THE ASSOCIATION OF THE INTIMA-MEDIA THICKNESS OF COMMON CAROTID ARTERY WITH CORONARY ARTERY DISEASE

By

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DEDICATION

To my wife who is always by my side and support my.

To my lovely son.

To my parents who provide me blessing and support.

To my father and mother in low who give me encouragement and blessing.

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ABBREVIATIONS

CAD	Coronary artery disease
1CAD	one vessel CAD
2CAD	two vessels CAD
3CAD	three vessels CAD
COROS	coronary angiography finding
CIMT	Intima media thickness of the carotid artery
DM	Diabetes mellitus
HDL	High density lipoprotein
IMT	Intima media thickness
LDL	Low-density lipoprotein
LDL-C	Low-density lipoprotein cholesterol

ABSTRAK

Tajuk: Menentukan kaitan diantara ketebalan intima-media daripada arteri "common karotid" dengan penyakit arteri koronori.

Latarbelakang: Penyakit arteri koronori berlaku kerana saluran darah arteri koronori yang sempit akibat penyakit "atherosklerosis". Penyakit arteri koronori mempunyai pelbagai ciri klinikal bermula dari keadaan praklinikal yang tiada tanda penyakit kepada keadaan lemah jantung yang mendadak. Penyakit arteri koronori adalah salah satu keaadan yang kerap mengakibatkan penyakit berterusan dan kematian. Penyakit arteri koronori merupakan penyakit yang mengakibatkan kematian yang terbanyak di Malaysia. Arteri-arteri "common karotid" dan arteri-arteri koronori mempunyai faktor-faktor risiko yang sama. Ini menunjukkan bahawa penyakit "atherosklerosis" boleh menentukan keaadaan arteri-arteri koronori pada seseorang individu dengan memeriksa dinding arteri karotid melalui "ultrasound B-mode , kuasa resolusi tinggi". Untuk mengukur arteri karotid "intima media". Untuk menentukan hubung kait diantara arteri "common karotid" dan arteri-arteri koronori, kajian ini mengharapkan indikasi mengenai individu yang mempunyai penyakit lemah jantung atau tidak boleh di tentukan. Kajian ini juga mengharap boleh mengelakkan atau menyokong daripada kemungkinan prosedur " koronori angiografi" dilaksanakan kepada seseorang individu.

Objektif: Kajian ini menentukan kaitan diantara ketebalan intima-media daripada arteri "common karotid" dengan penyakit arteri koronori. Kajian ini mengharapkan ketebalan intima-media daripada "common karotid" boleh digunakan sebagai suatu penentuan kepada penyakit lemah jantung.

Kaedah dan Bahan: "Ultrasound B-mode, resolusi tinggi" pada kedua-dua arteri "common karotid" dilakukan kepada 113 pesakit lelaki yang disyaki mempunyai penyakit lemah jantung dengan mungukur ketebalan "intima-media " masing-masing. Ketebalan intima-media daripada "arteri common karotid" diukur tiga kali 1 cm dari hujung "common karotid" masing- masing .Purata keenam-enam ukuran akan diambil sebagai purata ketebalan intima-media daripada kedua-dua "arteri common karotid". Prosedur ini disusuli dengan prosedur "koronori angiografi" kemudian hari. Maklumat mengenai risiko penyakit lemah jantung seperti umur, "Indeks body mass" , tekanan darah tinggi, kencing manis, kolesterol tinggi dan perokok diperolehi . Kaitan diantara purata ketebalan intima-media daripada arteri "common karotid" dengan keputusan "koronori angiografi" dianalisa menggunakan kaeadah "statistik"

Keputusan: Didapati bahawa ketebalan intima-media daripada arteri "common karotid" menunjukkan ukuran lebih tebal untuk individu yang mempunyai penyakit lemah jantung yang disah melalui prosedur "koronori angiografi" berbanding individu yang mempunyai ketebalan intima-media daripada arteri "common karotid" yang normal (p –value < 0.001) dan ukuran adalah lebih tinggi untuk individu yang mempunyai penyakit lemah jantung yang lebih teruk.(p-value < 0.001).Purata ketebalan intima-media daripada arteri

"common karotid" yang tiada penyakit lemah jantung adalah 0.72mm, yang mempunyai satu saluran darah koronori tersumbat adalah 0.87mm, yang mempunyai dua saluran koronori tersumbat adalah 0.93mm dan yang mempunyai tiga saluran darah tersumbat adalah 1.1mm. Sensitiviti dan specificiti untuk ketebalan intima-media daripada arteri "common karotid" adalah 81.3% dan 81.8% masing-masing. PPV dan NPV ukuran ini adalah 94.9% dan 51.5% masing-masing. Dalam kajian ini, kaitan yang " significant" diperolehi jika dibandingkan dengan umur, perokok, kencing manis dan kolesterol tinggi dan penyakit lemah jantung. Kaitan "significant" juga diperolehi diantara umur, perokok , kencing manis , dan ketebalan intima-media daripada arteri "common karotid" yang lebih tinggi.

Kesimpulan: Keputusan kajian ini menunjukkan bahawa " ultrasound B-mode, resolusi tinggi" boleh digunakan sebagai prosedur awal untuk mengukur ketebalan intima-media daripada arteri "common karotid" dan boleh menentukan samaada seseorang individu mempunayai penyakit lemah jantung atau tidak. Oleh kerana itu, prosedur ini boleh digunakan sebagai prosedur awal untuk mengesan penyakit lemah jantung yang tiada faktor risiko lemah jantung atau inidividu yang tiada ciri-ciri lemah jantung tetapi mempunyai faktor risiko lemah jantung. Individu yang mempunyai ketebalan intima-media daripada arteri "common karotid" yang tinggi boeh di syorkan untuk menjalani prosedur " koronori angiografi"

ABSTRACT

Topic: The association between intima-media thickness of the common carotid artery with coronary artery disease.

Background: Coronary artery disease (CAD) occurs due to coronary artery stenosis secondary to atherosclerosis. CAD presents differently ranges from silent preclinical stage to sudden acute myocardial infraction or sudden death. CAD is one of the most common diseases in the world and in Malaysia it is considered the number one killer. Common carotid arteries provide a "window" to the coronary arteries as both have similar risk factors. Thus, carotid atherosclerosis provide a window to the degree of coronary atherosclerosis in an individual by examining the carotid artery wall using a high-resolution B-mode ultrasound transducer to measure the carotid IMT (CIMT).

Objectives: 1- To demonstrate if there is any association between the increase in the CIMT and CAD. 2. To study whether CIMT can be used as a surrogate marker of CAD.

Methodology: High resolution B mode ultrasound examination of both common carotid arteries was performed on 113 male patients with suspected CAD. CIMT were measured three times from the distal 1 cm of each common carotid artery. Thereafter, the coronary angiography was done on the next day. Data about the traditional risk factors of CAD as age, body mass index (BMI), hypertension, diabetes mellitus, hyperlipidaemia and smoking were collected.

Results: It was found that CIMT was significantly higher in patients with CAD confirmed angiographically than in patients with normal coronary arteries (p-value < 0.001) and CIMT values were higher in patients with advanced CAD (three vessels CAD compared with one and two vessels CAD) (p-value < 0.001). The mean CIMT in patients without CAD was 0.72mm, in one vessel CAD was 0.87mm, in two vessels CAD was 0.93 mm and in three vessels CAD was 1.1mm. The sensitivity and specificity of CIMT were 81.3% and 81.8% respectively while PPV and NPV came out to be 94.9% and 51.5% respectively. In this study, the cardiovascular risk factors and their relation to CAD and CIMT revealed a significant association between age, smoking, DM and hyperlipidaemia with CAD and significant association was found between age, smoking and DM with increased CIMT (with p-value < 0.05).

Conclusion: The results of this study demonstrated that CIMT was significantly higher in patients with CAD especially in patients with advanced CAD. High resolution B-mode ultrasound measurement of CIMT can be used clinically as screening tool for early detection of patients with suspected CAD with no history of myocardial infarction or patients who are free of symptoms but with a number of cardiovascular risk factors.

SECTION 1

Introduction

1.0 Introduction

Atherosclerosis is a disease of large and medium-sized muscular arteries and is characterized by endothelial dysfunction, vascular inflammation, and the buildup of lipids, cholesterol, calcium, and cellular debris within the intima of the vessel wall. This buildup results in plaque formation, vascular remodeling, acute and chronic luminal obstruction, abnormalities of blood flow and diminished oxygen supply to target organs (Brain and Chowdhury, 2006).

Atherosclerosis is an evolving, progressive arterial disease that in earliest forms is present in young persons. 100% of subjects aged 25-34 years from autopsy study showed fatty streaks and fibrous plaques in the distal portion of the common carotid artery and 20% had calcified plaques. In older populations, there is a large number of subjects who have asymptomatic atherosclerosis. In the cardiovascular health study, 31% of adults at least 65 years of age had evidence of clinical cardiovascular disease and a further 37% of adults had subclinical cardiovascular disease. Interventions before the development of clinical disease may be indicated in these patients (Milan Halenka, 1999).

Ultrasonographic assessment of the peripheral arteries has evolved as a promising technique for non-invasive evaluation of atherosclerosis. B-mode ultrasound enables non-invasive, direct visualisation of the arterial wall. The intima media thickness of the carotid artery (CIMT) is a reliable marker of atherosclerotic burden. Furthermore, it

demonstrates greater sensitivity in detecting early atherosclerosis compared with angiography (Bots and Grobbee, 2002). Intima-media thickness of the carotid artery has been shown to be related to coronary risk factors in epidemiological and cross-sectional studies. In autopsy studies, a close relationship between carotid and coronary atherosclerosis has been reported (Held et al, 2001). The association between intima-media thickness of peripheral arteries and coronary artery disease are not well studied. The results regarding association between carotid intima-media thickness and the severity of coronary artery disease on coronary angiograms are conflicting. It is unsure whether the ultrasonographic changes due to atherosclerosis in peripheral arteries are good surrogate markers for coronary artery disease. Therefore, this association needs further investigation.

The carotid arteries may provide a "window" to the coronary arteries as both have similar risk factors. Therefore, carotid atherosclerosis could provide a window to the degree of coronary atherosclerosis by examining the carotid artery wall using a high-resolution B-mode ultrasound transducer to measure the carotid intima-media thickness (CIMT). Angiography is currently the gold standard technique for detecting coronary atherosclerosis by visualization of vessel stenosis. Stenosis, however, reflects an advanced stage of atherosclerosis, whereas early atherosclerosis progression cannot be reliably detected using angiography. Furthermore, due to the invasive nature of the procedure, high cost, morbidity and mortality risks and radiation exposure, it cannot be used as a coronary artery disease (CAD) screening tool and for tracking the progression of disease in a symptomatic subjects and hence alternative techniques have been sought.

These include B-mode (two-dimensional) ultrasound, magnetic resonance imaging and electron beam computed tomography.

The aim of this study is to investigate the association between common carotid intima-media thickness (CIMT) and the extent and severity of CAD and also to evaluate whether CIMT is a strong or weak predictive tool of coronary atherosclerosis. By evaluating this association, it will be of help to predict the patients with CAD from those without CAD. Consequently, this will be of help to avoid or support the indication of doing an invasive coronary angiography. Last but not least, the American Heart Association (AHA) Prevention Conference V, recommended CIMT scanning for patients who are over 45 years old and who require further clarification about their coronary heart disease risk (Sidney et al, 2000).

SECTION 2

Literature Review

2.0 LITERATURE REVIEW

2.1 Atherosclerosis

2.1.1 Definition of Atherosclerosis

Atherosclerosis is a disease of large and medium-sized arteries such as carotid, femoral, renal and coronary arteries. Atherosclerosis results in thickening or hardening of the arterial walls which is formed by a combination of damage to the endothelial lining, the deposition and accumulation of low-density lipoprotein (LDL) cholesterol and the development of atherosclerotic plaques within the walls, which advanced in size gradually over time and narrowed the vessel lumen (Rogers et al, 1997; Tegos et al, 2001 and Mathur, 2002). This process develops over many years, eventually causing the complete obstruction of the blood flow if left untreated (Davidson, 2000; Mathur, 2002 and Fox, 2002). Coronary artery disease (CAD) is a disease of the coronary artery wall where the blood supply to the heart muscle is partially or completely blocked, most commonly caused by atherosclerosis (Jamrozik, 2001). Other non-coronary manifestations of atherosclerosis disease include stroke, peripheral vascular disease and aortic aneurysm.

2.1.2 Anatomy of Arterial Wall

Arterial wall consist of three layers:

i- Tunica intima is the innermost layer made of endothelial lining (squamous cell) and associated connective tissue. Beneath the connective tissue, the internal elastic lamina separates the tunica intima from the tunica media.

ii- Tunica media is formed by a layer of circumferential smooth muscle and variable amounts of connective tissue. A second layer of elastic fibers, the external elastic lamina, is located beneath the smooth muscle. It separates the tunica media from the tunica adventitia.

iii- Tunica adventitia consist mainly of connective tissue fibers. The tunica adventitia blends with the connective tissue surrounding the vessel. (School of Anatomy and Human Biology: http://www.ucc.ie/bluehist/CorePages/Vascular/Vascular.htm, 30 JUN 2007)

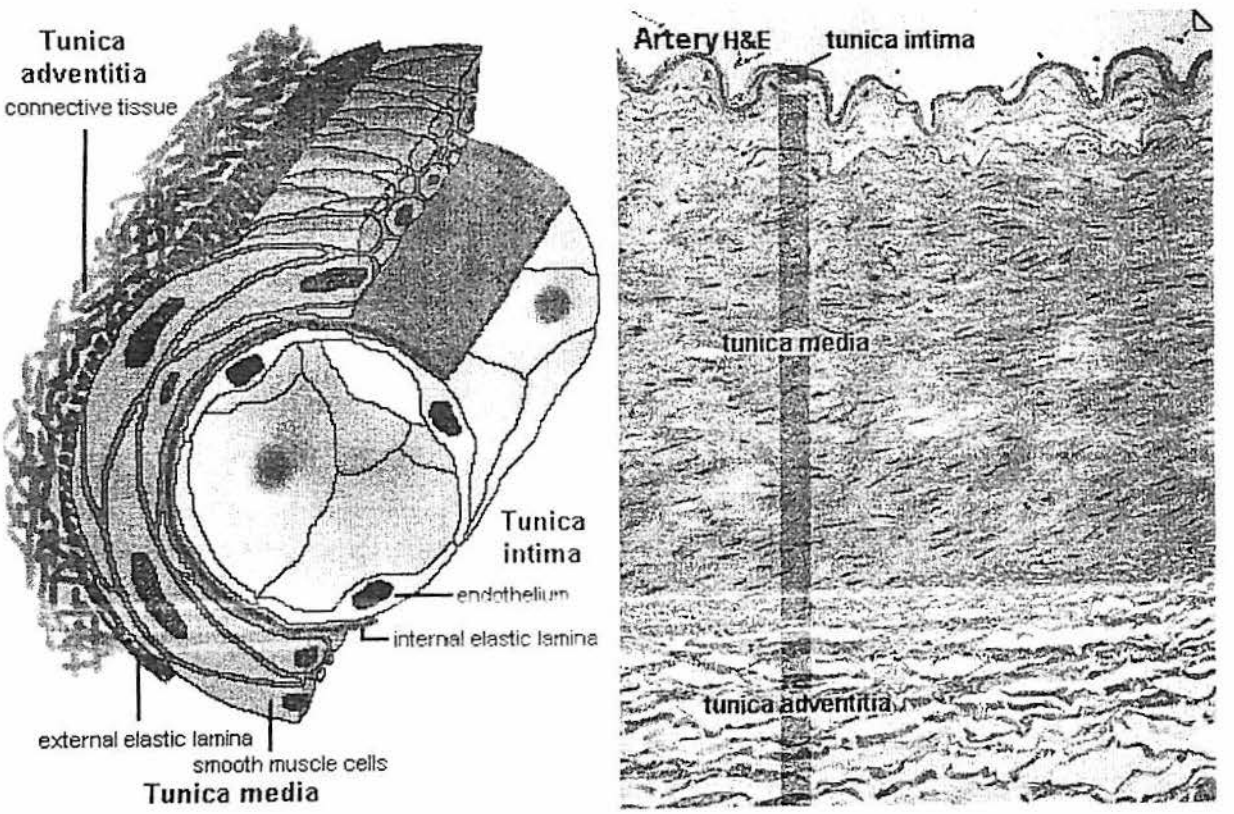

Figure 2.1 Histological anatomy demonstrates the three layers of the arterial wall.