Clinical Research

Need for surveillance of concomitant peripheral artery disease in patients with coronary disease: results of the AGATHA survey in Malaysia

Kui Hian Sim, 1 Kok Han Chee, 2 Inderjit Singh, 3 Choon Kiat Ang, 1 Houng Bang Liew, 1 Kim Heung Tan, 2 Omar Ismail 3

1 Department of Cardiology, Sarawak General Hospital, Sarawak, Malaysia
2 Department of Cardiology, Universiti Malaya Medical Centre, Petaling Jaya, Malaysia
3 Department of Cardiology, Penang General Hospital, Penang, Malaysia

Background For patients with cardiovascular disease (CVD), co-existence of peripheral artery disease (PAD) predicts increased mortality, and such patients are also more likely to benefit from aggressive therapy. Surveillance of PAD is often neglected at health clinics. Our aim is to highlight the importance and ease of surveillance of PAD in patients with CVD. Objective To determine the prevalence of symptomatic and asymptomatic PAD in a Malaysian patient population with documented CVD. Methods and Results A total of 393 subjects with established CVD were recruited from three centres (85 women and 308 men), as part of a larger international (AGATHA) survey. PAD, determined by presence of claudicant symptoms on interview and/or abnormal ankle-brachial index (ABI) score of less than 0.9, was present in 21.4% of patients - of whom 64% were asymptomatic. Abnormal ABI is associated with higher systolic blood pressure and number of arterial beds affected. Conclusions Concomitant PAD is prevalent among CVD patients in Malaysia. ABI screening is simple and yields a high proportion of patients with extensive atherosclerosis who may require more aggressive atherosclerotic risk management.(J Geriatr Cardiol 2007;4:195-199.)

Key words arteriosclerosis; atherothrombosis; Malaysia; cardiovascular diseases; epidemiologic factors; ankle-brachial index; peripheral arterial disease

Introduction

Coronary artery disease (CAD) and cerebrovascular disease (CBVD) account for nearly a third of total deaths worldwide.1,2 These diseases share a common underlying pathological process and are part of a spectrum of cardiovascular disease (CVD) that begins with atheroma formation, with or without rupture, leading on to acute thrombosis and resultant vascular luminal stenosis or occlusion. Clinically the acute thrombosis manifests as transient ischemic attacks (TIAs), unstable angina, stroke and myocardial infarction (MI).

Atherosclerosis is also a generalized and extensive vascular disease that may affect concurrently the coronary, cerebral and peripheral arterial beds to varying degrees. In the CAPRIE (Clopidogrel versus Aspirin in Patients at Risk of Ischaemic Events) trial, 26% of patients had at least two arterial beds involved.3 Furthermore, the risk of recurrent atherothrombotic events (whether in the same or separate arterial bed) in patients who survive their first episode is also increased many-fold. Between 16% and 24% of MI patients will suffer a stroke or TIA within a 10-year period, while 25% to 45% of stroke patients will develop CAD in the same period.4-6

With predisposing factors to atherosclerosis on the rise7-9 and incidence of first MI or CVD becoming more common and occurring at younger age, it is important from both a public health perspective to identify and treat at-risk patients early and optimally.10 While many patients can be assured of medical attention to CAD, they are less often screened for presence of peripheral artery disease (PAD).11 Hence the true prevalence of PAD, symptomatic and asymptomatic, in the general population and in high-risk established atherosclerotic disease patient groups is unknown.12 This is also true of Malaysia where, until now, there have been only a few papers on the prevalence of PAD and all were from single-centre studies.13

The objective of this multi-centre survey is to determine the prevalence of concomitant PAD among patients with established CAD in Malaysia by a simple bed-side measurement of ankle brachial index (ABI). We also compared the characteristics and ABI among patients who had
one, two or more arterial beds affected. This project was conducted as part of an international cross-sectional survey of patients with, or at risk of, atherothrombosis known as the AGATHA (A Global ATHerothrombosis Assessment) Study.14 We hope to highlight the need and ease of checking for PAD in health clinics through the findings of this paper.

Methods

Study population

The AGATHA study surveyed 8891 patients from 482 investigators in 24 countries. General practitioners, angiologists, cardiologists, neurologists, diabetologists, internists and vascular surgeons acted as referral agents. In Malaysia, 400 patients from three sites were enrolled consecutively from April to October 2002 with cardiologists and cardiac clinics as the referral source. Patients participated in only one study visit, without subsequent follow-up.

Patients were eligible for inclusion in the PAD survey if they had previous or current atherothrombotic symptoms, defined as prior ischemic stroke or TIA, prior MI, or history of stable or unstable angina (n=393). Seven patients with high-risk factors and without documented atherosclerotic disease were excluded from this study. Other exclusions include cerebral disease of non-atherothrombotic origin or neurological signs and symptoms due to a non-ischaemic cause (such as neoplasm). Written informed consent was obtained from every subject, and the study was conducted in accordance with the principles of the Declaration of Helsinki.

Baseline examination

At each centre, patients were seen by the investigator and had their sex, age, race, any history of previous vascular events, any current cardio-vascular or claudicant symptoms, and any current medications recorded. Subjects were evaluated via physical examination (weight, height, BMI, heart rate and blood pressure) and clinical tests including an electrocardiogram (ECG) and measurement of ankle-brachial index (ABI).

Ankle brachial index measurement

ABI was measured using an identical Doppler ultrasound probe for all AGATHA sites – an ELITE 100R 5MHz vascular probe (Nicolet Vascular, USA). Training was provided to all participating sites before patient enrolment. The brachial systolic pressure was recorded in the antecubital fossa in both arms, then at the left and right posterior tibial arteries and dorsalis pedis arteries. ABI was calculated for each side by taking the higher ankle pressure on the side measured, divided by the higher brachial pressure (from either side). The lower of the two resultant ABI values was used for risk classification. ABI values above 0.90 were considered normal; 0.71–0.9 indicated mild obstruction; 0.31–0.7 indicated moderate obstruction; and 0.0–0.3 indicated severe obstruction.10 Studies have shown ABI to correlate well with peripheral contrast angiography with a sensitivity and specificity above 90% for detection of significant PAD.15,17

Statistical Analysis

Data were stored on Microsoft Excel 2000. A descriptive analysis was performed on patient characteristics and extent of atherothrombosis. Patients with established PAD or symptoms of claudication on interview were regarded as having ‘symptomatic PAD’. Continuous parameters were summarized using median with minimum to maximum range given in brackets; categorical parameters were summarized using proportions and percentages. No statistical tests of significance were performed.

Results

All but two of the 393 patients had CAD. Baseline characteristics are shown in Table 1. Myocardial infarction was the most common CAD presentation, affecting 42% of patients, followed by unstable angina (27.5%), and stable angina (25.7%). CAD patients were treated by percutaneous transluminal coronary angioplasty (PCTA) with stenting (27.2%), coronary artery bypass graft surgery (17.3%), and PCTA without stent (9.9%). Twenty-four patients (6.1%) had prior documented history of cerebral vascular disease -18 with ischemic stroke, and 6 with TIA. Thirty patients (7.6%) had claudication symptoms (symptomatic PAD); 11.8% of patients had clinical involvement of two or more arterial beds.

All 30 symptomatic PAD patients had abnormal ABI. Another 54 out of the 363 patients without PAD symptoms also registered abnormal ABI values (asymptomatic PAD). (Figure 1) Overall, 21.4% of patients had an abnormal ABI. 47.6% of all patients with two arterial beds involvement and 80% of all patients with three arterial beds involvement had abnormal ABI (Figure 2).

Over 95% of patients were on at least 1 antihypertensive agent. Patients with abnormal ABI were more likely to be on an angiotensin-receptor blocker or ACE-inhibitor. Ninety-eight percent of patients were on a platelet aggregation inhibitory agent, most commonly aspirin. (Table 2)

Discussion

Atherosclerosis is increasingly being recognized as a generalised disease, even in the absence of symptoms.12 In this study, using ABI as a screening tool to detect the presence of atherothrombotic disease in the peripheral vascular bed of patients with a previous CV event, we found that over
one-fifth registered an abnormal ABI. This prevalence is similar to larger Caucasian surveys.5,16,18 What is interesting is that nearly two-thirds of patients with abnormal ABI do not have symptoms for PAD, a finding noted previously in a single-centre study.19 Our survey also noted that none of the 393 patients with CAD have been formally or objectively evaluated for concomitant PAD prior to the survey, including the 30 patients who had been complaining of limb claudication. Yet a diagnosis of concomitant PAD is significant to the patient. In one study, the combined risk of ischaemic stroke, MI or vascular death in patients with atherothrombotic involvement of two vascular beds was 25% higher than in patients with a single bed affected, and 51% higher in patients with involvement of three beds compared with those with single-bed disease.5 We are clearly not doing enough to screen for presence of PAD in our health clinics in Malaysia, which the use of a simple ABI measurement may address.

Indeed an abnormal ABI itself may serve as a prognostic tool. Leng and colleagues15 found that in patients with an ABI = 0.9, the relative risk of non-fatal MI, stroke and CV death in the 5 years post-baseline was 1.38, 1.98 and 1.85, respectively, compared with subjects in whom ABI was above 0.9. The CAPRIE investigators found a 10.2% increase in relative risk of CV events and deaths for every 0.1 decrease in ABI in patients.17 These studies all involved patients with abnormal ABI and definite claudicant symptoms.

Other studies and reviews have also shown the importance of adequate anti-platelet therapy for the prevention of atherosclerosis progression.7,20,21 Conventional risk factor control such as cessation of smoking, aggressive control of blood pressure, diabetes and dyslipidemia remain pivotal in prevention of atherothrombosis.6,12,18,22 Data are also emerging on the role of angiotensin-converting enzyme inhibitors (ACE-I) on reduction of cardiovascular events in asymptomatic PAD patients beyond blood pressure reduction. In the Health Outcomes Prevention Evaluation Study (HOPE) for example, ramipril reduced death and MI by 27%.6

Study limitations
We acknowledge that this survey is still relatively small with 393 patients. However, we believe this has been compensated in part by its multicentre design and consecutive patient recruitment process. It is also the largest survey of prevalence of PAD in CVD patients in Malaysia thus far.
The trends observed in the Malaysian sample with regard to ABI were also consistent with those of the overall Asia Pacific cohort as part of the larger AGATHA project. As it was a cross-sectional design, we were not able to determine the predictive and prognostic value of ABI nor that of blood pressure control. This has been ascertained convincingly in much larger case series and meta-analyses.

This study is also lacking in statistical tests of significance that is usual for a comparative study. However, the primary focus of this exploratory study is in the determination of percentages in various groups.

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References


