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Abdominal aortic aneurysm in patients affected by intermittent claudication: prevalence and clinical predictors

Giuseppe Giugliano¹, Eugenio Laurenzano¹, Carlo Rengo¹, Giovanna De Rosa¹, Linda Brevetti¹, Anna Sannino¹, Cinzia Perrino¹, Lorenzo Chiariotti², Gabriele Giacomo Schiattarella¹, Federica Serino¹, Marco Ferrone¹, Fernando Scudiero¹, Andreina Carbone¹, Antonio Sorropago¹, Bruno Amato³, Bruno Trimarco¹, Giovanni Esposito^{1*}

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Abstract

Background: Abdominal aortic aneurysm (AAA) is a frequent cause of death among elderly. Patients affected by lower extremity peripheral arterial disease (LE-PAD) seem to be particularly at high risk for AAA. We aimed this study at assessing the prevalence and the clinical predictors of the presence of AAA in a homogeneous cohort of LE-PAD patients affected by intermittent claudication.

Methods: We performed an abdominal ultrasound in 213 consecutive patients with documented LE-PAD (ankle/brachial index ≤ 0.90) attending our outpatient clinic for intermittent claudication. For each patient we registered cardiovascular risk factors and comorbidities, and measured neutrophil count.

Results: The ultrasound was inconclusive in 3 patients (1.4%), thus 210 patients (169 males, 41 females, mean age 65.9 ± 9.8 yr) entered the study. Overall, AAA was present in 19 patients (9.0%), with a not significant higher prevalence in men than in women (10.1% vs 4.9%, $p = 0.300$). Patients with AAA were older (71.2 ± 7.0 vs 65.4 ± 9.9 years, $p = 0.015$), were more likely to have hypertension (94.7% vs 71.2%, $p = 0.027$), and greater neutrophil count ($5.5 [4.5 - 6.2]$ vs $4.1 [3.2 - 5.5] \times 10^3/\mu\text{L}$, $p = 0.010$). Importantly, the c-statistic for neutrophil count (0.73, 95% CI 0.60 – 0.86, $p = 0.010$) was higher than that for age (0.67, CI 0.56–0.78, $p = 0.017$). The prevalence of AAA in claudicant patients with a neutrophil count $\geq 5.1 \times 10^3/\mu\text{L}$ (cut-off identified at ROC analysis) was as high as 29.0%.

Conclusions: Prevalence of AAA in claudicant patients is much higher than that reported in the general population. Ultrasound screening should be considered in these patients, especially in those with an elevated neutrophil count.

Introduction

Systemic atherosclerosis represents the leading cause of morbidity and mortality in the western countries [1-3], with increased prevalence in the elderly population [4,5]. The atherosclerotic disease may involved different part of vascular tree, in particular coronary arteries, carotid arteries and peripheral arteries [6,7].

Abdominal aortic aneurysm (AAA) is a frequent cause of death in the elderly and its incidence has increased during last decades because of the increasing life-expectancy and the development of easy and low-cost diagnostic tools like ultrasound [5,8-12]. The rising incidence of AAA and the severe prognosis in case of rupture with a mortality rate that can be as high as 90% [13] call for early identification and elective repair. However, opposing views have been published on the importance of ultrasound screening for AAA and there is still debate on

* Correspondence: espogiov@unina.it

¹Department of Clinical Medicine and Cardiovascular and Immunological Sciences, "Federico II" University, via Pansini 5, 80131, Naples, Italy
Full list of author information is available at the end of the article

the high-risk populations who need to be screened [14,15].

Lower extremity peripheral arterial disease (LE-PAD), one of the main expressions of atherosclerosis, affects about 27 million people in Europe and the United States [16] and is associated with a high risk of developing fatal and non-fatal ischemic cardiovascular events [2,17-19]. Patients affected by LE-PAD seem to be at particularly high risk for AAA development [20-22]. Accordingly, we aimed this study at assessing the prevalence and the clinical predictors of the presence of AAA in a homogeneous cohort of LE-PAD patients affected by intermittent claudication, the most frequent clinical expression of LE-PAD.

Methods

We performed an abdominal ultrasound in 213 consecutive patients with documented LE-PAD attending our outpatient complaining intermittent claudication. Using an Image Point Hx ultrasound system (Hewlett Packard) and a 3.0 MHz transducer, we measured in each patient both antero-posterior and transverse outer diameters at the largest portion of the infrarenal abdominal aorta. AAA was defined by an infrarenal abdominal aorta diameter ≥ 3 cm [23]. Infrarenal abdominal aortas 2.6 to 2.9 cm were defined ectatic.

The diagnosis of PAD was based on the presence of an ankle brachial index (ABI) ≤ 0.90 . ABI was measured after participants had rested supine for 5 minutes. The systolic blood pressure in both brachial arteries, and the ankle systolic blood pressure in the right and left posterior tibial and dorsalis pedis arteries were measured using a Doppler probe. The ABI for each leg was then determined using the higher of the two readings from either the posterior tibial or dorsalis pedis arteries, and the higher of the two brachial readings. The lower ABI of the two legs was used for diagnostic purposes.

In each patient, clinical history and risk factors were assessed. Smokers included current and former smokers. Hypertension was diagnosed if systolic arterial pressure exceeded 140 mmHg and/or diastolic arterial pressure exceeded 90 mmHg, or if the patient used antihypertensive drugs. Hypercholesterolemia was diagnosed if plasma total cholesterol exceeded 200 mg/dL, plasma low-density lipoprotein cholesterol exceeded 130 mg/dL, or if the patient used lipid-lowering drugs because of a history of hypercholesterolemia. Diabetes mellitus was diagnosed if plasma fasting glucose exceeded 126 mg/dL or if the patient used hypoglycaemic agents. A history of coronary artery disease, previous myocardial infarction, or ischemic stroke was documented by hospital records. All patients underwent ultrasound examination of carotid arteries.

All participants gave written informed consent to the study, which was approved by our institutional Ethics Committee.

Blood samples and laboratory assay

Blood was drawn from an antecubital vein using a 19-gauge needle in a Vacutainer system (Becton-Dickson, Franklin Lakes, NJ). Neutrophil count was measured with the Bayer H*2 hematology analyzer (Bayer Diagnostic Division, Tarrytown, NY).

Statistical analysis

Statistical analyses were performed using SPSS 12.0 (SPSS, Inc., Chicago, IL, USA). Variables were expressed as absolute numbers and percentage or mean \pm SD, with the exception of neutrophil count, which was expressed as median and inter-quartile range because of their skewed distribution. Comparisons were made by t-test for unpaired samples, χ^2 test, or Mann-Whitney U test, as appropriate. For continuous variables, receiver-operating characteristic (ROC) curve analysis was used to identify the threshold levels that provided the best cut-off for the prediction of the presence AAA. Correlations between continuous variables were evaluated by Spearman analysis.

All statistical tests were two-sided. For all tests, a p-value <0.05 was considered statistically significant.

Results

The ultrasound was inconclusive in 3 patients (1.4%), thus 210 patients (169 males, 41 females, mean age 65.9 ± 9.8 yr) completed the study. Table 1 shows baseline characteristics of the study population. Overall, AAA was present in 19 patients (9.0%), with a not significant higher prevalence in men than in women (10.1% vs 4.9%, $p = 0.300$). Furthermore, patients with AAA were older (71.2 ± 7.0 vs 65.4 ± 9.9 years, $p = 0.015$), were more likely to have hypertension (94.7% vs 71.2%, $p = 0.027$), and greater neutrophil count ($5.5 [4.5 - 6.2]$ vs $4.1 [3.2 - 5.5] \times 10^3/\mu\text{L}$, $p = 0.010$) (Table 2). The prevalence progressively increased with age (p for trend = 0.013), with a maximum of 15.8% in over 75-year-subjects (Table 3). Of note, in our population we observed a higher prevalence of carotid stenosis $>50\%$ in claudicant patients with AAA, although not significant (47.4 vs 29.3%, $p = 0.105$). No relationship was found between the ankle-brachial index and the presence of AAA. For continuous variables, which are associated to the presence of AAA at univariate analysis (i.e. age and neutrophil count), ROC curve analysis was performed to evaluate the best cut-offs to predict the presence of the disease (Figure 1). The best cut-offs were ≥ 66 years for age and $\geq 5.1 \times 10^3/\mu\text{L}$ for neutrophil count. Importantly, the c-statistic for neutrophil count (0.73, 95% CI 0.60 - 0.86, $p = 0.010$) was higher than that for age (0.67, CI 0.56-0.78, $p = 0.017$) (Figure 1). In our population the prevalence of AAA in claudicant patients with a neutrophil count $\geq 5.1 \times 10^3/\mu\text{L}$ (cut-off identified at ROC analysis) was as high as 29.0%. Of note,

Table 1 Baseline characteristics of the study population (n=210)

	Number	Percentage or mean (SD) or median [25 th -75 th percentiles]
Age (years)		65.9 (9.8)
Males	169	80.5
Height (cm)		167.4 (7.5)
Weight (Kg)		73.9 (11.7)
Risk factors		
Smoking	188	89.5
Hypertension	154	73.3
Hypercholesterolemia	137	65.2
Diabetes mellitus	75	35.7
BMI (kg/m ²)		26.2 (3.4)
WC (cm)		97.6 (9.4)
Metabolic syndrome	96	45.7
Comorbidity		
CAD	106	50.5
Previous MI	76	36.2
Previous stroke	8	3.8
Medications		
Antiplatelets	191	91.0
Beta blockers	47	22.4
ACE-inhibitors	104	49.5
Statins	130	61.9
Carotid status		
Carotid stenosis >50%	65	31
LE-PAD severity		
Bilateral LE-PAD	131	62.4
ABI		0.69 (0.22)
Aortic features		
Aortic diameter (mm)		20.7 (6.8)
Ectatic aorta	13	6.2
AAA	19	9.0
Inflammatory status		
Neutrophil count (x10 ³ /μL)		4.4 [3.3-5.7]

SD = standard deviation; BMI = body mass index; WC = waist circumference; CAD = coronary artery disease; MI = myocardial infarction; ACE = angiotensin converting enzyme; LE-PAD = lower extremity-peripheral arterial disease; ABI = ankle/brachial index; AAA = abdominal aortic aneurysm.

Spearman analysis showed that neutrophil count and age are not correlated ($\rho = -0.123$, $p = 0.230$).

Discussion

The present study demonstrates that prevalence of AAA in claudicant patients is much higher than that reported in the general population, with the highest clinical predictors being advanced age and an elevated inflammatory status.

To decrease the number of deaths from ruptured AAA, early detection by screening subjects at high risk is needed. Physical examination is not effective in identifying the presence of an AAA, while abdominal ultrasound is an accurate test to detect the presence of this life-threatening disease [23]. Elderly males are those who show the highest prevalence of the disease in the general population. Indeed there is evidence that screening programs involving males

with > 65 years are cost-effective [14,24,25]. The strong association with age has been confirmed also in our population of claudicant patients. Indeed, we observed that the prevalence of AAA dramatically increases after 65 years (optimal cut-off identified at ROC analysis being ≥ 66 years) and no AAA was found in patients younger than 55 years of age. Thus age cut-off to initiate screening for AAA in patients with intermittent claudication seems to be the same than in general population. These results might suggest that performing an abdominal ultrasound in all claudicant patients may not be advisable. However, in our study, we found that an elevated inflammatory status, evaluated by neutrophil count, is a powerful predictor of the presence of AAA in patients with intermittent claudication, and that the neutrophil count did not correlate with age. Initiating the screening in patients ≥ 65 years with intermittent claudication might consequently lead to

Table 2 Characteristics of claudicants according to the presence or absence of AAA.

	AAA (n = 19)	No AAA (n = 191)	p
Age (years)	71.2 ± 7.0	65.4 ± 9.9	0.015
Age ≥ 65 years	16 (84.2)	110 (57.6)	0.024
Males	17 (89.5)	152 (79.6)	0.300
Risk factors			
Smoking	18 (94.7)	170 (89.0)	0.437
Hypertension	18 (94.7)	136 (71.2)	0.027
Hypercholesterolemia	15 (78.9)	122 (63.9)	0.188
Diabetes Mellitus	4 (21.1)	71 (37.2)	0.162
BMI (kg/m ²)	26.5 ± 3.7	26.2 ± 3.4	0.742
WC (cm)	96.7 ± 9.6	97.7 ± 9.4	0.708
Metabolic syndrome	9 (47.4)	87 (45.5)	0.879
Comorbidity			
CAD	10 (52.6)	96 (50.3)	0.844
Previous MI	5 (26.3)	71 (37.2)	0.348
Previous stroke	1 (5.2)	7 (3.7)	0.729
Medications			
Antiplatelets	18 (94.7)	173 (90.6)	0.547
Beta blockers	2 (10.5)	45 (23.6)	0.194
ACE-inhibitors	11 (57.9)	93 (48.7)	0.444
Statins	10 (52.6)	120 (62.8)	0.383
Carotid status			
Carotid stenosis >50%	9 (47.4)	56 (29.3)	0.105
LE-PAD severity			
Bilateral LE-PAD	13 (68.4)	118 (61.8)	0.569
ABI	0.64 ± 0.11	0.69 ± 0.23	0.315
Inflammatory status			
Neutrophil count (x10 ³ /μL)	5.5 [4.5 – 6.2]	4.1 [3.2 – 5.5]	0.010

Values are n (%) or mean ± SD or median [interquartile range].

AAA = abdominal aortic aneurysm; BMI = body mass index; WC = waist circumference; CAD = coronary artery disease; MI = myocardial infarction; ACE = angiotensin converting enzyme; LE-PAD = lower extremity-peripheral arterial disease; ABI = ankle/brachial index; SD = standard deviation.

miss some diagnosis of AAA, and therefore in claudicant patients with an elevated inflammatory status the ultrasound screening should be performed irrespective of age. At this regard, pathophysiological studies are needed to evaluate whether the increased inflammation observed in our population of intermittent claudication patients affected by AAA is a cause or a consequence of the presence of AAA [19,26,27].

Table 3 Distribution of AAA by age.

	Total	AAA	Prevalence
Age < 55 years	25	0	0%
Age 55 – 64 years	59	3	5.1%
Age 65 – 74 years	88	10	11.4%
Age ≥ 75 years	38	6	15.8%

p for trend = 0.013

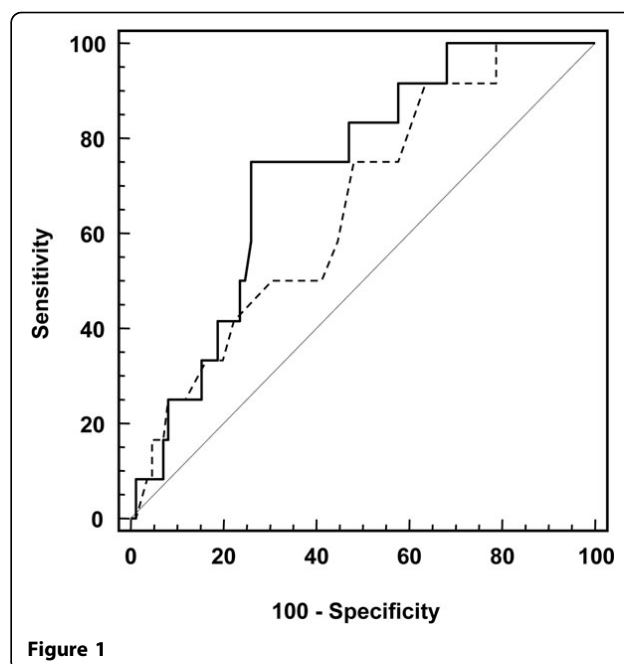


Figure 1

Conclusions

The high prevalence of AAA among patients affected by intermittent claudication makes them a suitable target population for AAA screening. In our opinion ultrasound screening should be considered in these patients, especially in those with an elevated neutrophil count. However, further studies are warranted to elucidate if screening all patients with intermittent claudication for of this life-threatening condition is cost-effective.

List of abbreviations

LE-PAD: Lower Extremity Peripheral Arterial Disease; AAA: Abdominal Aortic Aneurysm; ABI: ankle/brachial index.

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Author details

¹Department of Clinical Medicine and Cardiovascular and Immunological Sciences, "Federico II" University, via Pansini 5, 80131, Naples, Italy.

²Department of Biology and Cellular and Molecular Pathology, Federico II University, via Pansini 5, 80131, Naples, Italy. ³Department of General, Geriatric, Oncologic Surgery and Advanced Technologies, "Federico II" University, via Pansini 5, 80131, Naples, Italy.

Authors' contributions

GG, EL, CR, GDR, LB, AS, CP, LC, GGS, FS, AC, AS: conception and design, interpretation of data, given final approval of the version to be published, BA, BT: critical revision, interpretation of data, given final approval of the version to be published, GE: conception and design, critical revision, given final approval of the version to be published.

Competing interests

The authors declare that they have no competing interests.

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