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Ankle-brachial index and extent of atherothrombosis in 8891 patients with or at risk of vascular disease: results of the international AGATHA study

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KEYWORDS
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Myocardial infarction;
Peripheral arterial disease;
Stroke;
Patients at risk

Aims AGATHA (a Global Atherothrombosis Assessment) was designed to assess the extent of atherothrombosis and the use of the ankle-brachial index (ABI) in vascular patients. The principal hypotheses were that (1) in diseased patients, a low ABI was related to the number and site of vascular beds affected and (2) in at-risk patients without disease, a low ABI was related to the number of risk factors present.

Methods and results Patients were recruited consecutively by 482 clinicians in 24 countries and the ABI measurement was performed at a single visit. Of 8891 patients recruited, 1792 were defined as at risk and 7099 as with disease. Of the with-disease patients, 65.2% had one arterial bed affected, 27.6% two and 7.1% all three. Abnormal ABI ($\leq$0.9) was present in 30.9% of at-risk and 40.5% of with-disease patients. A lower ABI was weakly associated with an increasing number of risk factors in at-risk patients ($r = -0.056$, $P = 0.02$) and with the site and number of arterial beds affected in with-disease patients ($P < 0.001$).

Conclusion This large international study confirms that atherothrombotic disease often occurs at more than one site. The ABI is related to the risk factor profile and to the site and extent of atherothrombosis.

Introduction

For many years, vascular events, such as myocardial infarction (MI) and ischaemic stroke, and diseases, such as angina and peripheral arterial disease (PAD), have been the major causes of death and disability in the Western World.[1] Studies indicate that over the next two decades, cardiovascular and cerebrovascular diseases will become the most common cause of mortality and morbidity worldwide.[2,3] These arterial diseases and events are the result of atherothrombosis—a term used to indicate the contribution of both atherogenesis and clot formation to the disease process. Atherothrombosis can occur in any of the arterial beds (coronary, cerebrovascular, or peripheral arterial) and is frequently observed simultaneously in more than one bed.[4] Atherothrombotic disease in one bed may indicate an increased risk of disease in another.[5]

One of the major problems associated with atherothrombosis is the identification of patients at risk. Atherothrombosis is mostly a silent condition, and often the first sign of the disease is the occurrence of a major life-threatening event such as MI or stroke. Patients at risk are usually identified by the presence of risk factors, such as hypertension, diabetes, obesity, smoking, dyslipidaemia, or prior history of vascular disease. Recently, a number of clinical measurements such as C-reactive protein[6] have been proposed as having potential to aid in the diagnosis of atherothrombosis. Carotid intimal medial thickness (IMT) has also been proposed as a marker for risk, and studies have shown a good correlation with atherothrombotic conditions.[7–9] However, the measurement of IMT is complex and requires expensive equipment. Measurement of the ankle-brachial index (ABI), in contrast, is a simple and inexpensive test, and studies have indicated that the ABI can successfully identify patients with previously unrecognized PAD.[10,11] The technique has been shown to be reproducible and an indicator of the risk of generalized vascular mortality and morbidity.[12,13]

AGATHA (a Global Atherothrombosis Assessment), a prospective, international, multicentre study, was designed to assess in a wide variety of clinical settings the extent of atherothrombosis in two groups of patients: those presenting with a history of vascular events or current symptoms of vascular disease and those without disease but at increased risk of a future vascular event. More specifically,

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the main hypotheses were that (1) in diseased patients, a low ABI was related to the number and site of vascular beds affected and (2) in at-risk patients, a low ABI was related to the number of risk factors present.

Methods

AGATHA was an international, multicentre prevalence study based on clinical practice. Investigators were general practitioners and/or specialists (angiologists, cardiologists, neurologists, diabetologists, internists, and vascular surgeons) according to preference by country. Patients were recruited consecutively (and not sampled) from patient referrals to each centre. The need for truly consecutive recruitment was emphasized in the protocol and at investigators' meetings, which were held in order to ensure consistent understanding and implementation of the survey among the different sites and countries. A sample size estimation was not made for the study because it was considered that a target of over 8000 subjects would be more than adequate to provide precision and to test hypotheses. The number required was based more on the need to recruit a large number of representative subjects from different countries and clinical settings. Written informed consent was obtained from all patients and the study was conducted according to the principles of the Declaration of Helsinki (Edinburgh Amendment, 2000).

Patients

Patients were recruited into the study if they met the inclusion criteria listed in *Table 1*. Two patient groups were included: the patients with disease comprised those with prior evidence of cerebrovascular disease, coronary heart disease or PAD, or current cardiovascular symptoms and the patients at risk of vascular disease comprised those without a history of prior disease or current symptoms but aged >55 and with two or more risk factors. Patients were excluded from the study if they had cerebral disease of non-atherothrombotic origin (i.e. primary intracranial haemorrhage) or had neurological signs and symptoms due to a non-ischaemic cause.

Clinical evaluation

Table 2 shows the demographic data and medical history collected using a standard questionnaire and recording form. Data were derived both from the patient directly and from their medical records. The clinical assessments shown were mostly performed at the same visit. The methods of measurement were those used routinely in each centre except for the ABI, which was the key clinical measure in the study and was standardized. ECGs were interpreted locally by clinicians and the following were reported: conduction disturbances, ST-segment depression, ST-segment elevation, T-wave inversion, and abnormal Q-waves.

ABI was determined from blood pressure measurements in the arms and ankles with the patient supine. Systolic blood pressure in the brachial artery was measured in both arms using a blood pressure cuff and Doppler detection in the antecubital fossa. Systolic blood pressure at the left and right posterior tibial arteries and dorsalis pedis arteries was then measured with Doppler detection with a blood pressure cuff applied to the ankle just proximal to the malleoli. For each pressure measurement, the pulse was located using the Doppler probe and the cuff then inflated until the pulse was obliterated. The cuff was then deflated slowly and the pressure noted when the pulse detected by the Doppler probe re-appeared. ABI for each leg was calculated as the ratio of the higher of the two systolic pressures (posterior tibial or dorsalis pedis) in the leg and the average

Table 2 Medical history and clinical examination performed on each subject

Medical history	Clinical examination
Demography (age, sex, race)	Height
History of previous vascular disease	Weight
Current cardiovascular symptoms	Heart rate
Cardiovascular risk factors (including the presence of diabetes mellitus, dyslipidaemia, and smoking habit)	Blood pressure
	ECG (within 3 months of study entry)
	ABI
Currently prescribed medications	

Table 1 AGATHA study inclusion criteria for patients at risk and with vascular disease

Patients with vascular disease	Patients at risk of vascular disease
i.e. patients of any age with history of prior disease or with current symptoms	i.e. patients without history of prior disease or current symptoms but aged >55 (no upper age limit) and with two or more of following risk factors
Prior cerebrovascular disease	Diabetes mellitus
Ischaemic stroke	Type I or type II
TIA	Dyslipidaemia (lab tests within 3 months of study entry)
Carotid angioplasty or endarterectomy	Total cholesterol ≥6.21 mmol/L (≥240 mg/dL), LDL cholesterol ≥4.14 mmol/L (≥160 mg/dL), or HDL cholesterol ≤0.9 mmol/L (≤35 mg/dL), triglycerides ≥200 mg/dL, or current use of lipid-lowering agent for dyslipidaemia
Prior coronary heart disease	Hypertension
Stable angina	Systolic blood pressure ≥140 mmHg, diastolic blood pressure ≥90 mmHg, or current antihypertensive treatment
Unstable angina	Obesity
MI	BMI ≥30 kg/m^2 in males and ≥28.6 kg/m^2 in females
Coronary angioplasty or bypass graft	Smoking history
Prior PAD	Current or former smoker (≥10 packs of 20 cigarettes per year)
Intermittent claudication	
Previous abnormal ABI (≤0.9)	
Vascular lab diagnosis	
Lower-limb arterial revascularization	
Current cardiovascular symptoms	
Angina pectoris	
Intermittent claudication	

of the right and left brachial artery pressures, unless there was a discrepancy $\geq$10 mmHg in blood pressure values between the two arms. In such a case, the higher reading was used for the ABI. Each centre received an identical Doppler instrument (non-digital Nicolet ELITE 100R with a vascular probe of 5 MHz) for the ABI measurement.

Specific training in the measurement of ABI was carried out in all countries participating in the study. The training was based on a tool-kit prepared centrally and distributed to all participating sites. It comprised instructions from the manufacturer of the Doppler plus demonstration video and powerpoint slides showing a step-by-step approach to the measurement. This tool-kit was used in training meetings at each of the sites. In addition, in some countries such as Canada, further training in the measurement of ABI was included as part of other educational programmes.

Analysis of data

Statistical analysis was carried out using the SPSS software package for Windows, version 8.2. Data were summarized using mean, median, standard deviation and range for continuous parameters, and counts and percentages for categorical parameters. χ^2 tests (using Monte-Carlo estimation when needed) were performed to evaluate the general association between the ABI value and the site and number of vascular beds affected (patients with disease). Spearman rank correlation coefficient was calculated to test the association between the ABI and the number of risk factors present. Multivariate-regression analysis was used to test the association between the site of vascular bed affected and the ABI. Two-sided tests with significance level of $P < 0.05$ were used. Corrections for multiple testing were not considered necessary, given the extent of the analysis.

Results

Patient recruitment

Between March 2002 and March 2003, 8891 patients were recruited into the study by 482 clinicians in 24 countries. Nine European countries were represented, four South American countries, one Middle Eastern country, nine Asian countries, and one North American country. A full list of participating clinicians is included as Supplementary material.

The best represented group of the participating physicians (482) was general practitioners (177, 37%), with other well-represented groups including cardiologists (98, 20%), internal medicine specialists (80, 17%), neurologists (44, 9%), and vascular surgeons (44, 9%). The pattern of recruitment according to specialization varied from country to country, for example, 164 of the general practitioners were from Canada and 75 of the 80 internal medicine specialists were from Greece. Overall, ~20% of the study population was recruited by general practitioners and 80% by specialists.

Two patient populations were defined: those at risk of vascular events [1792 patients (20.2%), the at-risk population] and those with prior disease or current symptoms of vascular disease [7099 patients (79.8%), the with-disease population]. Patient profiles were missing for an additional 19 patients, who were excluded from the study.

Demographic and baseline characteristics

Most patients in the study were Caucasian (61.0%), with 32.3% defined as Asian, 2.0% as Black, and 4.7% as of other racial origin. The demographic and baseline characteristics of the patients in the at-risk and with-disease populations are shown in *Table 3*. There were more males than females in the with-disease population when compared with the at-risk population. Abnormal ECG was more than twice as common in the with-disease patients. Median age, body mass index (BMI), and systolic and diastolic blood pressures were similar between the two groups.

Presence of risk factors in patients at risk of vascular disease

Three or more risk factors were present in 62.5% of the at-risk patients, with over one-third of these having four or more risk factors present. *Table 4* shows that in the whole AGATHA at-risk population, hypertension was the most common risk factor followed by diabetes and dyslipidaemia. Among the hypertensives, 64.2% had an elevation in systolic blood pressure, 33.1% in diastolic, and 29.9% in both. In those with dyslipidaemia, 40.3% had elevated total cholesterol, 26.9% elevated LDL cholesterol, 15.6% reduced HDL cholesterol, and 30.9% elevated triglycerides, as defined in *Table 1*. Almost all the patients with diabetes as a risk factor had type II diabetes. Of the patients defined as smokers, just under one-half were current smokers, the remainder being subjects who had given up.

Geographical variations were observed in the distribution of risk factors in the at-risk patients (*Table 4*). Obesity was less prevalent in patients from Asian countries when compared with other geographical areas, but the prevalence of diabetes was higher in these patients. Smoking,

Table 3 Demographics and baseline characteristics of the patients at risk and with disease

Parameter	Patients at risk ($n = 1792$)			Patients with disease ($n = 7099$)		
	Median	Lower quartile	Upper quartile	Median	Lower quartile	Upper quartile
Age (years)	65.3	60.4	71.4	66.3	58.4	73.2
BMI (kg/m^2)	27.3	24.4	31.5	26.4	23.7	29.6
SBP (mmHg)	140	130	160	140	125	155
DBP (mmHg)	80	75	90	80	70	90
Sex (male/female, %)	47.6/52.4			66.5/33.5		
Abnormal ECG[a] (%, *n*)	27.5 (493) (7.7% ECG not done)			60.5 (4295) (3.5% ECG not done)		

[a]Abnormal ECGs comprised conduction disturbances (23.5% of total population), ST-segment depression (12.5%), ST-segment elevation (6.0%), T-wave inversion (20.5%), and abnormal Q-waves (15.6%). Note that SBP and DBP rounded to nearest 5 mmHg.

Table 4 Types of risk factor in patients at risk of vascular disease in different geographical areas[a]

Factor	Presence of risk factor: % of at-risk patients (*n*)			
	Asia ($n = 663$)	South America ($n = 139$)	UK/Canada ($n = 590$)	All countries in AGATHA study ($n = 1792$)
Hypertension	89.4 (593)	92.8 (129)	85.8 (506)	88.7 (1590)
Diabetes	88.1 (584)	51.5 (72)	57.5 (339)	70.0 (1254)
Dyslipidaemia	58.4 (387)	52.5 (73)	71.7 (423)	64.0 (1147)
Obesity	11.0 (73)	36.7 (51)	50.7 (299)	32.9 (590)
Smoking history	20.4 (135)	22.3 (31)	40.5 (239)	30.3 (543)

[a]Asia includes Taiwan, Hong Kong, Indonesia, South Korea, Malaysia, Philippines, Singapore, Thailand, and Pakistan; South America includes Brazil, Chile, Columbia, and Mexico. Figures for other European countries (Hungary, Romania, Bulgaria, Slovenia, Greece, Lithuania, Ukraine, and Russia) and the Middle East country (Lebanon) are not shown here because of considerable disparities between countries and small numbers for some countries.

dyslipidaemia, and obesity were most prevalent in the UK/Canada. Hypertension was the most prevalent risk factor in each of the geographical regions.

Number and type of vascular bed affected in the with-disease patients

In the with-disease patients, one-third had disease at more than one site and the number of vascular beds affected did not differ between the sexes: one site 64.2% males and 67.3% females; two sites 27.8% and 27.4%, and three sites 7.9% and 5.4%. The commonest categories of coronary disease ($n = 4521$) were stable angina and MI, of cerebrovascular disease ($n = 3437$) were ischaemic stroke and transient ischaemic attack (TIA), and of PAD ($n = 2112$) was intermittent claudication. Patients diagnosed with atherothrombosis in one arterial bed had a 35% chance of disease in one or more other arterial beds. *Figure 1* shows that among coronary disease patients, approximately one in three had cerebrovascular disease and one in five had PAD; in contrast, in cerebrovascular disease patients, one in two had coronary disease and one in four had PAD; PAD patients were the most likely to have disease at another site with one in two having coronary disease and one in two cerebrovascular disease. PAD patients also had the highest proportion with all three sites affected (one in four) when compared with cerebrovascular disease (one in seven) and coronary disease (one in nine) patients.

Presence of abnormal ABI

Abnormal ABI ($\leq$0.9) was seen in 30.9% of at-risk patients and 40.5% of with-disease patients. The distribution of ABI was similar between the sexes with 37.2% males and 34.4% females having an abnormal ABI of $\leq$0.9, although the proportion having a very low ABI of $\leq$0.7 was slightly higher in males (20.2%) than in females (15.8%).

Table 5 shows that in the at-risk patients, there was a weak but statistically significant correlation between the ABI and the number of risk factors ($P = 0.02$) with ABI tending to decrease as the number of risk factors increased. Also, the frequency of an abnormal ABI ($\leq$0.9) increased with the number of risk factors present from 15.0% with two risk factors to 29.3% with five risk factors. ABI was not related to the presence of any one particular risk factor

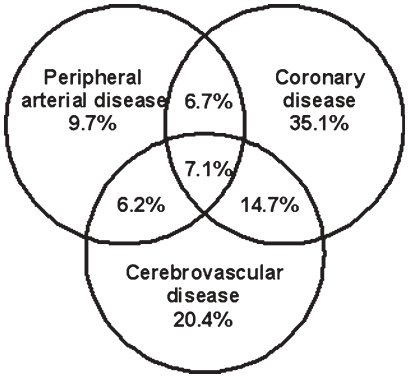

Figure 1 Type of arterial bed affected in the with-disease population. Note that figure is schematic and not to scale. Percentage values relate to % of whole with-disease population ($n = 7099$). Values in overlaps of circles are % of population with disease at more than one site.

(hypertension, diabetes, dyslipidaemia, smoking, and obesity) in this patient population (data not shown).

In the with-disease patients, the ABI profile was related to which arterial bed was affected (*Table 6*). Patients with PAD had the highest frequency of abnormal ABI: PAD alone 73.3%, cerebrovascular disease alone 26.1%, and coronary disease alone 20.2%. A combination of two affected beds increased the frequency of abnormal ABI, even in those not presenting with PAD (coronary and cerebrovascular diseases 32.5%). If all three beds were affected, 82.3% had an abnormal ABI. Multivariate-regression analysis showed that PAD was associated with mean reduction of 0.35 in ABI ($P < 0.001$), cerebrovascular disease with mean reduction of 0.04 ($P < 0.001$), and no association between coronary disease and the ABI ($P = 0.56$).

Medication received by patients

Most patients were receiving some type of cardiovascular medication (*Table 7*). Antihypertensive therapy was common in both at-risk and with-disease patients. Among those receiving antihypertensives, just over half were receiving an angiotensin-converting enzyme inhibitor. Antiplatelet therapy was twice as common in with-disease patients (80.7%) than in at-risk patients (39.6%). Lipid-lowering agents were prescribed to fewer than half of the patients in either category, although two-thirds of the patients with

Table 5 Percentage of abnormal and mean ABI by number of risk factors in at-risk patients

Number of risk factors present	Degree of ABI abnormality (%, *n*)					Mean ABI (SD)
	None >0.9	Mild ≤0.9 to >0.7	Moderate ≤0.7 to >0.3	Severe ≤0.3	Any ≤0.9	
2 ($n = 666$)	84.4 (562)	11.6 (77)	3.2 (21)	0.3 (2)	15.0 (100)	1.029 (0.172)
3 ($n = 710$)	82.1 (583)	12.1 (86)	5.1 (36)	0.1 (1)	17.3 (123)	1.008 (0.161)
4 ($n = 340$)	75.6 (257)	19.4 (66)	4.7 (16)	0.3 (1)	24.4 (83)	1.008 (0.193)
5 ($n = 58$)	70.7 (41)	22.4 (13)	6.9 (4)	0	29.3 (17)	1.006 (0.186)

Note that the table does not show eight subjects with missing ABI data and 18 subjects who had less than two risk factors present and should not have been included in the study. Formal analysis of the data showed a weak but statistically significant association between the ABI and number of risk factors present (Spearman rank correlation coefficient −0.056, $P = 0.02$).

Table 6 Percentage of abnormal and mean ABI by the number of vascular beds affected in patients with disease

Type/number vascular beds affected	Degree of ABI abnormality (%, *n*)					Mean ABI (SD)
	None >0.9	Mild ≤0.9 to >0.7	Moderate ≤0.7 to >0.3	Severe ≤0.3	Any ≤0.9	
Coronary alone ($n = 2497$)	79.7 (1990)	14.7 (368)	4.8 (120)	0.7 (17)	20.2 (505)	1.010 (0.188)
Cerebrovascular alone ($n = 1446$)	73.9 (1068)	16.8 (243)	8.4 (121)	0.9 (13)	26.1 (377)	0.985 (0.213)
Peripheral arterial alone ($n = 689$)	26.6 (183)	20.2 (139)	38.0 (262)	15.1 (104)	73.3 (505)	0.653 (0.346)
Coronary and peripheral arterial ($n = 478$)	25.7 (123)	24.1 (115)	40.2 (192)	10.0 (48)	74.3 (355)	0.697 (0.316)
Cerebrovascular and peripheral arterial ($n = 443$)	15.1 (67)	21.9 (97)	46.7 (207)	16.3 (72)	84.9 (376)	0.596 (0.326)
Coronary and cerebrovascular ($n = 1044$)	67.5 (705)	21.6 (225)	10.0 (104)	1.0 (10)	32.5 (339)	0.959 (0.222)
All three vascular beds affected ($n = 502$)	17.1 (86)	23.1 (116)	43.2 (217)	15.9 (80)	82.3 (413)	0.616 (0.328)

Note that the table does not show seven subjects with missing ABI data. χ^2 test for general association between the ABI and vascular bed affected: $\chi^2 2246$, df = 18, $P < 0.0001$. Multivariate-regression analysis showed that PAD was associated with mean reduction of 0.35 in the ABI ($P < 0.001$), cerebrovascular disease with mean reduction of 0.04 ($P < 0.001$), and no association between coronary disease and the ABI ($P = 0.56$).

Table 7 Medication classes received by patients at risk and with disease

Medication	% at-risk patients ($n = 1792$)	% with-disease patients ($n = 7099$)	% total patients ($n = 8891$)
Antihypertensive agents	82.8 (1484)	84.4 (5992)	84.1 (7477)
Vasodilator agents	5.2 (93)	43.6 (3095)	35.9 (3192)
Antiplatelet agents	39.6 (710)	80.7 (5729)	72.4 (6437)
Lipid-lowering agents	42.7 (765)	48.7 (3457)	47.5 (4223)
Antidiabetic therapy	61.6 (1104)	31.9 (2265)	37.9 (3370)

dyslipidaemia were prescribed such an agent. Nearly all those with type II diabetes were receiving an oral anti-diabetic drug.

Discussion

Given the overwhelming prevalence across the developed world of death and disability due to vascular events, identification and treatment of at-risk patients represent a medical challenge of the utmost importance. The AGATHA study was designed to evaluate the extent of atherothrombosis in patients presenting with vascular disease and to assess the ABI measurement in patients with or at risk of vascular disease in a multiregional setting involving both primary-care physicians and specialists from a variety of disciplines.

The study comprised both men and women but, in contrast to population prevalence studies, the relative proportions of each were dependent on the gender mix of the physicians' practices. The criteria for defining at-risk patients were chosen on the basis of well-recognized risk factors that are easy to detect. A minimum age cut-off of 55 years was selected, because it is unusual to find PAD at a younger age.[14] The criteria defining dyslipidaemia were based on those described in the National Cholesterol Education Program Report (2002).[15] Smoking as a criterion of risk included both current and ex-smokers because previous smoking is known to be associated with an increased risk for atherothrombosis.[5,16] Diabetes and hypertension are also well-established risk factors.[17]

Of the different arterial sites, the peripheral arterial bed is the one which, when clinically silent but affected by

atherothrombosis, is where disease is most easily detected. Furthermore, cardiovascular disease mortality in PAD patients has been shown to be higher than in subjects without PAD.[18] A number of studies have suggested that PAD is widely under-diagnosed and, even when a diagnosis has been made, PAD is often a poorly managed condition,[11] particularly in relation to prevention of major vascular events. The ABI measurement has been proposed as a simple and inexpensive procedure to identify patients with previously undiagnosed PAD and those at risk of future major cardiovascular events.[12,14]

Abnormal ABI was defined for this study as an ABI $\leq$0.9, particularly as this cut-off has been most commonly used in previous studies.[11,19] Although a low ABI is undoubtedly associated with a high prevalence of asymptomatic PAD, it should be recognized that its precise validity is unknown. However, it is known to have a close association with cardiovascular and cerebrovascular diseases[13] and is a good predictor of future cardiovascular events.[10,14,18,20] A standardized technique for measuring ABI was used across all centres in the study, and identical Doppler devices were supplied to all centres to ensure consistency in the measurements.

In the current study just over 30% of the at-risk patients had an abnormal ABI, suggesting undiagnosed PAD. Although a minimum of two risk factors were required for study entry, many of the at-risk subjects had three or more risk factors present. Prevalence and severity of abnormal ABI was related moderately to the number of risk factors present, but interestingly did not appear to be affected by the types of risk factor present. Previous studies have suggested that smoking has a greater association with PAD than with either coronary or cerebrovascular disease,[16] but abnormal ABI was not any more common in the current study in patients with current or prior smoking habit as a risk factor compared with patients with other risk factors. Although hypertension was the most common risk factor, it was also the risk factor most likely to be treated. Dyslipidaemia, however, was not treated pharmacologically in around one-third of at-risk patients, suggesting that optimal risk factor-reducing interventions may not have been applied.

Just over 40% of the with-disease patients had an abnormal ABI, indicating widespread presence of atherothrombosis in these patients. As might be expected, a greater frequency of abnormal ABI was seen with an increased number of vascular beds affected. Nevertheless, the number of patients with an abnormal ABI and previously diagnosed with coronary and/or cerebrovascular disease was relatively high, and it may be that PAD is widely underdiagnosed in patients with both conditions. Surprisingly, not all patients with a history of PAD presented with an abnormal ABI. This might reflect improved disease status (e.g. following angioplasty), measurement bias, or artefactual problems with the test, for example, in diabetics with rigid arteries.

The results seen in the AGATHA study are comparable to those seen with other similar registries. In the Polyvascular Atherothrombosis: an Observational Survey (PATHOS) study,[21] conducted in multiple centres in Italy, around one-third of patients with acute coronary syndrome (unstable angina and MI) or acute cerebral ischaemia (stroke and TIA) recruited into the study had an abnormal ABI. In contrast to our study, however, a larger proportion (20%) had a very low ABI of $<$0.6. In the Peripheral Arterial Disease Detection, Awareness and Treatment in Primary Care (PARTNERS) study,[11] which was conducted across a number of primary care sites in the USA, a high prevalence of PAD (29%) was found in higher risk patients as assessed using ABI measurement. This was very similar to the proportion of at-risk patients in our study who had a low ABI (*Table 5*). In the PARTNERS study,[11] around one-half of the patients with PAD were newly diagnosed during the study.

Overall the AGATHA study has confirmed that disease in one vascular bed often occurs with disease in another. Furthermore the ABI, which is a simple, inexpensive, and rapid measurement tool, has been shown to detect the likely presence of peripheral atherothrombosis both in many patients with current or prior history of other vascular disease and, more importantly, in at-risk patients. These findings suggest that the ABI has the potential in both at-risk and diseased patients to be used to contribute to more precise estimates of future risk of major cardiovascular events and death and to guide decisions on prevention and treatment. Indeed, a low ABI has been shown in several studies in the general population to be associated with approximately a two-fold increase in the risk of future fatal and non-fatal cardiovascular events, but the precise contribution which the ABI can make to delineating risk in conjunction with risk scoring systems using conventional risk factors, has yet to be established. Also, the accuracy of the ABI in predicting risk in young middle age needs to be evaluated.

Additional studies, such as the Reduction of Atherothrombosis for Continued Health (REACH) registry[22] and the getABI study,[19] will provide further insight into the risk, diagnosis, and treatment of atherothrombosis. In particular, these studies will follow patients for up to 2 years (REACH) and 3 years (getABI) and provide data that will enable the evaluation of the contribution of an ABI in the assessment of long-term risk of atherothrombosis in daily clinical practice in at-risk patients.

Supplementary material

Supplementary material is available at *European Heart Journal* online.

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