

Peripheral Artery Disease of the Lower Limbs and Morbidity/Mortality in Type 2 Diabetics

Magdalena Bundó Vidiella,^a Carmen Pérez Pérez,^a Juan José Montero Alia,^a María Dolores Cobos Solórzano,^a Josep Aubà Llambrich,^a and Carmen Cabezas Peña^b

Objective. To study the relationship between the presence of peripheral artery disease (PAD) and the morbidity and mortality at 6 years, and the ankle-brachial index (ABI) as a predictor of morbidity and mortality in type 2 diabetes mellitus.

Design. Retrospective cohort study. Six years follow-up.

Setting. Urban health centre.

Participants. A total of 269 type 2 diabetics, of which 63 had PAD in 1996: 20 were previously diagnosed and 43 had an ABI of ≤ 0.90 .

Principal measurements. An appointment was made with the patients to find out the incidence of fatal and non-fatal microvascular and macrovascular events and the histories were reviewed. Six patients were excluded as all their data were not available.

Results. Thirty nine patients had died, of whom 19 had PAD in 1996 (30.1%) and 20 did not (9.7%) ($P=.001$).

Sixteen patients died in the group with an ABI of ≤ 0.9 (30.2%) and 21 (10.1%) in the group with normal ABI values ($P=.001$). 7 (13.2%) patients died due to a cardiovascular cause with a pathological ABI, and 8 (3.9%) with a normal value ($P=.009$).

The presence of PAD has been associated with a higher probability of having a non-fatal episode of ischaemic cardiac disease ($P=.04$), a cerebrovascular accident (CVA) ($P<.001$) and ulcers ($P=.006$). A low ABI has been associated with a higher probability of presenting with a fatal or non-fatal cardiovascular event ($P<.001$). After the multivariate analysis an increase was observed in cardiovascular (odds ratio [OR] = 2.81; 95% confidence interval [CI], 1.16–6.78), CVA (OR=3.47; 95% CI, 1.19–10.07), and cardiac failure (OR=6.75; 95% CI, 1.34–33.81), morbidity and mortality in diabetics with an ABI of ≤ 0.90 .

Conclusions. The type 2 diabetics with PAD present with a higher morbidity and mortality. The ABI is a good predictor of cardiovascular disease and heart failure morbidity and mortality.

Key words: Peripheral artery disease. Ankle/brachial index. Type 2 diabetes mellitus. Cardiovascular disease.

ARTERIOPATÍA PERIFÉRICA DE EXTREMIDADES INFERIORES Y MORBIMORTALIDAD EN PACIENTES DIABÉTICOS TIPO 2

Objetivo. Estudiar la relación entre la presencia de arteriopatía periférica (AP) y morbilidad a los 6 años, y el valor del índice tobillo-brazo (ITB) como predictor de morbilidad en la diabetes mellitus tipo 2.

Diseño. Estudio de cohorte retrospectivo. Seguimiento de 6 años.

Emplazamiento. Centro de salud urbano.

Participantes. En total, 269 diabéticos no insulino dependientes, de los cuales 63 tenían AP en 1996: 20 estaban previamente diagnosticados y 43 presentaban un ITB $\leq 0,90$.

Mediciones principales. Se citó a los pacientes para conocer la incidencia de eventos microvasculares y macrovasculares mortales y no mortales y se revisaron las historias. Se excluyó a 6 por no disponer de todos los datos.

Resultados. Han fallecido 39 pacientes, 19 de los cuales presentaban AP en 1996 (30,1%) y 20 no (9,7%) ($p = 0,001$).

Fallecieron 16 pacientes en el grupo con ITB $\leq 0,9$ (30,2%) y 21 (10,1%) en el grupo con valores de ITB normales ($p = 0,001$). Murieron por causa cardiovascular 7 pacientes (13,2%) con ITB patológico y 8 (3,9%) con exploración normal ($p = 0,009$). La presencia de AP se ha asociado con una mayor probabilidad de presentar un episodio no mortal de cardiopatía isquémica ($p = 0,04$), un accidente cerebrovascular (ACV) ($p < 0,001$) y úlceras ($p = 0,006$).

Un ITB bajo se ha asociado con una mayor probabilidad de presentar un evento cardiovascular, mortal o no ($p < 0,001$). Tras el análisis multivariable se observa un aumento de morbilidad cardiovascular (odds ratio [OR] = 2,81; intervalo de confianza [IC] del 95%, 1,16–6,78), ACV (OR = 3,47; IC del 95%, 1,19–10,07) e insuficiencia cardíaca (OR = 6,75; IC del 95%, 1,34–33,81) en los diabéticos con ITB $\leq 0,90$.

Conclusiones. Los diabéticos tipo 2 con AP presentan una mayor morbilidad. El ITB es un buen predictor de morbilidad cardiovascular e insuficiencia cardíaca.

Palabras clave: Arteriopatía periférica. Índice tobillo-brazo. Diabetes mellitus tipo 2. Enfermedad cardiovascular.

Spanish version available at
www.atencionprimaria.com/99.499

A commentary follow
this article
(pág. 145)

^aRonda Prim Health Centre, Mataró PCS, Barcelonès Nord i Maresme Community and Family Medicine Teaching Unit, Mataró, Barcelona, Spain.

^bPrimary Care Research Unit, Gol i Gurina Foundation, Primary Care Division of the Catalan Health Institute, Barcelona, Spain.

Correspondence: Dra. M. Bundó. Centro de Salud Ronda Prim. Ronda Prim, 35. 0830 Mataró. Barcelona. España.
E-mail: mbundo.bnm.ics@gencat.net

Manuscript received December 14, 2004.

Manuscript accepted for publication December 12, 2005.

Introduction

Peripheral artery disease (PAD) is the name given to arteriosclerotic disease of the lower limbs. Of the 3 important clinical manifestations of arteriosclerosis, it has the most benign prognosis, but it has already been observed in the Framingham study that patients with intermittent claudication had a risk of cardiovascular mortality twice as high as those patients of the same age and gender without claudication.¹

Subsequent studies have also shown that asymptomatic PAD leads to an increased risk of presenting with cardiovascular events and total mortality.²⁻⁴

The pocket Doppler is an easy to use instrument and helps to make the diagnosis of PAD easier in the asymptomatic patient. With the help of a sphygmomanometer, it is possible to determine the systolic blood pressure (SBP) in the posterior brachial, pedis and tibial arteries and thus be able to calculate the ankle-brachial index (ABI).^{5,6} Many studies have been carried out to evaluate the validity of the ABI and its value as a predictor of total morbidity and mortality.^{2-4,7-9} The early diagnosis of PAD, when the patient is still asymptomatic, enables treatment to be started sooner and improves the prognosis.^{10,11}

The calculation of the ABI can be particularly useful in the patient with type 2 diabetes mellitus (DM2), who has a high cardiovascular risk. PAD is one of the complications of DM2 and an etiological factor and poor prognosis of diabetes foot.¹²⁻¹⁶

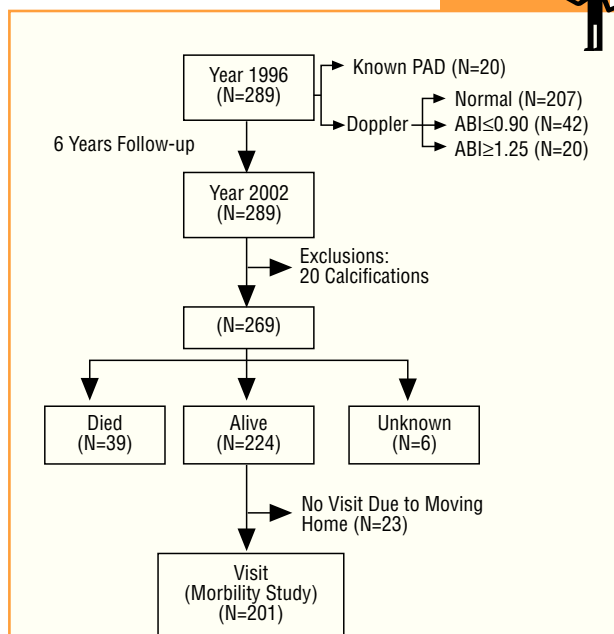
Few studies have been published on the prevalence of PAD in patients with DM2 where the Doppler has been used, and even less follow up studies on these patients to find out their prognosis.^{17,18} For this reason, a study was carried out in Mataró (Spain) in 1996 with the objective of finding out the prevalence of PAD in patients cared for in the health centre with DM2.¹⁹ A Doppler examination was carried out on diabetics without known PAD, to calculate the ABI of each lower limb. The prevalence of PAD was found to be 21.4%, higher than that diagnosed previously (6.9%).

In 2002 we set out to find out the state of the patients studied in 1996 and we began a new study with the objective of assessing the morbidity and mortality of the patients with DM2 after 6 years as regards the presence or not of PAD, and the value of the ABI as a predictor of cardiovascular and total morbidity and mortality in DM2.

Subjects and Methods

It is a retrospective follow-up study of a cohort over 6 years. The diabetics studied in 1996 participated in the study. Twenty patients who had signs of calcification, a fact that prevents find-

Material and methods



General Scheme of the Study

Retrospective study of a patient cohort with type 2 diabetes mellitus (DM2) ABI indicates anklebrachial index.

ing out the intraluminal state of the arteries, were excluded. Also excluded were those diabetics who could not be located and those where it was not known whether they were alive or dead, and in the morbidity study, those who had moved home and could not make the visit.

The data was collected from the 1st of July 2002 to the 28th of February 2003. An appointment was made with the patients and they all had an anamnesis performed, including a physical examination, an electrocardiogram, an ophthalmic examination, and a general laboratory analysis.

All the clinical histories were reviewed from when the Doppler examination was performed in 1996 up to the last visit to the centre and any new microvascular and macrovascular events were recorded.

The diagnostic criteria were the same as those used in 1996:

- PAD: a well documented diagnosis in the clinical history or an ABI of ≤ 0.90 in at least 1 of the lower limbs.
- Ischaemic heart disease: well documented episode of angina, acute myocardial infarction (AMI), or coronary surgical intervention.
- Ischaemic cerebrovascular accident (CVA): a well documented episode of ischaemic CVA or a stenosis of the supra-aortic trunks of $\leq 50\%$.
- Neuropathy: diagnosis present in the clinical history.
- Cardiac failure: diagnosis present in the clinical history.

- Nephropathy: confirmed presence of microalbuminuria (30–300 mg/24 h) or proteinuria (>300 mg/24 h) and/or creatinine >1.3 mg/dL.
- Retinopathy: diagnosis made by an ophthalmologist.
- Ulcers: recorded in the clinical history.
- Non-fatal cardiovascular event: new diagnosis of PAD or ischaemic heart disease or non-fatal CVA.
- Mortality: the passive files of the health centre and the only reference hospital (Mataró Hospital) were consulted to find out the cause of death of the patients who died during the study period. The causes were classified as: *a)* cardiovascular (AMI, ischaemic CVA, PAD, sudden death), and *b)* non cardiovascular (all the rest).

If the clinical histories were not found in the centre archives, the SIAP (Primary Care Computer System) database was consulted to find out if the patient had died or changed address.

The data was introduced into a computerised database and were analysed using the SPSS/PC, version 12 statistics program.

For the data analysis, the χ^2 test and binary logistic regression analysis (stepwise selection of the variables) were used. The variables introduced were: age, gender, years of evolution of the diabetes, blood pressure (BP), smoking habits, blood lipids, value of the ABI, and presence of cardiovascular disease in 1996 (known ischaemic heart disease, CVA, and PAD). As a test of goodness of fit, the Hosmer-Lemeshow test was used in all cases.

Patients without PAD in 1996 were compared with those who had PAD (well documented diagnosis in clinical history or ABI ≤ 0.90) and with those who had an ABI ≥ 0.90 .

Results

Of the 269 patients studied in 1996, 207 did not have PAD.

Of the 62 with PAD, 20 were previously diagnosed and 42 were diagnosed after an examination was made by Doppler. Table 1 shows the patient characteristics according to the ABI obtained. A higher prevalence of high BP and cerebrovascular disease was found among the patients with an ABI ≤ 0.90 .

Of the patients who did not have signs of calcification, the data of 6 were unknown, therefore they were excluded from the study (in 1996, 2 had a pathological ABI and 4 a normal ABI). The study of mortality was carried out with 263 diabetics.

Twenty three diabetics had moved home and were not able to come to the control visit, although it is known that they are alive. Of these, 2 belong to the known PAD group and 21 to the normal ABI group. There were no statistically significant differences between these patients and the patients in the study as regards age, gender, the presence of PAD, cardiovascular risk factors and the presence of ischaemic heart disease or CVA in 1996. After the exclusion, the morbidity study was carried out with 201 diabetics.

Mortality

Of the total diabetic patients studied, 39 (14.8%) had died, of whom 19 (31.6%) had PAD in 1996 and 20 (9.8%) did

TABLE 1 Principal Baseline Characteristics of the Diabetics Studied*

	ABI in 1996		
	0.91-1.24 (N=203)	≤ 0.90 (N=40)	P
Age (mean $\pm$ SD), y	62 $\pm$ 9.7	76 $\pm$ 9.8	.84
Males, N (%)	83 (40.8)	19 (47.5)	.28
Years with diabetes mellitus, mean $\pm$ SD	7.8 $\pm$ 7.8	9.5 $\pm$ 9.1	.07
Smoking, N (%)	62 (30.5)	17 (42.5)	.10
Hypertension, N (%)	109 (53.6)	29 (72.5)	.02
Ischaemic heart disease, N (%)	27 (13.3)	7 (17.5)	.3
Cerebrovascular accident, N (%)	22 (10.8)	14 (35)	<.01

*ABI indicates ankle-brachial index; SD, standard deviation.

TABLE 2 Relationship Between Peripheral Artery Disease Diagnosed Using Doppler in 1996 and Total and Cardiovascular Mortality at 6 Years*

Mortality	ABI in 1996			
	0.91-1.24 (N=203)	≤ 0.90 (n=40)	Difference of Proportions	95% CI
Total†	21 (10.3)	16 (40)	0.27	0.12-0.43
Cardiovascular†	8 (3.9)	7 (17.5)	0.12	0.01-0.24
Non-cardiovascular	10 (4.9)	4 (10)	0.04	-0.04 to 0.14

*ABI indicates ankle-brachial index; CI, confidence interval.

† $P < .001$

not have PAD ($P = .001$). Twenty one patients had died due to a cardiovascular cause, 12 (57.1%) with PAD and 9 (42.8%) without PAD ($P = .001$).

Of the 40 patients who had died 16 (40%) had a pathological ABI (≤ 0.90), and 21 (10.3%) with a normal ABI ($P = .001$). Seven (17.5%) with a pathological ABI had died due to a cardiovascular cause and 8 (3.9%) with a normal ABI (Table 2)

No statistically significant differences were found in the non-cardiovascular deaths.

Morbidity

Of the 201 patients who had been reviewed, those who had PAD in 1996 presented with a significantly higher number of ischaemic heart disease events ($P = .04$), CVA ($P < .001$), and ulcers ($P = .006$), as well as a higher probability of congestive heart failure ($P = .001$), neuropathy ($P = .01$), and retinopathy ($P = .05$). The differences were not significant for nephropathy (Table 3).

Morbidity and Mortality

On analysing the morbidity and mortality together, it was observed that 16 (29.1%) diabetics with PAD 1996 had a coronary event and 34 (61.8%) a cardiovascular event, as compared to 29 (14.6%) ($P = .01$) and 49 (24.6%) ($P < .001$) without PAD (Table 4). The patients who had

TABLE 3 Relationship Between Peripheral Artery Disease in 1996 and the Morbidity During the Follow-Up Period*

Mortality	PAD in 1996			
	No (N=162)	Yes (N=39) N (%)	Difference of Proportions	95% CI
Ischaemic heart disease	21 (12.9)	10 (25.6)	0.12	-0.01 to 0.27
CVA†	19 (11.7)	14 (35.9)	0.24	0.09-0.45
Cardiac failure†	4 (2.4)	6 (15.3)	0.12	0.11-0.73
Neuropathy†	17 (10.4)	10 (25.6)	0.15	0.01-0.39
Ulcers	6 (3.7)	6 (15.3)	0.11	0.03-0.61
Nephropathy	32 (19.8)	5 (12.8)	0.7	-0.05 to 0.19
Retinopathy	28 (17.3)	12 (30.8)	13.5	-0.02 to 0.29

*PAD indicates peripheral artery disease; CI, confidence interval; CVA, cerebrovascular accident.

† $P < .005$

TABLE 4 Relationship Between Peripheral Artery Disease in 1996 and Morbidity and Mortality Due to Ischaemic Heart Disease and Cardiovascular Disease*

Mortality	PAD in 1996			
	No (N=200)	Yes (N=55) N (%)	Difference of Proportions	95% CI
Ischaemic heart disease†	29 (14.6)	16 (29.1)	0.14	0.01-0.27
Cardiovascular†	49 (24.6)	34 (61.8)	0.37	0.23-0.51

*PAD indicates peripheral artery disease; CI: confidence interval.

† $P < .005$

TABLE 5 Relationship Between the Ankle-Brachial Index in 1996 and the Morbidity/Mortality Due to Ischaemic Heart and Cardiovascular Disease*

Mortality	ABI in 1996			
	0.91-1.24 (N=200)	≤0.90 (N=36) N (%)	Difference of Proportions	95% CI
Ischaemic heart disease	29 (14.5)	9 (25)	0.10	-0.04 to 0.25
Cardiovascular†	49 (24.5)	23 (63.9)	0.39	0.22-0.56

*ABI indicates ankle-brachial index; CI, confidence interval.

† $P < .001$.

a pathological ABI showed a higher probability of having a cardiovascular event ($P < .001$), but not a coronary one (Table 5).

In the multivariate analysis, a higher risk of cardiovascular morbidity and mortality (*odds ratio* [OR] =2.81; 95% confidence interval [CI], 1.16-6.78), CVA (OR=3.47; 95% CI, 1.19-10.07), and cardiac failure (OR=6.75; 95% CI, 1.34-33.81) was observed among the diabetics with an ABI≤0.90 (Tables 6 and 7). If the cardiovascular morbidity and mortality is analysed excluding the patients with known ischaemic heart disease, CVA and/or PAD in 1996, there is still an increased risk in patients with a pathological ABI (OR=3.01; 95% CI, 1.38-6.59; $P=.006$).

TABLE 6 Factors Associated With Different Types of Mortality in Type 2 Diabetics. Logistic Model With 236 Observations*

	OR	95% CI	P	Adjustment to the χ^2 de Hosmer-Lemeshow Model
Total mortality† (N=243)				
Age	1.08	1.03-1.14	.001	7.44
Woman	4.47	1.61-12.42	.004	$P=.489$
Cardiovascular mortality†				
Age	1.07	1.05-1.145	.035	10.05
Woman	5.14	1.26-20.97	.022	$P=.261$
MM due to IHD†				
Age	1.05	1.01-1.09	.012	10.412
Smoking	3.39	1.52-7.51	.003	$P=.237$
Cardiovascular MM†				
ABI	2.81	1.16-6.78	.021	10.04
Age	1.08	1.04-1.12	<.001	$P=.262$
Smoking	4.56	2.19-9.49	<.001	

*OR indicates odds ratio; CI, confidence interval; ABI, ankle-brachial index; MM, morbidity and mortality; IHD, ischaemic heart disease.

†Dependent variable of each type of mortality.

Patients with already known peripheral artery disease in 1996 and deaths by unknown cause (except in the total mortality section).

TABLE 7 Factors Associated With Different Types of Morbidity in Non-Insulin Dependent Diabetics. Logistic Model With 191 Observations

	OR	95% CI	P	Adjustment to the χ^2 de Hosmer-Lemeshow Model
CVA†				
ABI	3.47	1.19-10.07	.022	6.83
Age	1.08	1.02-1.13	.003	$P=.554$
Smoking	3.07	1.14-8.28	.026	
Cardiovascular disease	6.15	2.20-17.16	.001	
Ischaemic heart disease†				
Cardiovascular disease	25.5	8.96-72.5	<.001	Not estimated
Neuropathy†				
	—	—	—	—
Nephropathy†				
Years of evolution	1.05	1.00-1.09	.02	3.01
				$P=.884$
Cardiac failure†				
ABI	6.75	1.34-33.81	.02	Not estimated
Retinopathy†				
Years evolution	1.07	1.02-1.11	.001	10.05
				$P=.261$

*OR indicates odds ratio; CI, confidence interval; CVA, cerebrovascular accident; ABI, ankle-brachial index.

†Dependent variable of each type of morbidity. Reference category: males. Patients with already known peripheral artery disease in 1996 have been excluded.

Discussion

The results obtained in our study show an increase in cardiovascular morbidity and mortality and total mortality in patients with PAD in 1996 and also in those who just had an ABI of ≤ 0.90 .

The higher prevalence of high BP and cerebrovascular disease among patients with an ABI ≤ 0.90 has already been reported by other authors.^{8,9,17} On performing the multivariate analysis a higher risk of cardiovascular morbidity and mortality persists among patients with an abnormal ABI. We only know of 2 studies published on the prevalence and follow up of PAD in patients with DM2. Beach et al¹⁸ studied 252 diabetics using the ABI measurement and at 2 years of follow-up the mortality among diabetics with PAD was 22%, while in those who did not have PAD it was 4% ($P=.0005$). Kallio et al¹⁷ followed up 130 patients with NIDDM for 11 years and also found a higher mortality among those who had both symptomatic and asymptomatic PAD at the beginning of the study (58% compared to 16%; $P=.001$).

A large number of prospective studies have been carried out on non-diabetics that show a higher risk of cardiovascular and total mortality in patients with an ABI < 0.90 .^{2-4,20}

As regards morbidity, we have found that the presence of PAD is associated with a higher probability of not only suffering from coronary or cerebrovascular disease already reported by other authors,²⁰⁻²³ but also a higher prevalence of congestive cardiac failure, retinopathy, and neuropathy. Although Dolan et al²⁴ have already described the relationship between PAD and neuropathy, we know of no cohort study carried out only on patients with diabetes where the morbidity associated to the presence or not of PAD was studied.

One of the weak points of the study is the losses that occurred over the 6 years. If we exclude the patients with signs of calcification, only 10.7% of the patients have been lost and 2% in the mortality study.

Another point of conflict is the evaluation of events retrospectively, since the data has been collected basically from the clinical history. However, we believe that the information gathered has been correct, since the health centre has a very stable health staffing levels, and only one reference hospital, which makes the follow up the patient easier.

Another limitation of the study is the number of cases, which was adequate to study the relationship of ABI with mortality but inadequate for the study of the morbidity. It requires a follow-up with a much larger group of diabetics, as has been carried out on a general population, to find out the true value of the ABI as a predictor of complications in Type 2.

Important clinical studies have been published in recent years in the field of cardiovascular diseases. Some of them have newly introduced the use of ABI to make the diag-

Discussion
Key points

What Is Known About the Subject

- Patients with both symptomatic and asymptomatic PAD have an increased cardiovascular risk.
- The pocket Doppler is an easy to use instrument which can diagnose asymptomatic PAD.
- The ankle-brachial index is a good predictor of cardiovascular events, since it indicates the presence of arteriosclerotic disease.
- PAD is a complication of non-insulin dependent diabetes mellitus.

What This Study Contributes

- There are few follow up studies of non-insulin dependent diabetics with PAD diagnosed using the pocket Doppler, and none published in Spain.
- At 6 years of follow up a higher morbidity/mortality has been found among diabetic patients with both symptomatic and asymptomatic PAD.
- The results suggest that the ABI is a good predictor of total and cardiovascular mortality in non-insulin dependent diabetics.

nosis of PAD and to be able to analyse these patients within separate sub-groups, similar to that carried out with ischaemic heart disease and CVA.²⁵ Others have considered PAD among the principal events studied^{26,27} and, along with other studies,²⁸ they have also demonstrated the efficacy of the strict control of risk factors for arteriosclerosis in these patients. These studies are the ones that have led to the publication of the most important recommendations for the prevention and treatment of cardiovascular disease by advising the application of secondary prevention measures in the patient with PAD, both symptomatic as well as that diagnosed solely using the ABI.²⁹⁻³¹ The American Heart Association³² recommends measuring the ABI on all those over 50 years old, with the intention of identifying patients with a high cardiovascular risk and thus be able to treat them more aggressively, and also to be more active in looking for coronary and cerebral disease.

All this data leads us to emphasise the importance of incorporating the Doppler into Primary Care clinics, thus

being able to identify, with a simple examination, the patients with a higher cardiovascular risk and be able to offer them a treatment which has shown to be efficient.

References

1. Kannel WB, Skinner JJ, Schwartz MJ, Shuerleff D. Intermittent claudication. Incidence in the Framingham study. *Circulation*. 1970;XLI:875-83.
2. Criqui M, Langer RD, Fronek A, Feigelson HS, Klauber MR, et al. Mortality over a period of 10 years in patients with peripheral arterial disease. *N Engl J Med*. 1992;326:381-6.
3. Vogt MT, Cauley JA, Newman AB, Kuller LH, Hulley SB. Decreased ankle/arm blood pressure index and mortality in elderly women. *JAMA*. 1993;270:465-9.
4. Leng GC, Fowkes FG, Lee AJ, Dunbar J, Housley E, Ruckley CV. Use of ankle brachial pressure index to predict cardiovascular events and death: a cohort study. *BMJ* 1996;313:1440-4.
5. Yao ST, Hobbs JT, Irvine WT. Ankle systolic pressure measurements in arterial disease affecting the lower extremities. *Br J Surg*. 1969;56:676-701.
6. Prineas RJ, Chairman PD, Harland WR, Janzon L, Kannel W. Recommendations for use non-invasive methods to detect atherosclerotic peripheral arterial disease in population studies. American Heart Association Council on Epidemiology. *Circulation*. 1982;65:A1562-5.
7. Ouriel K, Mc Donnell AE, Metz CE, Zarins CK. A critical evaluation of stress testing in the diagnosis of peripheral vascular disease. *Surgery*. 1982;91:686-93.
8. McKenna M, Wolfson S, Kuller L. The ratio of ankle and arm arterial pressure as an independent predictor of mortality. *Atherosclerosis*. 1991;87:119-28.
9. Hooi JD, Kester AD, Stoffers HE, Rinkens PE, Knottnerus JA, van Ree JW. Asymptomatic peripheral arterial occlusive disease predicted cardiovascular morbidity and mortality in a 7-year follow-up study. *J Clin Epidemiol*. 2004;57:294-300.
10. Hiatt AJJ. Medical treatment of peripheral arterial disease and claudication. *N Engl J Med*. 2001;344:1608-21.
11. Criqui MH, Denenberg JO, Langer RD, Fronek A. The epidemiology of peripheral arterial disease: importance of identifying the population at risk. *Vascular Med*. 1997;2:221-6.
12. Brand FN, Abbott RD, Kannel WN. Diabetes, intermittent claudication, and the risk of cardiovascular events. *Diabetes*. 1989;38:504-9.
13. Orchard TJ, Strandness E. Assessment of peripheral vascular disease in diabetes. Report and recommendations of an International Workshop. *Circulation*. 1993;88:819-28.
14. Becks PJ, Mackay AJC, Neeling JND, de Vries H, Bouter LM, Heine RJ. Peripheral arterial disease in relation to glycemic level in an elderly Caucasian population: the Hoorn Study. *Diabetologia*. 1995;38:86-96.
15. Miettinen H, Salomaa V. Diabetes and macrovascular disease. *J Cardiovascular Risk*. 1997;4:76-82.
16. Jude EB, Oyibo SO, Chalmers N, Boulton AJ. Peripheral arterial disease in diabetic and nondiabetic patients. A comparison of severity and outcome. *Diabetes Care*. 2001;24:1433-7.
17. Kallio M, Forsblom C, Groop PH, Groop L, Lepantalo M. Development of new peripheral arterial occlusive disease in patients with type 2 diabetes during a mean follow-up of 11 years. *Diabetes Care*. 2003;26:1241-5.
18. Beach KW, Bedford GR, Bergelin RO, Martin DC, Vandenberghe N, Zaccardi M, et al. Progression of lower-extremity arterial occlusive disease in type II diabetes mellitus. *Diabetes Care*. 1988;11:464-72.
19. Bundó M, Auba J, Vallés R, Torner O, Pérez AM, Massons J. Arteriopatía periférica en la diabetes mellitus tipo 2. *Aten Primaria*. 1998;22:5-11.
20. Ogren M, Hedblad B, Isacson SO, Janzon L, Jungquist G, Lindell SE. Non-invasively detected carotid stenosis and ischemic heart disease in men with leg arteriosclerosis. *Lancet*. 1993;342:1138-41.
21. Abbot RD, Petrovitch H, Rodríguez BL, Yano K, Schatz IJ, Popper JS, et al. Ankle-brachial blood pressure in men >70 years of age and the risk of coronary heart disease. *Am J Cardiol*. 2000;86:280-4.
22. Abbot RD, Rodríguez BL, Petrovitch H, Yano K, Schatz IJ, Popper JS, et al. Ankle-brachial blood pressure in elderly men and the risk of stroke. The Honolulu Heart Program. *J Clin Epidemiol*. 2001;54:973-8.
23. Zheng ZJ, Sharrett AR, Chambless LE, Rosamond WD, Nieto FJ, Sheps DS, et al. Associations of ankle-brachial index with clinical coronary heart disease, stroke and preclinical carotid and popliteal atherosclerosis: the Atherosclerosis Risk in Communities (ARIC) Study. *Atherosclerosis*. 1997;131:115-25.
24. Dolan NC, Liu K, Criqui MC, Greenland P, Guralnik JM, Chan CH, et al. Peripheral artery disease, diabetes, and reduced lower extremity functioning. *Diabetes Care*. 2002;25:113-20.
25. The Heart Outcomes Prevention Evaluation Study Investigators. Effects of an angiotensin-converting-enzyme inhibitor, ramipril, on cardiovascular events in high-risk patients. *N Engl J Med*. 2000;342:145-53.
26. MRC/BHF Heart Protection Study of cholesterol lowering with simvastatin in 20536 high-risk individuals: a randomised placebo-controlled trial. *Lancet*. 2002;360:7-22.
27. Adler A, Stevens R, Neil A, Stratton I, Boulton A, Holman R. UKPDS 59: hyperglycaemia and other potentially modifiable risk factors for peripheral vascular disease in type 2 diabetes. *Diabetes Care*. 2002;25:894-9.
28. Mehler PS, Coll JR, Estacio R, Esler A, Schier RW, Hiatt WR. Intensive blood control reduces events in patients with peripheral arterial disease and type 2 diabetes. *Circulation*. 2003;107:753-6.
29. Dormandy JA, Rutherford RB. Management of peripheral arterial disease (PAD). TASC Working Group. Transatlantic Inter-Society Consensus (TASC). *J Vasc Surg*. 2000;31:S1-296.
30. The Seventh Report of the Joint National Committee on prevention, evaluation, and treatment of the high blood pressure. *JAMA*. 2002;289:2560-72.
31. Linton MF, Fazio S; National Cholesterol Education Program (NCEP)-Adult Treatment Panel (ATP III). A practical approach to risk assessment to prevent coronary artery disease and its complications. *Am J Cardiol*. 2003;92:i19-26.
32. Pearson TA. New tools for coronary risk assessment. What are their advantages and limitations? *Circulation*. 2002;105:886-92.

COMMENTARY

Peripheral Artery Disease and the Usefulness of the Ankle-Brachial Index in the Diabetic Patient

Ramón Veras Castro

Family Medicine, San Xosé Health Centre, A Coruña, Spain.

Both symptomatic and sub-clinical peripheral artery disease causes a large decrease in functional capacity and quality of life, leads to limb amputations and increases the risk of death. These patients most probably have other ischaemic cardiac diseases, such as myocardial infarction or stroke. It is, in fact, a marker of atherothrombotic disease in other vascular regions.

In patients with diabetes, the presence of arterial disease is increased. It is particularly localised in distal zones (femoral, popliteal, and tibial area), unlike other risk factors such as smoking and hypertension, associated with disease in the aorta-iliac-femoral vessels. Owing to this localisation of the disease and its association with neuropathy, which reduces the sensitivity of the lower limbs, patients with diabetes are diagnosed later with peripheral artery disease. By the time the symptoms appear they have a higher risk of amputation and other fatal cardiovascular diseases.

The study by Bundó et al characterises the vascular risk of the diabetic patient with symptomatic or asymptomatic peripheral artery disease very well. It is a study carried out in Spain in a primary care setting, with a follow-up of 6 years on patients with diabetes and peripheral artery disease, in which it demonstrated the increased prevalence of clinical and sub-clinical disease, which goes from 6.9% to 21.4% on measuring the ankle-brachial index (ABI), on all known diabetics in their health centre. The follow-up of these patients showed an increase in the morbidity/mortality to be seen and a higher probability of microvascular and macrovascular complications of diabetes: ischaemic heart disease, stroke, cardiac failure, neuropathy and retinopathy as well as skin ulcers. An increase in nephropathy was not found, perhaps because this association required a larger number of cases in the study. Finally, the incorporation of this technique into daily clinical practice is recommended.

The ABI is a non-invasive, quantitative and reliable diagnostic method, as well as a prognostic predictor of peripheral artery disease. It is validated in relation with the di-

Key Points

- The prevalence of peripheral artery disease is increased in diabetic patients and is associated with a higher risk of cardiovascular morbidity and mortality.
- The diagnosis of arterial disease should not change the treatment of the diabetes, but reinforce the therapeutic approach by the doctor faced with a patient with a high cardiovascular risk.
- The ankle-brachial index could be incorporated routinely into daily clinical practice in primary care if the nursing staff took it on as their task.
- The ankle-brachial index should be indicated in the study of the patient with diabetes, so as to be able to carry out a prognostic staging of arterial disease and check its evolution, but not a screening test if no therapeutic changes are introduced.

agnostic reference, angiography, with a sensitivity of 95% and a specificity of almost 100% for a cut off point of abnormality of <0.91 . This method also has limitations, on giving false negative results in some symptomatic patients with moderate aorta-iliac stenosis and in people who have calcified, difficult to compress arteries, as happens in older people and in some patients with diabetes.

The American Diabetes Association recommends measuring the ABI in patients >50 years old with diabetes and a repeat test every 5 years if it is normal, with the purpose of obtaining an early sub-clinical diagnosis and to begin applying preventive measures which may prevent an amputation.^{1,2} However, according to the PAPPs (Preventive Activities and Health Promotion Program) recommenda-

tions (adaptation of the European Cardiovascular Prevention Guide) a few changes should be made, as regards aggressive therapy and special care of the feet, whether the patient with diabetes, may have arterial disease or not.³ We should remember that the guide places non-insulin dependent diabetes and insulin dependent diabetes with microalbuminuria in the high cardiovascular risk group, with treatment recommendations similar to established peripheral artery disease. The general impression is that these recommendations are sub-optimal and that the diagnosis of artery disease reinforces a more aggressive attitude by the doctor. In the SMART study, screening of asymptomatic cardiovascular disease is carried out with non-invasive imaging techniques in patients classified as high or low risk according to the European Cardiovascular Prevention Guide. In this, an ABI<0.90 was only found in 5 patients out the 545 initially classified as low risk. In other words, only 0.91% of the low risk patients were reclassified to high risk by the sub-clinical diagnosis of artery disease.⁴

The measurement of ABI in primary care is feasible. The technique takes 10-15 minutes to perform, but to be used routinely it would be necessary for the nursing staff to assume this task. The ABI enables a diagnosis of artery disease to be made, to establish the baseline value and to make a prognostic staging of the disease. Its follow-up enables us to understand the evolution of the disease and it is a prognostic factor of cardiovascular mortality (Bundó et al). In any case, it is difficult to recommend it as a screening test, since the diagnosis of artery disease should not change the therapeutic approach, unless diabetes with arterial disease in future investigations is classified as very high risk and may change the treatment objectives or different treatments may be used for this diabetic group. To insist that the doctor complies with the recommendations of the guides, it would be more logical to introduce this

test as a screen now. Future lines of investigation is the presence of an abnormal ABI in patients with impaired fasting glucose or glucose intolerance.⁵ These have lower vascular risk and an abnormal ABI could lead to a change in the therapeutic approach. Another possible line is the prognostic significance of a high ABI, since in some studies it has also been associated with an increase in cardiovascular mortality.⁶

References

1. American Diabetes Association. Peripheral arterial disease in people with diabetes. *Diabetes Care*. 2003;26:3333-41.
2. Hirsch et al. ACC/AHA 2005 guidelines for the management of patients with peripheral arterial disease (lower extremity, renal, mesenteric, and abdominal aortic): executive summary a collaborative report from the American Association for Vascular Surgery/Society for Vascular Surgery, Society for Cardiovascular Angiography and Interventions, Society for Vascular Medicine and Biology, Society of Interventional Radiology, and the ACC/AHA Task Force on Practice Guidelines. *J Am Coll Cardiol*. 2006;47:1239-312.
3. Villar-Álvarez F, Maiques-Galán A, Brotons-Cuixart C, Torcal-Laguna J, Banegas-Banegas JR, Lorenzo-Piqueres A, et al. Recomendaciones preventivas cardiovasculares en atención primaria. *Aten Primaria*. 2005;36 Suppl 2:11-26.
4. Goessens B, Visseren F, Algra A, Banga JD, van der Graaf Y. Screening for asymptomatic cardiovascular disease with non-invasive imaging in patients at high-risk and low-risk according to the European Guidelines on Cardiovascular Disease Prevention: The Smart study. *J Vasc Surg*. 2006;43:525-32.
5. Barzilay J, Sprekermeyn CF, Fuller JH, Burke GL, Bittner V, Gottdiener JJ, et al. Prevalence of clinical and isolated subclinical cardiovascular disease in older adults with glucose disorders. The Cardiovascular Health Study. *Diabetes Care*. 2001;24: 1233-9.
6. O'Hare A, Katz R, Shlipak M, Cushman M, Newman A. Mortality and cardiovascular risk across the Ankle-Arm Index spectrum. Results from the Cardiovascular Health Study. *Circulation*. 2006;113:388-93.