disease in children despite the concerns regarding fertility and other side effects.

Methotrexate was effective in inducing remission in 81% of 16 patients with steroid resistant disease. Over half of these patients had a sustained response [54]. Despite this agent being widely used especially in developing countries (including our own centre) there is very little evidence of it efficacy.

There have been a number of recent report of the efficacy of TNF blockers in steroid resistant TA cases. Although there are no controlled trials and no long term data regarding their effectiveness or side effects, there appears to be a high initial response rate to these agents [64-69]. A recent review of this literature which included 84 TA patients revealed complete remission in 37%, partial remission in 53.5%, and 9.5% non responders [70].

In a recent report one out of two two patients showed good clinical response to Rituximab after being resistant to methotrexate and TNF alpha inhibitors [71]. Hoyer et al reported three patients with refractory TAK despite prednisone, mycophenolic acid, cyclosporine and adalimumab, who responded to rituximab. Of note, response and relapse correlated to plasma cell precursors [72].

Nine recent cases of the use of anti-interleukin 6 (Tocilizumab) therapy for the treatment of resistant Takayasu’s disease (one naïve case) have been reported in the literature. These are summarized in a recent article [73]. All cases achieved disease remission and steroids were either tapered or discontinued. One case relapsed on therapy and another three months after stopping.

Refractory disease in 12 TA patients was recently shown to respond to leflunamide therapy in a recent prospective study from Brazil. Clinical disease as well as inflammatory markers improved significantly after 9 months of therapy. Steroid therapy had however not been stopped at the end of the study and two cases had radiological progression despite clinical and laboratory remission [74].

As for all patients with hypertension it is imperative to control other cardiovascular risk factors such as hyperlipidaemia etc. Although often used in certain parts of the world the role of oral anticoagulants, antiplatelet agents and vasodilators has not been established. Despite positive mantoux test in these patients anti-tuberculous therapy is probably unwarranted unless there is evidence of tuberculous disease or contact. In endemic areas like South Africa we feel anti-tuberculous prophylaxis is warranted when using immunosuppressive drug.
Surgical Treatment Takayasu’s

When medical treatment alone fails, or when patients present with advanced disease, then surgical treatment of takayasu arteries lesions may be indicated. Indications for surgery in takayasu arteritis would be intractable hypertension not responding to treatment, severe symptomatic cerebral or coronary artery disease, limb ischaemia or risk of organ loss, aneurysms with a risk of rupture, severe aortic regurgitation or coarctation. In these cases the risk benefit of surgery is good [75-77]. A one size fits all approach does not work and the type of surgery needs to be individualized for each patient because of the individual degree and site of lesions that occur. In children 80% of patients require surgical treatment for stenotic lesions [78] compared with adult patients where approximately 20% require surgical management [75,76]. Miyata demonstrated that in patients with major complications and progressive disease surgery increased the long term survival of patients with TA [77]. Conversely survival was decreased in patients with mild disease who underwent surgery. The published literature also indicates that re-stenosis is common so it is therefore vital to select patients carefully for surgery and the decision should not be based on the radiographic features alone without considering clinical parameters.

Children with Takayasu arteritis are often inflamed on presentation. Inflammation at the time revascularisation was shown to be associated with increased vascular complications [77,79,80]. It is therefore advisable to wait (if possible) until remission before embarking on vascular procedures. This usually can be achieved within 2 weeks to one month.

The Thoracic and abdominal aorta are the most common vessels affected in children with TA with renal artery involvement in 70-80% of cases [16,81]. Unlike in developed countries, in South Africa and Asian populations TA is the most common cause of renovascular hypertension [46,82]. Surgical options include Percutaneous transluminal angioplasty, autotransplantation, in situ arterial bypass surgery using other arteries (eg splenic, hepatic) grafts (saphenous vein, internal iliac) or synthetic conduits.

In adult studies benefit of revascularization procedures in TA induced RVH has shown benefit in terms of hypertension and preservation of renal function [83,84]. Corbetta et al demonstrated good outcome in five TA children with RVH using autotransplantation [85]. In the largest series of surgical management of RVH in children (non TA) Stanley reported increased incidence of aneurysmal dilatation when using autologous saphenous veins for bypass surgery. This has led to decreased use of this modality [86]. Outcome after splenorenal, gastroduodenal-renal and iliorenal bypass surgery has been documented as poor in some reports with early development of new stenotic disease in the inflow arteries or at the anastomosis [86,87] in children with non-TA RVH.

PTA use although still controversial is becoming more popular and has become first line treatment in some large centres in children with mainly non TA RVH [87,88]. Efficacy of PTA in children with RVH secondary to TA has been shown in children from India both in terms of technical success and for treatment of renovascular hypertension with benefit being shown in terms of hypertension in up to 90% of patients [82,89]. Benefit (cure or improvement) in hypertension was also demonstrated in seven TA patients with RVH from South Africa who were treated with PTA [15]. Restenosis rates were higher in reported TA paediatric patients (16-20%) [82,89] than in non TA patients [88]. Similar benefit in terms of blood pressure control and re-stenosis were seen in adult TA patients with RVH treated with PTA [90,91]. Ham reported on renal artery interventions in a cohort of 79 pts with non atherosclerotic renal artery disease (55% TA). Surgical revascularization was shown to have better one and 5-year outcomes including patency rates (91% and 80%, resp.) compared to endovascular intervention (73% and 49%) [84]. Endovascular treatment may have a better outcome rate in discrete lesions and extra renal lesions [88,90-94]. Sharma’s group [91] concluded in their study that PTA without stenting in TA patients is preferential and they cite small vessels with difficult access, frequent spasm, coexisting periaortic stenosis, long length of stenosis, difficult stent expansion due to tough nature of stenosis and increased risk if in stent re-stenosis as reasons. They also feel that stents may make subsequent surgical treatment more complicated. Shroff’s group also found increase restenosis with stents in non TA RVH children and they give specific indications for stenting. Their group do not feel that stenting complicates later surgery [87,88,93]. The use of high pressure balloon or
cutting balloon may be an option for difficult stenoses [93]. A report from Harvard medical School in the States this year found that children with mid-aortic stenosis (including 19% of patients with Takayasu’s) treated with PTA had a higher re-intervention rate compared to surgery [94].

With regard to carotid and subclavian artery lesions Kim demonstrated superior patency of supra-aortic vessels with surgical bypass versus endovascular treatment (12.5% vs 53% restenosis). This was despite only doing PTA on the short stenotic lesions. These lesions often have long, irregularly fibrosed narrowing which is not ideal for PTA and stenting [95].

In a report from Japan coronary artery involvement was reported to be low (23%) in a cohort of 130 Takayasu patients (including some children). Coronary artery stenosis or occlusion was the more common than aneurysmal coronary ectasia and coronary steal phenomenon. They recommend treatment of coronary stenosis, as coronary ischemia can be one of the main causes of death. Surgical treatment was satisfactory with an actuarial survival rate, including in-hospital deaths, of 86.5% at 5 years [96]. In 90 TA patients also from Japan, with Aortic regurgitation Matsuura demonstrated a 15 year survival rate of 76% with surgical treatment [97].

Complications of both endovascular and surgical approaches include restenosis (75.7%), thrombosis (10%), bleeding (8.6%), and stroke (5.7%). In terms of post operative complications and re-stenosis, surgical treatment had better outcome compared to PTA in adult reports [80,98].

Despite the high restenosis rate and slight higher complication rate endovascular treatment may be an attractive option in children who are too small for surgery and to prevent the need for (and complications of) secondary procedures after the growth spurt in adolescence, especially when using synthetic grafts with no potential for growth. In developing countries the procedural simplicity and cost effectiveness of endovascular procedures is also attractive.

Conclusion

This review of childhood TA from the developing world perspective highlights some of the information available to us but also shows many areas where there are deficiencies in knowledge. Data from developing countries, where TA appears to be more prevalent are sparse. Where healthcare systems are under strain from lack of resources and communicable diseases such as HIV and TB, the accurate diagnosis of TA, is likely to be a major challenge. Indeed the imaging techniques required for the diagnosis of TA are completely inaccessible in many parts of the developing world. There is a need for better epidemiological data from developing countries to better assess the disease spectrum in different populations. The role of tuberculosis in TA in the developing world needs to be clarified. Biomarkers and clinical scores of disease activity need to be developed and validated in this setting. Therapeutic options, both surgical and medical, deserve further study to deliver affordable effective therapies that are accessible to patients in need.

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