ARTERIAL FUNCTION IN PREADOLESCENT CHILDREN FOLLOWING KAWASAKI DISEASE: A SYSTEMATIC REVIEW

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Background Kawasaki disease (KD) is a paediatric systemic vasculitis, which may alter arterial structure and function and predispose affected patients to long-term cardiovascular sequelae. Increased arterial stiffness is an independent predictor of cardiovascular morbidity and mortality and could be used as a biomarker of cardiovascular risk in KD patients.

Objectives To systematically review available literature in order to understand whether KD impacts arterial stiffness.

Methods This review was performed following PRISMA guidelines. PubMed was searched using the terms: ‘pulse wave velocity’ (PWV), ‘carotid intima-media thickness’ (cIMT), ‘arterial stiffness index’ (SIx), ‘flow-mediated dilation’ (FMD), ‘flow imaging’, ‘laser flow Doppler’, ‘venous plethysmography’, ‘cardi’ magnetic resonance imaging’, ‘aortic intima-media thickness’, ‘vascular ultrasound’ and ‘neonate’; ‘paediatric’, ‘infant’; ‘child’. Case reports, case series, reviews, commentaries, conference proceedings, animal studies, articles not in English and articles with children >12 years old were excluded. Reference lists of relevant studies were searched for additional eligible studies. Studies assessing arterial structure and function in children affected by KD were included.

Results 12/1087 studies identified were included. Brachio-radial (brPWV) and aortic PWV (aPWV) were performed as measures of arterial stiffness in four studies, using techniques including echocardiography, photoplethysmography and magnetic resonance imaging. Five studies assessed cIMT and four studies measured flow-mediated dilation (FMD), as arterial wall structure and endothelial dysfunction can both affect arterial stiffness. Eight studies assessed biophysical properties of the aorta relating to stiffness (such as Sx and distensibility).

brPWV and aPWV were significantly higher in children with KD than healthy controls in all studies. This was independent of the presence of coronary artery lesions (CALs) in all but one study, which suggested a dose-response relationship between coronary involvement and brPWV. cIMT and Sx were also increased in children with KD except in one study. Children with KD had lower aortic distensibility than controls, and this was even lower in children with CALs compared to those without (0.6±0.2 vs 0.9±0.3 cm²/dyne x 10⁻⁴, p=0.001).

All four studies showed FMD was impaired in children with KD, and most impaired in children with CALs or longer disease duration. Impaired FMD was suggestive of a genotype-modulating effect on the pro-inflammatory state that may mediate the increased risk of developing higher arterial stiffness in KD.

Conclusions Clearly, arterial stiffness measurements are increased in patients with KD, though the effect of presence of CALs on stiffness is yet to be conclusively determined. Variability between studies can be explained by the wide variety of techniques, patient demographics, and time from disease onset studied. An improved understanding of the pathophysiological mechanisms behind increased arterial stiffness may allow more targeted interventions to mitigate future cardiovascular risk. We recommend long-term cardiovascular monitoring of patients with KD as well as further longitudinal observational and interventional studies aimed at better understanding and offsetting the long-term arterial sequelae of KD.