Kawasaki disease (KD) is an acute systemic inflammatory illness that occurs predominately in children <5 years of age. The reported incidence varies widely depending on the ethnicity of the population and the method of case ascertainment. Recent reports would suggest the annual incidence is ~20 to 25 per 100,000 children <5 years of age in North America, with the highest reported incidence of 188 being in Japan, where the disease was first described in 1967.1 The illness is self-limited and of unknown cause, but is complicated by a systemic vasculitis with a predilection for small- to medium-sized arteries, particularly the coronary arteries. The majority of patients will have either transient coronary artery dilation or no coronary artery luminal changes as noted on echocardiography. Long-term prognosis for these patients is considered to be excellent. Coronary artery aneurysms occur in 25% of patients, but the prevalence is reduced to ~4% for patients treated with intravenous immunoglobulin infusion within 10 days of illness onset. Aneurysms are associated with an intense inflammatory cell infiltrate, destruction of the internal elastic lamina, and smooth muscle cell death. Coronary artery involvement is usually maximal within 6 to 8 weeks after the acute episode. Regression of aneurysms can occur primarily through myointimal proliferation, although the arterial structure and function remains abnormal,2 and there is an important ongoing risk of stenoses and occlusions.3 Long-term cardiology assessment and management is required, and some of these patients may require revascularization procedures or, rarely, cardiac transplantation. KD has become the most prevalent acquired cardiac disease in children in developed countries.

Although coronary artery complications are the predominant cause of morbidity and mortality, other cardiovascular abnormalities can occur. Valvulitis is a less prevalent complication, and there have been case reports of important long-term aortic and mitral valve dysfunction. Pericarditis occurs, and small pericardial effusions are often noted during the early course of the disease, but they resolve spontaneously without sequelae in nearly all patients. Myocarditis occurs, most frequently manifested as signs of diastolic dysfunction and myocardial thickening and more rarely as systolic dysfunction and cardiovascular collapse or ventricular dysrhythmias. These abnormalities resolve spontaneously, although systemic steroids are often given. There have been isolated reports of ongoing histological changes noted on biopsy specimens and pathological specimens, but cardiomyopathy has only been reported in the presence of important coronary artery involvement with myocardial ischemia or infarction. Aortic root dilation has been described in pediatric patients from baseline up to 1 year after diagnosis with KD, but the magnitude of change was in the order of 1 SD, with few having associated mild aortic valve regurgitation.4

In this issue of Circulation, Kitamura et al5 specifically describe their expert experience and excellent long-term outcomes for that subset of patients with KD who develop important stenoses or obstructions and who underwent surgical revascularization with bypass grafting. The primary purpose of revascularization is to salvage myocardium at risk of ischemia and infarction. Indications may include the presence of obstructions or important stenoses (>75% of lumen), previous myocardial infarction or the presence of ventricular dysfunction, and symptoms of ischemia or signs of ischemia noted on stress myocardial perfusion/functional imaging. Young children are predisposed to develop important collateral vessels, particularly in the presence of obstructions, and symptoms and signs of ischemia may be masked. Obstructions and stenoses most often occur at the inlet or outlet of an aneurysm. The decision to perform percutaneous coronary intervention (PCI) or bypass grafting may depend on the accessibility of the lesion to PCI, the total extent of involvement both proximal and distal to the target lesion, and the presence of obstructions and stenoses in other branches. Considerations regarding bypass grafting include growth potential of the graft relative to somatic growth, long-term patency, and factors that may influence it (such as the presence of competitive flow from the native vessel or collaterals, atherosclerosis), the presence of abnormal coronary artery structure and function at the site of anastomosis, and the need for possible future revascularization in other branches. Involvement of the graft vessel from the episode of KD is very unlikely. Kitamura et al5 have shown that bypass grafting can be performed in pediatric patients as young as 1 year of age, with no operative or hospital deaths, and a 25-year patient survival rate of 95%. Cardiac event-free survival at 25 years was 60%, with the majority of events being PCI or reoperation. Long-term patency rates for internal thoracic artery grafts were better than those for saphenous vein grafts, with no impact of the coronary artery branch or age of the patient at surgery.
PCI has been used to address restenoses in bypass grafts and as primary therapy in selected patients. These procedures are best performed by a team that includes both adult and pediatric interventional cardiologists. When these procedures are used as primary therapy, there should be no ostial lesion and no important ventricular dysfunction, and the stenosis should be relatively localized and not over a long segment. The time since the acute episode and the degree of lesion calcification guide which PCI technique is indicated, and intravascular ultrasound has proven useful to characterize lesions. Balloon angioplasty is useful if the procedure is performed earlier after the acute episode when the lesion has no or mild calcification. The creation of new aneurysms at the site of angioplasty is a concern. For older and larger patients, stent implantation is a useful adjunct, particularly at the entry and exit points of giant aneurysms. For lesions with severe calcification, rotational ablation is indicated and may be combined with stent implantation. Immediate results have been promising, short-term follow-up suggests a high rate of restenosis, and data regarding long-term outcomes are needed.

Cardiac transplantation has been performed rarely in the setting of KD. Cardiac transplantation is reserved for those patients with severe ventricular dysfunction and intratable arrhythmias, or those with ischemia but severe distal vessel disease not amenable to revascularization procedures. Outcomes have been good.

What the Adult Cardiologist May Expect
Adult cardiologists will increasingly become the cardiology care providers for adult patients with cardiovascular sequelae related to childhood KD. The majority of these patients will be those with known coronary artery aneurysms who have been assessed and managed by pediatric cardiologists. The adult cardiologist will be responsible for ongoing medical management, including anticoagulation, and surveillance and management of abnormalities of myocardial perfusion and function. There is an ongoing and constant risk of stenoses, particularly for aneurysms 6 mm or more in diameter. Concomitant with the risk of stenoses and obstructions is an ongoing risk of myocardial infarction, ventricular dysfunction, ventricular dysrhythmias, and sudden death. New aneurysms may rarely appear in patients with existing aneurysms, reflecting poststenotic dilation or the effects of superimposed atherosclerosis. Markers of early atherosclerosis are prevalent in patients with important coronary artery involvement. The clinical relevance of other noncoronary artery abnormalities into adulthood remains speculative and reports are rare, few with long-term follow-up or a known denominator.

An unknown proportion of adults will present with cardiovascular complications without a recognized history of having had KD, although the current literature is limited to case reports and small case series. The differential diagnosis for coronary artery aneurysms in a young adult should include KD, particularly if there is important coronary artery calcification and intima-media thickening consistent with arteriosclerosis. Recollection of a childhood illness with clinical features consistent with KD is useful, but often unlikely, given the young age at which the acute episode would have occurred.

The largest group of patients will be those with either transient coronary artery dilation or no coronary artery luminal changes as noted on echocardiography after acute KD in childhood. These patients are currently recommended to require no pharmacological therapy beyond 6 to 8 weeks after the acute episode, no invasive cardiologic testing, and ongoing cardiovascular risk factor assessment and counseling at 3- to 5-year intervals, which may be performed by the patient’s cardiologist or primary care provider. In case-control cross-sectional studies of small number of patients, subtle ongoing abnormalities have been variously and sometimes inconsistently reported. Relative to controls, these include increases in markers of inflammation, decreases in high-density lipoprotein, the presence of varying degrees of endothelial dysfunction in both the coronary and systemic arteries, decreases in myocardial blood flow reserve, increases in carotid intima-media thickness, decreases in arterial compliance and distensibility, increases in aortic root size, increases in myocardial fibrosis, and alterations in the coronary artery microvasculature. The clinical relevance of these findings is unknown for patients without important coronary artery involvement, although for patients with either persistent or regressed aneurysms, these findings are more marked and consistent and may indicate an increased risk of accelerated atherosclerosis, ventricular dysrhythmias, and ischemic cardiomyopathy. Graded attention to management of cardiovascular risk factors has been recommended. After 4 decades, there have been no signs of increased morbidity or mortality for these patients. Few longitudinal cohort studies have been performed, but are essential to determine whether patients are at increased risk for premature atherosclerotic cardiovascular disease, cardiomyopathy, or arrhythmias, regardless of their level of coronary artery involvement. A Japanese cohort with 6576 patients and up to 26 years of follow-up has shown that the standardized mortality ratio for those patients without coronary artery involvement is 0.71. For males but not females with cardiac sequelae, the standardized mortality ratio was elevated at 2.55.

The majority of patients with KD will be expected to survive into adulthood. Successful transition to adult care is an important issue. Outcomes must be tracked seamlessly into adulthood if ongoing concerns about prognosis are to be resolved. In the meantime, advocacy for healthy lifestyle and screening and management of cardiovascular risk factors for all patients is prudent and recommended.

Disclosures
None.

References

McCrindle Outcomes into Adulthood After Kawasaki Disease


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