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Ankle-brachial index, risk of clinical fractures, mortality and low bone mass in nursing home residents

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Abstract. – OBJECTIVE: To assess whether the ankle-brachial index is related to functional impairment, clinical fractures and mortality in nursing home residents, and whether this effect is associated or not with low bone mass.

PATIENTS AND METHODS: Prospective, observational, non-interventional cohort study in non-dependent nursing home residents. The following determinations were made: BUN, creatinine, cholesterol, triglycerides, calcium, phosphorous 25-hydroxyvitamin D, parathyroid hormone and cystatin C in blood and microalbuminuria in urine. Bone mass was determined by measuring the peripheral densitometry of the calcaneus. The Katz Index of independence, the Tinetti Balance and Gait evaluation and functional tests were administered. The ankle-brachial index was measured and patients divided into three groups (ankle-brachial index > 1.40, 1.40-0.90, and < 0.90). Clinical fractures and general and vascular mortality were measured for 20 months.

RESULTS: Seventy-two patients were included. There was an inverse relationship between age and the ankle-brachial index (p = 0.022) but no association with bone mass, biochemical tests, clinical fractures and the degree of independence. There was increased mortality in patients with increased or reduced ABI.

CONCLUSIONS: An altered ankle-brachial index is a marker of vascular mortality in elderly nursing home residents.

Key Words:
Ankle brachial index, Low bone mass, Elderly, Mortality.

Introduction

Studies have shown an association between osteoporosis and atherosclerosis[1-3]: persons with low bone mass, significantly-reduced bone mass and those presenting fractures have increased overall mortality and, specifically, vascular mortality. It has been reported that low bone mass is a predictor of coronary heart disease, with an odds ratio greater than that of traditional risk factors. This relationship was observed only in non-vertebral sites, and remained after adjusting for age and traditional cardiovascular risk factors[4]. Cohort studies have found a relationship between peripheral artery disease and reduced bone mass, primarily at the femur, in postmenopausal women[5]. Other prospective studies have found that the rate of bone loss at the hip and spine was greater in women, who had greater reductions in the ankle-brachial index (ABI)[6].

A prospective study of 2,262 postmenopausal women found that aortic calcification was an independent risk factor for hip fracture (odds ratio = 2.3), together with age and the body mass index (BMI). This may be due to various factors: asymmetry of the femoral blood flow caused by atherosclerosis which could result in greater demineralization in the affected side, greater bone loss in women with a reduced ABI, atherosclerosis in the vessels reaching the hip in patients with hip fractures and a negative bone equilibrium accompanied by a reduction in formation in patients with atherosclerotic involvement of the hip vessels[7].

An association between peripheral arterial disease and low bone mineral density (BMD) was reported by the Rotterdam study[8], which investigated the relationship between BMD and peripheral arterial disease in Caucasians of both sexes aged > 55. The results showed that women with low BMD at the femoral neck had an increased risk of peripheral arterial disease, but that men

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did not. A posterior study showed an association between peripheral arterial disease and BMD in in both non-Caucasian men and women[6], with peripheral arterial disease being an indirect measure of generalized atherosclerosis.

Reduced mobility is a common cause of vitamin D deficiency, which has a negative impact on the progression of peripheral arterial disease. Symptoms of fatigue, muscle and bone pain, weakness and difficulty walking are common symptoms in peripheral arterial disease, contributing to the immobilization so prevalent in advanced stages of the disease[9]. Patients with peripheral arterial disease have low levels of 25-hydroxyvitamin D (25(OH)D), with up to 70% having levels of < 9 ng/ml. The stages of peripheral arterial disease are inversely associated with 25(OH)D levels, suggesting that patients with restricted mobility secondary to vascular pathology have less exposure to the sun and, thus, lower levels of vitamin D[9,10].

Bone loss is associated with the progression of aortic calcification, suggesting a common factor which may act by promoting atherosclerosis and osteoporosis in the vascular and bone cells. Proinflammatory cytokines have pro-atherogenic effects on the vascular wall and are potent modulators of osteoclasts and accelerated bone loss. The RANK/RANKL system plays a role in osteoclast differentiation and vascular calcification[11].

The aim of this study was to assess whether the ankle-brachial index was associated with functional impairment, clinical fractures and mortality in elderly nursing home residents and whether this was associated with or independent of low bone mass.

Patients and Methods

We made a non-interventional, prospective, observational cohort study in non-dependent elderly residents of the Parquesol nursing home (Valladolid, Spain). Inclusion criteria were age ≥ 65 and residence in the nursing home. Exclusion criteria were people who were bedridden or had diminished mobility that precluded functional testing and those who did not wish to participate.

At inclusion, blood was extracted from all participants and a urine sample was collected. The following determinations were made: BUN, creatinine, total cholesterol, triglycerides, glucose, calcium, phosphorous and microalbuminuria using a Hitachi 917 automated analyser. Parathyroid hormone (PTH) was measured by electrochemiluminescence (Roche Diagnostics GmbH®, Mannheim, Germany), 25(OH)D by high performance liquid chromatography, and cystatin C by immunonephelometry (N Latex Cistatin C, Dade Behring GmbH Marburg, Germany). The presence of cardiovascular diseases and treatments were also recorded. Clinical fractures and mortality were recorded for 20 months.

Independence was measured using the Katz Index of Independence in Activities of Daily Living (Katz ADL)[12-14]. The Tinetti Balance and Gait Evaluation was used to detect the risk of falls[12,15-17]. Lower extremity function was evaluated by examining the ability to stand with the feet together in the side-by-side, semi-tandem, and tandem positions, time to walk 8 feet, and time to rise from a chair and return to the seated position 5 times. These tests are predictors of falls, disability, institutionalization and death[18-20]. For accuracy, these tests were made using a Van Allen chronometer and a 3-metre tape measure.

Bone mass was determined by peripheral densitometry of the calcaneus using a PIXI-Lunar® DXA peripheral densitometer (Madison, WI, USA). BMD was expressed in g/cm^2 and the T-score.

The ABI was measured using a BOSO ROID I sphygmomanometer, a 120 Vascutrack Doppler 8 MHz ultrasound transducer and transducer gel. Briefly, the patient was placed in the supine decubitus position and systolic blood pressure (BP) was measured in both arms and in both legs (anterior and posterior tibial artery). The right ABI was calculated by dividing the maximum systolic BP in the right ankle by the maximum systolic BP of the arms. The left brachial index was calculated using the same procedure[21]. The lowest of the two values was used to represent the ABI in each patient. Patients were classified into three groups: ABI (ABI) < 0.90 (diagnosis of peripheral arterial disease), ABI 0.90-1.40, and ABI > 1.40 (indicating the presence of non-compressible arteries in the legs). The presence of non-compressible arteries may indicate calcification of the media of the artery (a common situation in patients with diabetes, those receiving chronic steroid treatment, those with chronic kidney disease and the elderly) which is associated with increased mortality[22-24].

The study was approved by the Clinical Research Committee of the Hospital Universitario Río Hortega Valladolid, Spain. All patients or their representatives gave written informed consent to participate in the study.

Statistical Analysis

Quantitative variables were described as means ± standard deviation (SD) in the case of normal distributions, and medians and interquartile range (IQR) for non-normal distributions. The Kolmogorov-Smirnov test was used to establish the normality of distribution. Qualitative variables were described using absolute and relative frequencies (percentages). The 95% confidence intervals (CI) of the parameters obtained were calculated. Missing values were expressed as percentages or absolute values. Associations between qualitative variables were studied using the 2 test with Yates correction, Fisher's exact test or the likelihood ratio, depending on the operating conditions. Differences between independent means were assessed using parametric or non-parametric statistical tests required by the operating conditions (Student's *t* or Mann-Whitney U tests for two groups, and ANOVA or Kruskal-Wallis H test for comparisons between > 2 groups). Logistic regression analysis was made to assess falls during the study follow up, including the median age of the study sample, sex and variables that were significant in the bivariate analysis. Statistical significance was established as $p \leq 0.05$. The analysis was made using SPSS for Windows v. 15.0 (SPSS Inc. 1989-2006 Chicago, IL, USA).

Results

Of the 183 elderly nursing home patients considered, 80 met the inclusion criteria, and the ABI was obtained in 72 patients, who were included in the final analysis. Eight patients had an ABI > 1.40, 64 an ABI of 0.90 and 1.40, and 18 an ABI < 0.90.

Of the 72 patients included, 56 (77.8%) were female, the mean age was 84.7 years and the mean BMI was 29 ± 5 kg/m^2. The mean age was 88 ± 5 years in patients with an ABI < 0.90, 83 ± 7 years in those with an ABI of 0.90-1.40, and 82 ± 7 years in those with an ABI > 1.40 (p = 0.022). More females had a reduced ABI (ABI > 1.40, 50% vs ABI 1.40-0.90, 83% vs ABI > 0.90 78%) although the differences were not statistically significant.

Peripheral densitometry showed that reductions in the ABI were accompanied by reductions in the BMD and the T-score, although the differences were not significant (Table I). Statistically significant higher levels of microalbuminuria were associated with reductions in the ABI (Table II).

No significant differences were found in the Katz index or the functional tests according to the ABI (Table I). No significant differences were found in clinical fractures at 20 months according to the ABI (ABI > 1.40, 0% vs ABI 0.90-1.40, 16% vs ABI < 0.90, 6%; p = NS).

Analysis of mortality at 20 months of follow-up showed that patients with an ABI > 1.40 and those with an ABI < 0.90 had higher mortality than other patients, although the differences were not significant (Table I). Analysis of the causes of death showed that patients with an ABI < 0.90 had significantly more deaths due to cardiovascular accidents than the other groups and patients with an ABI > 1.40 had significantly more cardiac deaths than the other groups (Table III).

Table I. Ankle-brachial index, bone mineral density, T-score, degree of independence, function and mortality.

Variable		ABI > 1.40 (N=8)	ABI 1.40-0.90 (N=46)	ABI < 0.90 (N=18)	SIG
Bone mineral density (g/cm^2)		0.43 ± 0.09	0.37 ± 0.14	0.37 ± 0.18	NS
T-score		-1.38 ± 0.70	-1.60 ± 1.40	-1.97 ± 1.88	NS
Degree of independence:					
Katz index	A	7 (87.5%)	34 (65.2%)	12 (66.7%)	NS
	B	1 (12%)	13 (28.3%)	4 (22.2%)	
	C	0	2 (4.3%)	0	
	G	0	1 (2.2%)	2 (11.1%)	
Degree of functionality	Tinetti gait[12]	11.75 ± 0.71	10.56 ± 2.05	10.59 ±1.94	NS
	Tinetti balance[16]	15.38 ± 1.19	13.36 ± 2.85	12.76 ± 3.95	NS
	Balance[4]	3.13 ± 1.25	2.36 ± 1.21	2.12 ± 1.27	NS
	Gait[4]	2.50 ± 0.54	2.13 ± 1.06	2.12 ± 1.17	NS
	Chair test[4]	2.75 ± 0.71	2.42 ± 1.34	2.47 ± 1.24	NS
Mortality	No	6 (75%)	41 (89.1%)	14 (77.8%)	NS
	Yes	2 (25%)	5 (10.9%)	4 (22.2%)	

Table II. Ankle-brachial index and biochemical variables.

Variable	ABI > 1.40 (N=8)	ABI 1.40-0.90 (N=46)	ABI < 0.90 (N=18)	SIG
BUN (10-50 mg/dl)	46.43 ± 15.37	46.89 ± 13.38	55.89 ± 22.68	NS
Total cholesterol (110-240 mg/dl)	216.00 ± 49.37	209.95 ± 36.96	203.89 ± 47.29	NS
Triglycerides (50-170 mg/dl)	104.86 ± 59.49	108.41 ± 38.45	108.17 ± 43.56	NS
Creatinine 0.6-1.1 mg/dl	0.90 ± 0.20	0.77 ± 0.20	0.85 ± 0.33	NS
Calcium (8.1-10.4 mg/dl)	9.57 ± 0.53	9.46 ± 0.43	9.41 ± 0.44	NS
Phosphorous (2.7-4.5 mg/dl)	3.67 ± 0.46	3.68 ± 0.52	3.70 ± 0.60	NS
High density lipids (35-70 mg/dl)	55.14 ± 11.94	57.91 ± 16.06	56.00 ± 13.50	NS
Cr in urine (66-132 mg/dl)	84.04 ± 24.17	66.05 ± 38.03	64.59 ± 27.99	NS
Parathyroid hormone (12-72 pg/ml)	56.39 ± 17.51	59.79 ± 33.57	75.07 ± 47.64	NS
Albumin (2.5-4.5 g/dl)	4.01 ± 0.31	3.91 ± 0.30	3.81 ± 0.26	NS
Microalbuminuria (0-30 mg/L)	4.76 ± 4.23	14.68 ± 31.27	59.06 ± 104.29	0.018
Cistatin C (0.53-0.95 mg/L)	1.10 ± 0.30	1.03 ± 0.24	1.20 ± 0.34	NS
25 OH vitamin D (30-155 nmol/L)	19.95 ± 6.82	19.07 ± 8.23	17.01 ± 6.56	NS

Discussion

The results of this study show that patients with an ABI of < 0.90 were significantly older than patients with an ABI > 0.90, consistent with the results of other studies which found that peripheral arterial disease increased with age, which was the main risk marker[22]. We found no significant differences in ABI according to sex.

Our results show that reductions in the ABI were related to reductions in BMD and the T-score, although the differences were not significant. However, other studies have found an association between low BMD and peripheral arterial disease[6,8]. However, the population analyzed in the Mr and Ms Os study were Asian[6] and those included in the Rotterdam studies were younger than our patients and bone mass was determined by central DXA[8].

We found that reductions in the ABI were accompanied by reductions in 25(OH)D although the differences were not significant. Likewise, patients with an ABI > 1.40 and those with an ABI < 0.90 had and increased levels of cystatin C, although the differences were not significant. Microalbuminuria levels were significantly associated with reduced ABI. As previously stated, up to 70% of patients with peripheral arterial disease have 25(OH)D levels < 9 ng/ml (22.5 nmol/L), and there is an inverse association between 25(OH)D levels and peripheral arterial disease[9,10]. Microalbuminuria is a marker of impaired renal function and a marker of cardiovascular risk, and increases in patients with reduced ABI, indicating peripheral arterial disease. Cystatin C is a marker of renal function and cardiovascular risk, and is sometimes used as a biomarker in the diagnosis of asymptomatic or atypical manifestations of peripheral arterial disease[25,26]. In one study, cystatin C was associated with a rapid reduction in renal function and an increased risk of heart failure and peripheral artery disease[27].

We found no significant association between tests measuring the degree of independence and function with the ABI. Likewise, there was no significant association between the ABI and fractures at 20 months of follow up.

Table III. Ankle-brachial index and causes of mortality.

Mortality	ABI > 1.40 (N=2)	ABI 1.40-0.90 (N=5)	ABI < 0.90 (N=4)	SIG
Cardiovascular accident	0	0	3 (75%)	$p = 0.029$
Hip fracture	0	2 (40%)	0	
Suicide	0	2 (40%)	0	
Cardiac death	1 (50%)	1 (20%)	0	
Unknown	0	0	1 (25%)	
Necrotic ulcer	1 (50%)	0	0	

We found a higher mortality rate in patients with an ABI > 1.40 and an ABI < 0.90, with cardiovascular deaths being the most frequent cause in both groups. ABI values > 1.40 indicate non-compressible arteries in the legs, which prevents correct measurement of systolic pressure at the ankle. Non-compressible arteries imply calcification of the intima media of the artery (a common situation in patients with diabetes mellitus, those receiving chronic steroid treatment, those with chronic kidney disease and the elderly), which is associated with increased mortality[22-24]. A Spanish multicentre study of patients aged 65-85 years with prior atherothrombotic events [chronic ischemic heart disease or cardiovascular disease), but without diagnosed peripheral arterial disease found that 30% of patients had an ABI < 0.9 and 7% an ABI > 1.40. In both groups an association was found with an increase in cardiovascular events and death from cardiovascular causes[28]. The Strong Heart Study found that a baseline ABI of > 1.40 was associated with a 1.8-fold increase in total mortality and a 2-fold increase in cardiovascular mortality compared with a normal ABI; these findings were observed in both diabetic and nondiabetic patients and were independent of atherosclerotic risk factors for cardiovascular disease[23].

Although the small sample size and the fact that all patients had low levels of vitamin D, the strengths of the study are the uniformity of the population observed and the complete record of mortality.

Conclusions

We found no association between bone mass measured at the calcaneus and the ABI but we found a U-shaped association between ABI and mortality[23,24,29], with patients with an ABI < 0.90 or with an ABI > 1.40 having increased total and cardiovascular mortality[23,24,28].

Conflict of Interest

The Authors declare that there are no conflicts of interest.

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