Monitoring of vascular health in children at risk for atherosclerosis

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7.2.1 Study design

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7.3.1 Study design

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<table>
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<th>Abbreviation</th>
<th>Description</th>
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<tbody>
<tr>
<td>aIMT</td>
<td>Aortic intima media thickness</td>
</tr>
<tr>
<td>BMI</td>
<td>Body mass index</td>
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<tr>
<td>CAH</td>
<td>Congenital adrenal hyperplasia</td>
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<tr>
<td>CGMS</td>
<td>Continuous glucose monitoring system</td>
</tr>
<tr>
<td>cIMT</td>
<td>Carotid intima media thickness</td>
</tr>
<tr>
<td>CONGA</td>
<td>Continuous overall net glycaemic action</td>
</tr>
<tr>
<td>CSII</td>
<td>Continuous subcutaneous insulin infusion</td>
</tr>
<tr>
<td>DCCT</td>
<td>Diabetes Control and Complications Trial</td>
</tr>
<tr>
<td>ECG</td>
<td>Electrocardiogram</td>
</tr>
<tr>
<td>EDIC</td>
<td>Epidemiology of Diabetes Interventions and</td>
</tr>
<tr>
<td></td>
<td>Complications Trial</td>
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<tr>
<td>FMD</td>
<td>Flow mediated dilatation</td>
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<td>GTN</td>
<td>Glyceryl trinitrate induced dilatation</td>
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<tr>
<td>HDL</td>
<td>High density lipoprotein</td>
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<tr>
<td>HOMA-IR</td>
<td>Homeostasis model of assessment of insulin</td>
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<tr>
<td></td>
<td>resistance</td>
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<tr>
<td>Hs-CRP</td>
<td>High sensitive C-reactive protein</td>
</tr>
<tr>
<td>ICC</td>
<td>Intra-class correlation coefficient</td>
</tr>
<tr>
<td>LDL</td>
<td>Low density lipoprotein</td>
</tr>
<tr>
<td>LGBI</td>
<td>Low glucose blood index</td>
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<tr>
<td>MAGE</td>
<td>Mean of glycaemic excursions</td>
</tr>
<tr>
<td>Abbreviation</td>
<td>Definition</td>
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<tr>
<td>-------------</td>
<td>------------------------------------</td>
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<tr>
<td>MDI</td>
<td>Multiple daily injections</td>
</tr>
<tr>
<td>MODD</td>
<td>Mean of daily difference</td>
</tr>
<tr>
<td>NO</td>
<td>Nitric oxide</td>
</tr>
<tr>
<td>PCOS</td>
<td>Polycystic ovarian syndrome</td>
</tr>
<tr>
<td>ROS</td>
<td>Reactive oxygen species</td>
</tr>
<tr>
<td>T1D</td>
<td>Type 1 diabetes</td>
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<tr>
<td>T2D</td>
<td>Type 2 diabetes</td>
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ABSTRACT

Adult cardiovascular disease has its origins in childhood, and adolescence is a critical period in determining lifetime risk. Early changes in arterial structure and function measured non-invasively have prognostic significance. Assessment of vascular structure and function provide an opportunity to test intervention strategies at an age when vascular damage is potentially reversible. Understanding the relative sensitivity of these markers of vascular damage is essential in identifying children at risk and enabling evaluation of clinical and public health interventions.

In a cross-sectional study, aortic and carotid intima media thickness were assessed in 66 children with type 1 diabetes and 32 healthy children. Aortic intima media thickness (aIMT) was significantly greater in the children with type 1 diabetes and related to age, glycosolated haemoglobin and low-density lipoprotein cholesterol concentrations. In contrast, there was no significant difference in carotid intima media thickness between groups, suggesting that aIMT is an earlier marker of subclinical atherosclerosis in children with type 1 diabetes.

An interventional trial of 22 children with type 1 diabetes was performed to evaluate whether reduction in glucose variability with initiation of continuous subcutaneous insulin infusion (CSII) therapy would improve vascular function. At 3 weeks post commencement of CSII, vascular function improved associated with a reduction in glucose variability; however the effects on vascular function over 6 to 12 months were not sustained, with deterioration of glycaemic control.

Finally, in a cross-sectional study, vascular function and structure was assessed in 14 children with congenital adrenal hyperplasia (CAH), a relatively novel
patient population, whose risk for atherosclerosis has not been previously investigated. The results from the children with CAH were compared to 28 obese and 53 healthy controls. The children with CAH had evidence of vascular dysfunction, comparable to the obese cohort, despite having a lower body mass index.

It was concluded that use of non-invasive ultrasound markers of preclinical atherosclerosis can allow early detection of changes in vascular structure in children at known risk for future atherosclerosis, identify novel groups of children with medical conditions not previously recognized to have future cardiovascular risk, and is a valuable tool that can be used to test interventions in a timely manner.
DECLARATION

I certify that this work contains no material which has been accepted for the award of any other degree of diploma in any university or other tertiary institution and, to the best of my knowledge and belief, contains no material previously published or written by another person, except where due reference has been made in the text. In addition, I certify that no part of this work will, in the future, be used in a submission for any other degree of diploma in any university or other tertiary institution without the prior approval of the University of Adelaide and where applicable, any partner institution responsible for the joint-award of this degree.

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Jennifer Harrington  
Date

Jennifer Harrington, January 2014
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The children, adolescents and families who so generously participated in the studies, without whose time and commitment, the research would not have been possible

Finally to my family, who continue to provide me with the love and support for me to pursue my aspirations.