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Carotid artery intimal medial thickness, brachial artery flow-mediated vasodilation and cardiovascular risk factors in diabetic and non-diabetic indigenous Australians

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Abstract

Background: Indigenous Australians are at high risk for cardiovascular disease and type 2 diabetes. Carotid artery intimal medial thickness (CIMT) and brachial artery flow-mediated vasodilation (FMD) are ultrasound imaging based surrogate markers of cardiovascular risk. This study examines the relative contributions of traditional cardiovascular risk factors on CIMT and FMD in adult Indigenous Australians with and without type 2 diabetes mellitus.
Method: One hundred and nineteen Indigenous Australians were recruited. Physical and biochemical markers of cardiovascular risk, together with CIMT and FMD were meausred for all subjects.
Results: Fifty-three Indigenous Australians subjects (45%) had type 2 diabetes mellitus. There was a significantly greater mean CIMT in diabetic versus non-diabetic subjects ($p = 0.049$). In the non-diabetic group with non-parametric analyses, there were significant correlations between CIMT and: age ($r = 0.64$, $p < 0.001$), systolic blood pressure ($r = 0.47$, $p < 0.001$) and non-smokers ($r = -0.30$, $p = 0.018$). In the diabetic group, non-parametric analysis showed correlations between CIMT, age ($r = 0.36$, $p = 0.009$) and duration of diabetes ($r = 0.30$, $p = 0.035$) only. Adjusting for age, sex, smoking and history of cardiovascular disease, Hb_{A1c} became the sole significant correlate of CIMT ($r = 0.35$, $p = 0.01$) in the diabetic group. In non-parametric analysis, age was the sole significant correlate of FMD ($r = -0.31$, $p = 0.013$), and only in non-diabetic subjects. Linear regression analysis showed significant associations between CIMT and age ($t = 4.6$, $p < 0.001$), systolic blood pressure ($t = 2.6$, $p = 0.010$) and Hb_{A1c} ($t = 2.6$, $p = 0.012$), smoking ($t = 2.1$, $p = 0.04$) and fasting LDL-cholesterol ($t = 2.1$, $p = 0.04$). There were no significant associations between FMD and examined cardiovascular risk factors with linear regression analysis
Conclusions: CIMT appears to be a useful surrogate marker of cardiovascular risk in this sample of Indigenous Australian subjects, correlating better than FMD with established cardiovascular risk factors. A lifestyle intervention programme may alleviate the burden of cardiovascular disease in Indigenous Australians by reducing central obesity, lowering blood pressure, correcting dyslipidaemia and improving glycaemic control. CIMT may prove to be a useful tool to assess efficacy of such an intervention programme.

Keywords: Type 2 diabetes mellitus; Carotid artery intimal medial thickness; Indigenous Australians; Flow-mediated vasodilation; Cardiovascular risk

1. Introduction

Indigenous Australians have a life expectancy 16–20 years less than that of the general Australian population

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[1]. In concordance with the general Australian population, cardiovascular death is the single greatest contributor to mortality among Indigenous Australians, however, the majority of excess death in Indigenous Australians is also accounted for by cardiovascular causes [2]. The high prevalence of type 2 diabetes, obesity, and dyslipidaemia coupled with generally poor control of disease are major contributing factors to increased mortality and morbidity in this population [3]. To compound this problem, there is a growing body of evidence that genetic predisposition is a substantial contributor to cardiovascular disease among Indigenous Australians [4]. Identifying indices of cardiovascular risk other than traditional risk factors in the high risk Indigenous Australian population is therefore of importance, especially in risk stratification for planning primary prevention and monitoring of management efficacy. We investigate the use of carotid artery intimal medial thickness (CIMT) and brachial artery flow-mediated vasodilation (FMD) as non-invasive indices of cardiovascular risk by correlating them to established traditional markers of cardiovascular risk.

High-resolution carotid artery ultrasonography has been gaining acceptance as a non-invasive measure of preclinical atherosclerosis since the late 1980s [5]. CIMT has been correlated with traditional markers of cardiovascular risk such as total cholesterol, type 2 diabetes mellitus and age [6]. CIMT is a strong predictor of future cardiovascular events, in particular myocardial infarction and stroke [7]. CIMT is also correlated with the extent of atherosclerosis in other arterial beds and prevalence of cardiovascular disease in the general population [8].

On the other hand, endothelial dysfunction has been postulated to be the key precursor of atherosclerosis. Atherosclerosis has been demonstrated in asymptomatic young adults exposed to risk factors, e.g., smoking, and its amelioration may have important prognostic implications in cardiovascular disease [9,10]. Non-invasive testing of endothelial function is based on measuring the degree of hyperaemia in response to shear stress caused by blood flow after an occlusive cuff is released off the investigated artery [11]. This flow-mediated vasodilation has been shown to reflect endothelial dependent blood flow in the coronary arteries, and is regulated by the endothelial nitric oxide (eNOS) system [12,13].

In this paper, conventional cardiovascular risk factors such as smoking, diabetes, glycaemic control, past history of cardiovascular disease, dyslipidaemia, hyperhomocysteinaemia and central adiposity will be contrasted with the imaging based surrogate markers of cardiovascular disease, CIMT and FMD. While several studies have examined CIMT in diabetics of varied ethnicity [14–16], to our knowledge, this is the first study of its kind examining the use of both CIMT and FMD in Indigenous Australians. The aim of our study is to assess the relevance of CIMT and FMD in the Indigenous Australian population, by correlating them to established cardiovascular risk factors.

2. Methods

2.1. Subjects and study design

The Australian Families Against Diabetes programme was conducted by our research group in three Indigenous Australian communities across south-east Queensland in 1997 with the aim of identifying the genetic component of type 2 diabetes mellitus in the examined population [17]. It included screening for diabetes, central obesity, hypertension, dyslipidaemia, smoking and hyperhomocysteinaemia. As such, these indigenous communities were well defined clinically and our ongoing association with them presented us with a unique opportunity to investigate their predisposition to cardiovascular disease.

Indigenous Australian participants of the Australian Families Against Diabetes programme over 20 years of age and living on North Stradbroke Island were invited to participate in this study. Participants were divided into groups based on fasting glycaemic status according to WHO criteria [18]. Individuals were considered diabetic if they met one of the following criteria: (i) previously diagnosed type 2 diabetes on medical therapy or (ii) fasting plasma glucose $\geq$7.0 mmol/l. Participants not previously diagnosed with type 2 diabetes mellitus and with a fasting plasma glucose level $\leq$6.0 mmol/l were classified as non-diabetics. Participants with a fasting plasma glucose reading >6 and <7 mmol/l were classified as impaired fasting glucose.

One hundred and nineteen Indigenous Australian participants were recruited in total. Sixty-six of these subjects were non-diabetics, 53 had type 2 diabetes mellitus. None of the participants were classified as having impaired fasting glucose. The study was approved by the ethical review boards of the indigenous community and the Princess Alexandra Hospital. All participants were required to provide written informed consent for this study.

2.2. Clinical and biochemical data

The baseline measurements included a medical history, physical examination and laboratory testing. Particular attention was paid to the presence of diabetes mellitus, past history of stroke or coronary heart disease and smoking. Presence of cardiovascular disease in participants was defined as a historical presence of stroke, angina or myocardial infarction or peripheral vascular disease. Validation of clinical history was through examination of charts in the local community health centre.

Physical parameters recorded included: body mass index (BMI), waist to hip circumference ratio (WHR), systolic blood pressure (SBP) and diastolic blood pressure (DBP). Body mass index was defined as weight (kg) divided by height (m) [2], waist circumference was measured at the midpoint between the iliac crest and lowest ribs and hip circumference was recorded around the point of maximum protuberance of the buttocks. Blood pressure was measured using an