

Symptomatic peripheral arterial disease: the value of a validated questionnaire and a clinical decision rule

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ABSTRACT

Background

If a validated questionnaire, when applied to patients reporting with symptoms of intermittent claudication, could adequately discriminate between those with and without peripheral arterial disease, GPs could avoid the diagnostic measurement of the ankle brachial index.

Aim

To investigate the Edinburgh Claudication Questionnaire (ECQ) in general practice and to develop a clinical decision rule based on risk factors to enable GPs to easily assess the likelihood of peripheral arterial disease.

Design of study

An observational study.

Setting

General practice in The Netherlands.

Method

This observational study included patients of ≥ 55 years visiting their GP for symptoms suggestive of intermittent claudication or with one risk factor. The ECQ and the ankle brachial index were performed. The prevalence of peripheral arterial disease, defined as an ankle brachial index < 0.9 , was related to risk factors using logistic regression analyses, on which a clinical decision rule was developed and related to the presence of peripheral arterial disease.

Results

Of the 4790 included patients visiting their GP with symptoms suggestive of intermittent claudication, 4527 were eligible for analyses. The prevalence of peripheral arterial disease in this group was 48.3%. The sensitivity of the ECQ was only 56.2%. The prevalence of peripheral arterial disease in a clinical decision rule that included age, male sex, smoking, hypertension, hypercholesterolemia, and a positive ECQ, increased from 14% in the lowest to 76% in the highest category.

Conclusion

This study indicates that the ECQ alone has an inadequate diagnostic value in detecting patients with peripheral arterial disease. The ankle brachial index should be performed to diagnose peripheral arterial disease in patients with complaints suggestive of intermittent claudication, although our clinical decision rule could help to differentiate between extremely high and lower prevalence of peripheral arterial disease.

Keywords

ankle brachial index; atherosclerosis; clinical decision rule; Edinburgh Claudication Questionnaire; intermittent claudication; peripheral vascular disease.

INTRODUCTION

Atherosclerosis is a systemic disease leading frequently to myocardial infarction, stroke, and disease of the aorta and peripheral arteries. Peripheral arterial disease, that is atherosclerosis of the lower extremities, although a chronic condition with a relatively benign prognosis locally, is an important marker for generalised atherosclerosis and is closely associated with cardio- and cerebrovascular disease.¹ The incidence of acute (non-) fatal cardiovascular disease is two to three times higher in patients with arterial disease in the lower extremities compared with people with no atherosclerosis in the peripheral arteries.² It has been shown that individuals with an ankle brachial index below 0.9 were twice as likely to have cardiovascular disease,³ and men with an ankle brachial index below 0.9 have a fourfold risk of cerebrovascular disease compared with those with normal pressure indexes.² However, the majority of patients with peripheral arterial disease are asymptomatic or have leg symptoms other than

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classic intermittent claudication, the main symptom of peripheral arterial disease. It is estimated that only 22% of patients with peripheral vascular disease are symptomatic.⁴

GPs can and must play a key role in recognition, diagnosis and treatment of risk factors of patients with peripheral arterial disease. Assessment of the ankle brachial index in patients with symptoms suggestive of intermittent claudication is an effective diagnostic tool for peripheral arterial disease and is the clinical standard in primary care.⁵ However, it has been shown that in only 10% of the patients referred to a vascular out-patient clinic a prior ankle brachial index measurement had been performed.⁶

The Edinburgh Claudication Questionnaire (ECQ) is a validated questionnaire to diagnose intermittent claudication in epidemiological surveys of peripheral arterial disease.⁷ It has an established effectiveness for the use in epidemiological studies of peripheral arterial disease. If this questionnaire, when applied to patients reporting with symptoms of intermittent claudication, could adequately discriminate between those with and without peripheral arterial disease, GPs could avoid the diagnostic measurement of the ankle brachial index. Furthermore, a clinical decision rule could be useful to differentiate between patients reporting with symptoms having a low or a high likelihood of the presence of peripheral arterial disease.

The aim of this study was threefold: to investigate the clinical applicability of the ECQ in daily general practice, using a large population presenting with symptoms suggestive of intermittent claudication among a representative number of general practices; to develop a clinical decision rule based on generally accepted risk factors for peripheral arterial disease to easily assess the likelihood of peripheral arterial disease; and to evaluate a combination of the final decision rules to assess their diagnostic value.

METHOD

Study population

This observational study was conducted from October 2002 to February 2005 among 955 general practices. Patients of ≥ 55 years, visiting with symptoms deemed to be suggestive of intermittent claudication by the GP (but without confirmation by ankle brachial index) were eligible and were asked for informed consent.

Assessment of risk factors

The following risk factors were assessed by the GP: smoking; diabetes; hypertension; hypercholesterolemia; a family history of vascular disease (<60 years); previous myocardial infarction; history of angina pectoris; angioplasty; coronary by-pass surgery; and a prior ischaemic stroke. Smoking was recorded as current, former (a history of ≥ 10 pack

How this fits in

A diagnostic questionnaire for peripheral arterial disease that has been used in epidemiological studies could be valuable in daily general practice to avoid the time-consuming measurement of the ankle-arm-index. However, this study indicates that the Edinburgh Claudication Questionnaire has no added diagnostic value to diagnose peripheral vascular disease in symptomatic patients. Since a more aggressive prophylactic treatment of risk factors is only advocated in subjects with a high risk for cardiovascular disease, an ankle brachial index measurement to confirm the diagnosis of peripheral arterial disease in patients with complaints suggestive of intermittent claudication seems a necessity.

years), and never smoked. Diabetes was present if the serum fasting glucose level was ≥ 6.0 mmol/l and/or if glucose lowering medication was prescribed. Patients using glucose lowering medication with a fasting glucose level <6.0 mmol/l were considered to be adequately treated. A blood pressure of $\geq 140/90$ mmHg, and/or the use of antihypertensive medication were defined as hypertension. Adequately treated hypertension was defined as a blood pressure 140/90 mmHg while using antihypertensive medication. Hypercholesterolemia was defined as a serum total cholesterol of ≥ 5.0 mmol/l and/or the use of cholesterol lowering medication, and was considered as adequately treated when <5.0 mmol/l. If a first-grade relative had experienced a cardiovascular event aged <60 years, a family history of vascular disease was considered to be present.

Assessment of the Edinburgh Claudication Questionnaire

In all patients the ECQ was completed (Box 1). Patients were not be considered to have intermittent claudication if pain was complained of in the hamstrings, feet, joints or appeared to radiate, in the absence of any calf pain.

Assessment of the ankle brachial index

First the systolic brachial blood pressure was measured by auscultation or Doppler sound of 8 MHz

Box 1. Edinburgh Claudication Questionnaire.

- ▶ Do you get a pain or discomfort in either leg on walking?
- ▶ Does this pain ever begin when you are standing till or sitting?
- ▶ Does this pain occur if you walk uphill or hurry?
- ▶ Does this pain occur if you walk at an ordinary pace on the level?
- ▶ What happens if you stand still?
- ▶ In what part of your leg do you feel the pain?

Table 1. Demographic and clinical characteristics of the total population with complaints suggestive of intermittent claudication.

	Total population (n = 4527)	ABI<0.9 (n = 2187)	0.9≤ABI≤1.4 (n = 2340)	OR for ABI<0.9 (95% CI)	P-value
Age (years), mean (SD)	68.8 (8.5)	70.1 (8.5)	67.7 (8.3)	1.04 (1.03 to 1.04)	<0.001
Men, n (%)	2448 (54.1)	1318 (60.3)	1130 (48.3)	1.63 (1.45 to 1.83)	<0.001
BMI, mean (SD)	27.3 (11.6)	26.9 (11.9)	27.8 (11.3)	0.95 (0.94 to 0.97)	0.009
Current smokers, n (%)	1570 (34.7)	938 (42.9)	632 (27.0)	2.05 (1.81 to 2.33)	<0.001
Ever smoked, n (%)	1532 (33.8)	743 (34.0)	789 (33.7)	2.25 (1.97 to 2.57)	<0.001
Never smoked, n (%)	1319 (29.1)	454 (20.8)	865 (37.0)	0.44 (0.39 to 0.51)	<0.001
Hypertension, n (%)	3428 (75.7)	1758 (80.4)	1670 (71.4)	1.82 (1.56 to 2.12)	<0.001
Diabetes mellitus, n (%)	1330 (29.4)	664 (30.4)	666 (28.5)	1.12 (0.99 to 1.28)	0.084
Hypercholesterolemia, n (%)	2147 (47.4)	1081 (49.4)	1066 (45.6)	1.23 (1.08–1.40)	0.002
Family history, n (%)	1721 (38.0)	788 (36.0)	933 (39.9)	0.85 (0.75 to 0.96)	0.008
Coronary heart disease, n (%)	1153 (25.5)	591 (27.0)	562 (24.0)	1.17 (1.03 to 1.34)	0.02
Stroke or TIA, n (%)	406 (9.0)	206 (9.4)	200 (8.5)	1.11 (0.91 to 1.37)	0.300
No vascular risk factor present, n (%)	137 (3.0)	28 (1.3)	109 (4.7)	0.27 (0.17 to 0.40)	0.001
Two risk factors present, n (%)	1579 (34.9)	758 (34.7)	821 (35.1)	0.95 (0.84 to 1.08)	0.463
Three or more risk factors present, n (%)	1768 (39.1)	987 (45.1)	781 (33.4)	1.70 (1.50 to 1.92)	0.001

ABI = ankle brachial index. BMI = body mass index. OR = odds ratio. SD = standard deviation. TIA = transient ischaemic attack.

at both arms, after which the systolic pressures of the dorsalis pedis and posterior tibial arteries were measured at malleolar level by Doppler sound. The ankle brachial index was calculated for each leg by dividing the highest systolic ankle pressure by the highest brachial systolic pressure. The practice assistant was able to perform the ankle brachial index measurement. Peripheral arterial disease was defined

Table 2. Ankle brachial index related to the ECQ.

	ABI<0.9	0.9≤ABI≤1.4	Total
ECQ ^a positive	1153	788	1941
ECQ negative	898	1388	2286
Total	2051	2176	4227

^aDefinite and atypical intermittent claudication; ECQ = Edinburgh Claudication Questionnaire.

as an ankle brachial index of <0.9 in one or both legs.

Analyses

The primary outcome measurement was peripheral arterial disease. The used cut-off point of the ankle brachial index was 0.9. This is used in the majority of recent studies and is reported to have a sensitivity of 95% and a specificity of 99% for angiographically confirmed peripheral arterial disease.⁸ All patients with an ankle brachial index between 0.9 and 1.4 in both legs were considered normal. Since a high ankle brachial index (>1.4) appears to correlate similarly to a low ankle brachial index to mortality,⁹ we excluded patients with an ankle brachial index above 1.4 in one or both legs and without peripheral arterial disease as defined above from the reference group. This was to prevent underestimation of the peripheral arterial disease prevalence.

The characteristics of patients with symptoms suggestive of intermittent claudication were compared between participants with and without peripheral arterial disease using the Students' *t*-test for continuous variables and the χ^2 test for binary variables. Statistical analyses were performed using SPSS 11.0.

The prevalence of peripheral arterial disease was compared to the risk factors and ECQ using multivariate logistic regression analyses. The β -coefficients that resulted from the regression analyses were converted into odds ratios (OR). Based on these OR, a clinical decision rule was developed. Finally, the outcomes of this clinical decision rule were compared to the presence of peripheral arterial disease.

RESULTS

The study included 4790 patients with symptoms deemed suggestive of intermittent claudication by the GP. Of these, 181 (3.8%) patients had to be excluded from the analyses since their ankle brachial index was above 1.4 in one or both legs (without an ankle brachial index below 0.9 in the other leg). In addition, ankle brachial index ratio data were missing in 82 (1.7%) patients, leaving 4527 patients for analyses. The general demographics are shown in Table 1.

The prevalence of peripheral arterial disease in the study group was 48.3%. As shown in Table 1 most of the risk factors were statistically significantly more prevalent in patients with peripheral arterial disease. There was no significant difference in the prevalence of diabetes between the participants with a low and a normal ankle brachial index.

Edinburgh Claudication Questionnaire

For 300 (6.6%) patients data were incomplete to assess the ECQ, resulting in an analysis of 4227 patients. The sensitivity of the ECQ for detecting an

Table 3. Clinical decision rule according to the logistic regression analyses.

Risk factor points	Age	Sex	Smoking behaviour	Hypertension	Hypercholesterolemia	ECQ
0	55–59 years (n = 822)	Female (n = 1993)	Never smoked (n = 1319)	No hypertension (n = 928)	No hypercholesterolemia (n = 2019)	Negative ECQ (n = 2286)
+1	60–64 years (n = 722)	Male (n = 2448)		Hypertension adequately treated (n = 941)	Hypercholesterolemia (n = 2147)	
+2	65–69 years (n = 851)			Hypertension not adequately treated (n = 2487)		
+3	70–74 years (n = 880)		Ever smoked (n = 1532)			Positive ECQ (n = 1941)
+4	75–79 years (n = 716)					
+5	80–84 years (n = 409)					
+6	≥85 years (n = 127)					
+8			Currently smoking (n = 1570)			

ankle brachial index below 0.9 was 56.2%, resulting in a positive predictive value of 59.4% and a negative predictive value of 60.7%. The sensitivity of the ECQ appeared to increase with the number of risk factors present. The relationship between the ankle brachial index and the ECQ is depicted in Table 2.

Multivariate model

Using the stepwise logistic regression analysis, diabetes ($P = 0.05$), a positive family history ($P = 0.35$), a prior cardio- ($P = 0.66$) or neurovascular event ($P = 0.30$), and the body mass index ($P = 0.18$) were consistently removed from or not included in the final model. The final model showed a significantly increased risk of peripheral arterial disease with increasing age (OR = 1.28 per 5 years; 95% confidence interval (CI) = 1.23 to 1.36; $P < 0.001$), male sex (OR = 1.22; 95% CI = 1.05 to 1.42; $P = 0.009$), smoking, both former (OR = 1.87; 95% CI = 1.56 to 2.25; $P < 0.001$) and currently smoking (OR = 3.78; 95% CI = 3.17 to 5.52), the presence of hypertension (OR = 1.67; 95% CI = 1.39 to 2.00; $P < 0.001$), adequately treated hypertension (OR = 1.35; 95% CI = 1.20 to 1.61; $P = 0.001$), the presence of hypercholesterolemia (OR = 1.33; 95% CI = 1.15 to 1.54; $P < 0.001$), and a positive ECQ (OR = 1.92; 95% CI = 1.67 to 2.22; $P < 0.001$). To translate the OR to an easy clinical decision rule, an OR of 1 was taken as 0 risk factor points, increasing with 1 risk factor point per increase of the OR with

approximately 0.33. The clinical decision rule is shown in Table 3.

Prevalence of peripheral arterial disease in relation to clinical rule

The prevalence of peripheral arterial disease according to the clinical decision rule increases proportionately to increasing score, with a prevalence of peripheral arterial disease of 14% in the lowest category to 71% in the highest category (Table 4).

Table 4. Risk profile for peripheral arterial disease in patients with leg symptoms suggestive for intermittent claudication.

Score	Prevalence, n	ABI < 0.9, n (%)
0–3	228	33 (14.5)
4	179	36 (20.1)
5	262	67 (25.6)
6	392	142 (36.2)
7	436	189 (43.3)
8	406	209 (51.1)
9	450	237 (52.7)
10	437	279 (63.8)
11	351	229 (65.2)
12	252	163 (64.7)
≥13	259	184 (71.0)

ABI = ankle brachial index.

DISCUSSION

Summary of main findings

The prevalence of ankle brachial index verified peripheral arterial disease was 48.3% in a large cohort of patients with complaints suggestive of intermittent claudication in primary care setting. This non-specificity of complaints for peripheral arterial disease is consistent with findings in previous studies.¹⁰ Since more aggressive prophylactic treatment of risk factors is only advocated in patients with a high risk for cardiovascular diseases, an ankle brachial index measurement to confirm the diagnosis of peripheral arterial disease seems necessary.

Among patients with complaints suggestive of intermittent claudication, higher age, male sex, smoking, hypertension and hypercholesterolemia were significantly associated with peripheral arterial disease. However, even in the lowest risk category the prevalence of peripheral arterial disease was still 14% and only 71% in the highest category.

In 43.8% of the patients with peripheral arterial disease the diagnosis would have been unjustly rejected if physicians had relied solely on the ECQ. This suggests that the ECQ is of limited value in diagnosing peripheral arterial disease in general practice.¹¹ The ECQ was earlier reported to have a high sensitivity (82.8%) and specificity (100%).⁷ However, this study used the patient history taken by a physician as a reference. In our study, where the ankle brachial index was used as a reference, the sensitivity appeared to be only 56.2%.

Strengths and limitations of the study

First, our study was population-based, was performed in a substantial number of general practices, and included a large number of both men and women.

While the ability of GPs to identify peripheral arterial disease seems good (positive predictive value of 48.3%), we are unable to report on the negative predictive value based on the design of the study.

The presence of hypertension, hypercholesterolemia and diabetes were based on a single measurement or on the established diagnosis of the GP, and not verified according to the criteria of established guidelines.¹²⁻¹⁴ Hence, misclassification could have occurred, resulting in the underestimation of the role of the particular risk factors with respect to the prevalence of peripheral arterial disease.

Furthermore, palpation of the peripheral arteries has a high negative predictive value,¹⁵ which could have lead to a more specific population if it had been performed. However, it has been shown that this examination is prone to spurious results, even in experienced hands, resulting in many unidentified patients with peripheral arterial disease.^{15,16}

Since the ankle brachial index measurement was

performed by multiple GPs or practice assistants, a larger observer variation could have occurred when compared to a central ankle brachial index measurement assessment. However, it is reported that this kind of bias appears to be low.¹⁷ Moreover, the ankle brachial index measurement should have been repeated twice according to the guideline of the Dutch College of GPs¹⁸ and in this study, the ankle brachial index measurement was only performed once. Both biases would lead to an underestimation of the role of the risk factors in relation to the prevalence of peripheral arterial disease. In addition, the assessment of the ECQ and ankle brachial index measurement were not performed by independent observers. This might have introduced a diagnostic suspicion bias.

Since the study attempted to derive a prediction rule for patients with symptoms suggestive of intermittent claudication, one could argue that a true validation study of the developed clinical decision rule on a different population is necessary. However, validation of a clinical decision rule, showing that an ankle brachial index measurement is necessary and independent of the risk score, seems to be worthless due to the expectation that it would produce even lower prediction scores.

Comparison with existing literature

Sole use of the ECQ without measurement of the ankle brachial index, would mean risk-factor management would not be performed in many patients with peripheral arterial disease, which is associated with a high morbidity and mortality due to other atherosclerotic manifestations like myocardial infarction and stroke.

In our study more men were included, suggesting that men more often report complaints suggestive of intermittent claudication.⁴ Once again this study indicated that smoking is a very important risk factor of peripheral arterial disease. The percentages of current and past smoking are comparable with results reported previously.¹⁹

We showed a significant association between the presence of vascular risk factors and a low ankle brachial index, in accordance with most previous investigators.¹⁶ The Framingham Heart Study documented a 2.5-fold increase in the risk of peripheral arterial disease in hypertensive men and a 3.9-fold increase in women with hypertension.²⁰ We were able to show the influence of adequate treatment of hypertension, which gave a 0.4-fold decrease in the risk of peripheral arterial disease and is similar to an earlier report.²¹

Our study confirmed the association of high cholesterol levels with atherosclerosis with an OR of 1.4, which is slightly lower compared with the results of an earlier study that found an OR of 1.7.²²

No statistically significant association was shown between a low ankle brachial index and the presence of diabetes. It is documented that in about 5% of diabetics the ankle brachial index is over 1.10, despite the presence of peripheral arterial disease.²² The sensitivity and specificity of the ankle brachial index in patients with type 2 diabetes are lower (70.6 versus 90% and 88.5 versus 99%, respectively).²³ However, a small study of patients with type 2 diabetes showed little additional benefit of toe pressure measurement.²⁴

Although it is suggested that a high rate of comorbidity in patients with peripheral arterial disease is the rule in primary care,²⁵ our cohort showed no significant association between the presence of coronary heart disease or stroke and a low ankle brachial index after multivariate analyses. Among patients with peripheral arterial disease, prior evidence of coronary heart disease is more common (27%) than a prior stroke (9.4%). No statistically significant relation is shown between a low ankle brachial index and ischaemic stroke, which is comparable with our study.²⁶ With the diagnosis of peripheral arterial disease, indicating the presence of general atherosclerosis, antiplatelet therapy should be started and risk factors have to be treated.²⁷

Implications for clinical practice

This study indicates that the ECQ alone has an inadequate diagnostic value in general practice in patients with symptoms suggestive of intermittent claudication. Based on the high risk of the presence of peripheral arterial disease in even our lowest category (14.5%) it seems that in every patient with complaints suggestive of intermittent claudication the ankle brachial index should be performed in order to diagnose peripheral arterial disease. However, our clinical rule could differentiate between patient groups with extremely high and lower prevalence of peripheral arterial disease.

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Ethics committee

The study protocol was approved by the medical ethical committee of the Atrium Medical Centre Parkstad, Heerlen, The Netherlands

Competing interests

The authors have stated that there are none

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