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KAWASAKI PATIENTS WITH CORONARY ARTERY CALCIFICATIONS DETECTED BY ULTRAFAST CT SCAN: A POPULATION AT RISK FOR EARLY ATHEROSCLEROSIS

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Background: Kawasaki disease produces a vasculitis which may injure the coronary arteries and predispose these patients to early atherosclerosis. Previously, case reports have documented that Kawasaki patients may develop coronary calcifications and may die of sudden death many years after their acute illness. Ultrafast computer tomography (UCT) has been successful at detecting coronary calcifications in adults with atherosclerosis. The goal of this study is to show that UCT can be utilized as a non-invasive technique to identify Kawasaki patients at high risk for coronary disease and who would require long-term surveillance through adulthood.Methods and Results: Eighteen patients ages five to twenty-one years old with a history of Kawasaki disease were enrolled. Each patient had an UCT of the heart. There were four patients with calcifications noted. All of the four patients had: a previous history of an aneurysm, were at least five years from their acute illness, and had the calcification correlate to the previous site of aneursym formation. A calcium score was determined by the Agaston method for each calcification. The Mayo clinic guidelines for adult atherosclerosis were then used to correlate these scores with the risk of future coronary artery disease. All four patients were at moderate or greater risk of future coronary disease.Conclusion: This study indicates that UCT can be used as an effective non-invasive methodology in Kawasaki patients to successfully identify the high-risk patients predisposed to developing potential early atherosclerotic coronary artery disease.

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PERCUTANEOUS TRANSLUMINAL CORONARY ANGIOPLASTY IN KAWASAKI DISEASE; EFFICACY IN ANASTOMOTIC STENOSIS AFTER CORONARY ARTERY BYPASS GRAFTING

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Objectives. To evaluate the efficacy of percutaneous transluminal coronary angioplasty (PTCA) for anastomotic stenosis after coronary artery bypass grafting (CABG) in patients with Kawasaki disease (KD). Subjects and Methods. From September 1993 to April 2000, 8 boys with KD underwent PTCA for anastomotic stenosis in 9 lesions following CABG using the left internal thoracic artery (LITA) or the right internal thoracic artery (RITA). Progressive severe stenosis of grafts in the follow-up angiograms and some ischemic signs were regarded as indications for PTCA. Aspirin or cilostazol was given after CABG. Age at PTCA ranged from 4.2 to 16.7 years (median, 11.0), while it was performed from 0.1 to 5.6 years (median, 0.6) after the operation. Nifedipine had been given for 3 days before PTCA and nitroglycerin was administered intravenously prior to PTCA. The graft ostium was cannulated with 5 or 6 F guiding catheter and the dilating catheter passed across the lesion under biplane fluoroscopy. The balloon diameter ranged from 1.5 to 2.5 mm and the pressure of inflation ranged from 6 to 14 atm. Results. The balloon was successfully dilated at the lesion in all patients. During the procedure transient ischemic signs appeared on electrocardiogram in two patients. The stenosis rate decreased from 63 - 100 % (median, 90 %) to 0-40 % (median, 20%). All patients underwent the follow-up angiogram 3-14 months after PTCA. Although 6 of 8 were revealed no restenosis. One patient had a new stenosis at the distal portion of anastomosis. One had the occlusion of the graft. The last case underwent PTCA again.The follow-up angiogram after 3 months revealed no restenosis. Conclusion. PTCA is a feasible procedure to prevent occlusion of the grafts after CABG in patients with KD.

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IMPAIRMENT OF THE FIBRINOLYTIC SYSTEM IS PRESENT AND IS A MARKER FOR ENDOTHELIAL DYSFUNCTION IN ADOLESCENTS AFTER KAWASAKI DISEASE

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Impairment of the fibrinolytic system is one of the most sensitive markers of endothelial dysfunction, and a major risk factor for future cardiovascular disease in adults. Persistent endothelial dysfunction, which is an early pathophysiological event in atherogenesis, occurs in some patients following Kawasaki disease (KD). The aim of this study was to assess whether impaired fibrinolysis is present in long-term survivors of KD. The study included 42 children with a documented history of KD presenting without coronary lesions (n = 22), with resolved coronary aneurysms (n = 13), or with persistent giant aneurysms (n = 7), and 26 healthy age-matched teenagers as controls. Blood samples were collected from all patients and controls prior to and following venous occlusion (VO) stress testing, and assayed for tissue plasminogen activator (tPA), plasminogen activator inhibitor (PAI)-1, plasminogen, alpha2-antiplasmin (a2-AP), alpha2-macroglobulin (a2-M), D-Dimer, fibrinogen, and von Willebrand factor (vWF). Significantly decreased fibrinolytic activity following VO was detected in patients compared to controls due to decreased tPA antigen, and increased PAI-1 activity. In addition, patients had significantly increased plasma concentrations of plasminogen and fibrinogen, which were related to similar increases of a2-M compared to controls. Decreased fibrinolytic activity was found in patients with coronary aneurysms but also in those without coronary lesions. In summary, a decreased fibrinolytic activity reflects persistent endothelial damage following acute KD, potentially predisposing these patients to accelerated atherosclerosis and cardiovascular disease in early adult life.

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GIANT ANEURYSMS IN KAWASAKI DISEASE: IS OUTCOME AFFECTED BY ANTICOAGULATION ?

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Background: Kawasaki Disease (KD) has potentially serious cardiac complications including coronary artery aneurysms. Giant aneurysms (GAs) (diameter 0.8cm) increase the risk of thrombosis, and to reduce the ischemic risks, anticoagulation with warfarin is recommended, but its efficacy has not been studied. **Hypothesis:** Anticoagulation alters the outcome of patients with GAs. **Objectives:** To determine 1) If anticoagulation is cardioprotective for myocardial ischemia 2) Whether anticoagulation affects the size of GAs. **Method:** A retrospective cohort study of all KD patients who had a 2D echo at the Hospital for Sick Children between 05/90 and 04/00 were performed. **Results:** Twenty-two of 997 patients (2.2%) had GAs. Patients were divided into two groups: 1) Therapeutic anticoagulation with warfarin (with or without antiplatelet agents); 2) No anticoagulation (with or without antiplatelet agents). There were no significant demographic differences between the groups for sex distribution (11M:2F and 7M:2F), and age at diagnosis (5.2 vs. 3.8 yr). Mean duration of follow-up was significantly longer for the no anticoagulation group (6.9 vs. 13.3 yr, p=0.008) In the anticoagulation group, there were 22 GAs (1.7/pt), and 20 non-giant aneurysms (>0.4 cm <0.8 cm) (1.5/pt). In the no anticoagulation group there were 17 GAs (1.9/pt) and 13 non-giant aneurysms (1.4/pt). These numbers were not significantly different. Early ischemic events (<1 year) occurred in four patients: two patients had MIs on warfarin, one patient had an MI on no anticoagulation, and one patient had a coronary thrombosis and stroke at presentation with KD. Late ischemic events were monitored by stress thallium or sestamibi scanning. Of four patients in the anticoagulation group followed by scanning, at mean f/u 82 months there were no perfusion defects noted. In the anticoagulation group, at 126 months, only 1/9 patients had reversible defects, subsequently requiring CABG surgery. Regression of aneurysms (GAs and non-giant) was observed in both groups. GAs regressed a mean 22% vs 32% (p=0.24), and non-giant aneurysms regressed a mean of 28% vs 25% (p=0.74). Compliance with anticoagulation was good, with INRs in range 52% of the time. There were no major bleeding complications of anticoagulation, but most patients had minor bleeding (epistaxis, bruising). **Conclusions:** Early ischemic events occurred independent of anticoagulation, and late ischemic changes were rare. Regression of GAs was observed regardless of anticoagulation. No benefit for long-term anticoagulation was observed, but long term follow-up studies are needed to further evaluate the potential benefits of anticoagulation vs. its potential serious complications.

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LONG-TERM OUTCOME OF PATIENTS WITH KAWASAKI DISEASE

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Objectives; The purpose of this study is to clarify the long-term outcome of patients with Kawasaki disease(KD). Methods; We investigated the outcomes of the patients with KD who were examined in our institute and already reached eighteen years old by reviewing their clinical records. Results; 375 patients with KD(female/male; 140 / 235)reached eighteen years old, fifty-two of them are followed up regularly. Their ages range from 18 to 31 years old (median; 21years old). Age at onset of KD is 1.8 (median)years old(0.2～11.8 years old). Thirty-eight patients(10%) had coronary artery lesions on the first examination, Twelve(32 %) of them developed stenotic lesions, and ten of them(26 %) were regressed later. Three patients had aneurysmal lesions of another arteries in addition to coronary artery lesions, two of them had an aneurysm in iliac artery and one of them had in bilateral axillary arteries and abdominal aorta. Myocardial infarction occurred in five patients (1%). One patient suddenly died while walking at the age of eighteen. Epileptic attack occurred in two patients, one of them was resulted from the cerebral infarction at the onset. Acute leukemia developed later in two patients. Nineteen patients were managed with prophylactic anticoagulant medications (antiplatelet agents), and five of them also received a vasodilator. The medications were omitted in four male patients. Conclusions; KD patients with coronary artery lesions presented a variety of clinical course, therefore an appropriate management and a carefull follow-up are considered to be necessary.

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SYSTEMIC HETEROGENEITY OF ENDOTHELIAL FUNCTION AFTER KAWASAKI DISEASES

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Coronary arteritis associated with Kawasaki disease (KD) raises concern about the premature development of arteriosclerosis. Accordingly, we investigated endothelial function in the epicardial, resistance CAs, and femoral arteries (FAs) after KD during long-term observation. We assessed the responses of left epicardial and resistance CAs to serial intracoronary infusions of acetylcholine (final concentrations, 0.1 and 1 micromol/L) and nitroglycerin in subjects by using quantitative angiography and a Doppler flow wire system. Three age-matched groups were evaluated: 8 control subjects (group 1), 10 KD patients with normal left CA from the onset (group 2), and 8 KD patients with a persistent or regressed aneurysm in the left anterior descending CA (L AD) (group 3). Acetylcholine (1 micromol/L) changed the LAD area to 114.0+/-2.6%, 72.7+/-3.9% (P<.05 versus group 1), and 88.9+/-4.3% (P< .05 versus groups 1 and 2) of baseline in groups 1, 2, and 3, respectively, with a similar degree of increased coron ary blood flow in each group. Nitroglycerin increased the LAD area to 143.5+/-7.7%, 132.3+/-1.9%, and 120.8+/-5.6% (P< .05 versus group 1), respectively. Nextly, we evaluated the reactive hyperemia- or sublingual nitroglycerin-induced FA dilatation b y high-resolution ultrasound in two age-matched groups: 13 controls, and 13 KD patients with persistent or regressed aneurysms in 4 and normal CAs in 9 patients. There were no differences in the FA responses to reactive hyperemia or nitroglycerin betwee n the two groups. Results demonstrate a persistent endothelial dysfunction in the "uninvolved" epicardial but neither in resistance CAs nor in FAs after KD, suggesting systemic heterogeneity of endothelial function in this disorder.