Frequency of Peripheral Artery Disease in association with Coronary Artery Disease: a cross-sectional monocentric study in eastern Algeria

Fréquence de l'association artériopathie oblitérante des membres inférieurs et coronaropathie : résultats d'une étude transversale monocentrique à l'est algérien

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RÉSUMÉ

Introduction. Les coronariens ayant une atteinte vasculaire périphérique ont un pronostic cardiovasculaire plus sévère. Il paraît donc intéressant de dépister cette association, notamment en mesurant l'index de pression systolique qui est un moyen simple, non invasif, et non coûteux ayant un apport diagnostic important, afin de détecter des lésions silencieuses, mais menaçantes, et d'identifier un sous-groupe de coronariens à plus haut risque cardiovasculaire, nécessitant une prise en charge plus spécifique. **Objectifs.** Estimer la fréquence de L'artériopathie oblitérante des membres inférieurs (AOMI) chez les patients coronariens, recrutés en cardiologie dans les centres hospitalo-universitaires de la ville de Constantine et déterminer les facteurs de risques de cette association. **Patients et méthodes.** Notre étude est descriptive, transversale, mono centrique réalisée en unités des explorations cardiovasculaires de l'hôpital militaire régional universitaire de Constantine. Les sujets inclus avaient aux moins une lésion coronaire significative ≥ 50% sur une artère coronaire principale, pour chaque patient, une anamnèse orientée et un examen clinique cardiovasculaire ont précédé la mesure de L'index de pression systolique (IPS). L'AOMI était définie par un IPS inférieur à 0.90 sur une des quatre artères distales des membres inférieurs. Le traitement et l'exploitation des données ont fait appel au logiciel Epi Info Statistics V7. **Résultats.** 300 patients coronariens, âgés en moyen de 61 ans à prédominance masculine nette, ont été inclus. La fréquence de l'association AOMI et coronaropathie était de 34,7%, asymptomatique dans 18% des cas. L'âge ≥ 65 ans, le tabac, le diabète, l'HTA, la dyslipidémie, la sédentarité, l'accident vasculaire cérébral (AVC) et l'atteinte coronaire sévère étaient les facteurs indépendants de l'association. L'odds ratio ajusté (ORa) est à : 3,67 (âge ≥ 65 ans), 4,10 (tabac), 3,48 (diabète), 3,30 (HTA), 2,32 (dyslipidémie), 2,14 (sédentarité), 6,40 (AVC) et 2,36 (atteinte coronaire sévère). **Conclusion.** L'IPS, en plus d'être un outil de dépistage précoce de l'AOMI, sa diffusion en pratique médicale aiderait à l'approche et l'affinement du risque vasculaire des patients coronariens.

Mots-clés : IPS, AOMI, coronaropathie.

ABSTRACT

Introduction. Patients with both Coronary Artery Disease (CAD) and Peripheral Artery Disease (PAD) have a worse cardiovascular prognosis. It therefore seems interesting to detect this association, in particular by measuring the ankle-brachial systolic pressure index (ABI) which is a simple, inexpensive and non-invasive way with a significant diagnostic input that can detect silent but threatening lesions. It can also identify a subgroup of patients with coronary artery disease at a higher cardiovascular risk requiring a more specific management. **Aims.** Estimate the frequency of peripheral artery disease (PAD) in patients with Coronary Artery Disease CAD who were recruited at the department of cardiology at the university hospital of Constantine. This study also aims to detect the risk factors of this association. **Patients and methods.** Our study is descriptive, cross-sectional, single-centered in cardiovascular exploration units of the of the regional military university hospital of Constantine. The included subjects had at least one significant coronary lesion in a major coronary artery using radial Coronary angiography. Guided medical history and a cardiovascular clinical examination preceded the measurement of the ABI for each patient. PAD was defined by an ABI of less than 0.90 in one of the four distal arteries of the two lower limbs. Data was analyzed and processed by Epi-Info Statistics V7. **Results.** 300 coronary patients, an average age of 61 years, mostly males, took part in the study. The frequency of the combination PAD and coronary artery disease was 34.7% using the ABI, asymptomatic in 18% of cases. independent factors of the association were : Age≥ 65 [aOR 3,67, P <0,0001], tobacco [aOR 4,10, P<0,002], diabetes [aOR 3,48, P<0,0001] , AHT [aOR 3,30, P<0,0001], dyslipidemia [aOR 2.32, P<0,009], inactivity [aOR 2,14, P<0,015] , stroke [aOR 6,4, P<0,015] and severe coronary impairment [aOR 2,36, P<0,015]. **Conclusion.** ABI, in addition to being an early detection tool for PAD, its dissemination in medical practice would help in the approach and refinement of vascular risk in coronary heart patients.

Keywords : ABI, PAD, CAD.

INTRODUCTION

Atherosclerosis and its corollary atherothrombosis are widespread in both developed and developing countries [1]. International registries, recruiting patients with at least arterial disease, record between 16 and 28% of multisite arterial disease, of which about one third of these atheromatous patients are, in fact, asymptomatic and at very high cardiovascular risk [2]. Wanted by measurement of the ankle-brachial systolic pressure index (ABI) in coronary patients, the prevalence of peripheral arterial disease (PAD) can reach more than 30% according to the age of the subjects and can even exceed 40% in hospitalized subjects [3].

MATERIELS AND METHODS

Study population

Our epidemiological study is descriptive, analytical and monocentric conducted on a sample of 300 consecutive coronary patients, at the regional military university hospital of Constantine, with at least one lesion of 50% in

a major coronary artery, using radial coronary angiography regardless of their age and gender, excluding those who refused to participate in the study and patients with acute ischemia of the lower limbs.

Study

The patients received a collection of anthropometric measurements (weight, height, calculation of BMI), a collection of information (cardiovascular risk factors, cardiovascular and cerebral pathologies), a comprehensive clinical examination, a biological balance including complete lipid profile (HDL-C ,Total cholesterol, triglyceride, LDL-C), fasting blood glucose, creatinine levels, calculated creatinine clearance according to the MDRD formula and HBA1C for diabetic patients. we measured the ABI in dorsal decubitus, the upper limbs undressed, in a patient relaxed for more than 10 minutes, by a pocket doppler (Sonotrax Vascular Lite, brand: EDAN), equipped with a probe of 8 MHz , with a sphygmomanometer (brand: Riester) . After obtaining a stable Doppler signal, the cuff was inflated by 20 mm Hg beyond the signal removal pressure and then slowly deflated by 2 mm Hg per second until an audible signal reappeared. The retained value was equivalent to systolic ankle blood pressure. The recorded arteries were classically, for each lower limb, the posterior tibial artery in the back-malleolar gutter, the Dorsalis pedis artery at the foot [4]. This procedure was performed twice on each limb; at each arm. The Doppler signal was picked up at the humeral or radial level, with the cuff positioned as when measuring the usual blood pressure (BP). We chose the most sensitive method to calculate the ABI. The ratio between the lowest levels of systolic pressure on the highest brachial systolic pressure of both arms. The ABI was calculated for each of the arteries of each limb [5]. The lowest index of the two lower limbs was the one considered, making the diagnosis of PAD if lower or equal 0.9 in the presence or absence of symptomatology.

If ABI ankle was limited to 0.91 -0.99, a hemodynamic treadmill walking test (Skinner Strandness test) with taking distal pressures at rest and after an effort was indicated in search of an subclinical PAD; the diagnosis was retained when the distal pressure dropped by at least 20% from the first minute after stopping the effort. In the case where the ABI ankle was strictly greater than 1.3, a supplement of hemodynamic exploration was performed by measuring the systolic pressure index in toe (TBI) for each member using a photoplethysmograph. All of our coronary patients have benefited from a Trans thoracic cardiac ultrasound with measurement of the LV mass, overall left ventricular systolic ejection fraction using the Simpson Biplan method and evaluation of LV diastolic function by measuring LV filling pressures.

Data analysis

All patient examinations were performed by the same cardiologist (lead investigator), which were then initially recorded on a data sheet prepared for this purpose, later transferred to a database (EXCEL 2013 file) designed for the same purpose. Statistical analysis was performed using Epi Info Statistics V7. The results are presented with 95% confidence intervals, in the form of average, median, standard deviation, and minimum and maximum values, for quantitative variables. In the form of percentages with their standard deviation for qualitative variables.

RESULTS

Characteristics demographics of our sample

Between June 2015 and March 2016, we collected 300 consecutive coronary patients. The average age of this population was 61.3±11.3 years, extremes of age ranging from 23 to 85 years, and a median of 62 years, with a significant male predominance (P<0,0001). This population was relatively small (average BMI 27.9 ±4.7 kg/m2, Average waist circumference 95.6±11.2 cm). The majority of our coronaries had more than three cardiovascular risk factors (CVRF) (72.7%). The predominant CVRF were arterial hypertension (AHT) (58.7%), sedentarity (57.3%), dyslipidemia (52.7%), overweight (49%), and diabetes (47.4%). The least observed CVRF were active smoking (32.3%), obesity (29.3%), and Familial Coronaropathy (26.4%). Diabetes was associated with AHT and dyslipidemia in 36%, 47.3% of cases respectively; triple association was observed in 37.7%. Personal antecedents of cerebrovascular disease (ischemic stroke, hemorrhagic stroke), were observed in 2.7%. The majority of our patients (60.7%) went through coronary angiography for an acute coronary syndrome, the rest for stable ischemic heart disease, an increased left ventricular mass (LVM), was found in 54%. The left ventricular ejection fraction (LVEF), using the Simpson biplane method, was retained in 83.34% and 54.3% of our patients had an alteration of LV diastolic function. 41.67% had Single vessel disease, 30.7% double vessel disease, 22% triple vessel disease.

Peripheral arterial exploration

As a result of this investigation, it was found that the frequency of Symptomatic PAD was 16%, and the frequency of intermittent claudication of the lower limbs according to the Edinburgh questionnaire 11.67%. The intake of the clinical examination was poor, finding a decrease or abolition of pulse 11% and pathological auscultation in 7.34%. For 300 patients and on the basis of four ABI for each of them, we totaled 1200 ABI with an average ABI of 1.07±0.26 on the right side and 1.08 ± 0.24 on the left side. The ABI profile according to TASC II and AHA [6] was normal in 44.7%, ABI ≤ 0, 9 evoking PADS in 17.3%. A dodgy ABI in 17%, an ABI> 1.3 evoking arterial incompressibility in 21%. After measuring the ABI of stress in situations where the ABI is questionable (0.9-ABI -1), and measuring the systolic pressure index to the big toe in situations where the ABI was 1.3, the definitive ABI profile of our population was in 57% in favor of the absence of PAD, a Media calcinosis observed in 21%, in relation to an isolated mediacalcosis (8.3%) or mixed impairment (12.7%) and the presence of PAD in 34.7% for either an isolated PAD, diagnosed after measuring resting ABI in 52 patients (17.3%), a PAD diagnosed after measuring stress ABI in questionable cases in 14 patients (4.7%), or a mixed impairment (calcose media and associated PAD) in 38 patients (12.7%). In total, ABI was pathological in 129 coronary scans, representing a frequency of 43% of the overall population. The frequency of the combination PAD and coronary artery disease, diagnosed using the ABI is 34.7% ±5,3, 95% CI (29.3% - 40%). This population is therefore composed of 104 patients including 48 with symptomatic PAD and 56 with asymptomatic PAD.

Analysis of the factors correlated with the occurrence of PAD in our coronary heart

Multi-varied analysis, with a type of logistic regression, was carried out by the SPSS 22. The risk of PAD related to each factor, adjusted for all other factors, was represented by Odds Adjusted Ratio (ORa) estimated with its confidence interval at 95%. The various parameters predisposing to the installation of PAD in our coronary artery have been identified and are in order of frequency: personal antecedents of brain events type ischemic stroke or transient ischemic attack (TIA) (ORa 6.40), smoking (ORa 4.10), age advanced age 65 (ORa 3.67), diabetes (3.48), AHT(ORa 3.30), severe coronary impairment (0Ra 2.36), aorto-coronary bypass surgery (ORa 3.20), and to a lesser degree dyslipidemia and inactivity (ORa 2.32, 2.14).

However, some factors, which were found to be significant in the bi-varied analysis, no longer stood out in the multivariate analysis; these are: male sex, normal BMI, severe kidney failure, systolic LV dysfunction, diastolic LV dysfunction and increased LV mass (Table1 and 2).

Tableau 1. Comparative study between different coronary populations

Variables	without PAD (n=196)	with PAD (n=104)	P	with PAD		P
				asymptomatic (n=56)	symptomatic (n=48)	
Sex (n - %)						
Men	145(74)	90(86,5)		50(89,2)	40 (83,3)	*NSD*
Women	51(26)	14(13,5)	*NSD*	6(10,8)	8(16,7)	
Age						
Average (years)	58,14±11,25	67,2±8,4	0,0001	67,8±7	66,9±8	*NSD*
range (years)						
≥65	64(32,6)	68(65,4)	0,0001	36(64,2)	32(66,7)	*NSD*
<65	132(67,4)	36(34,6)		20(35,7)	16(33,3)	
Number of CVRF						
≥ 3CVRF	124(63,3)	94(90,4)	0,0001	49(87,5)	45(93,8)	*NSD*
< 3CVRF	72(36,7)	10(9,6)		7(12,5)	3(6,52)	
BMI (Kg/m2)						
BMI average	28,7 ± 4,63	26,3 ± 43	0,0001	26,08	26,71	*NSD*
BMI≥30 (n-%)	78(39,8)	10(9,6)	0,0001			
BMI<30(n - %)	118(60,2)	94(90,4)				
Diabetes (n-%)						
Diabetic	74(37,8)	68(65,4)	0,0001	40(71,4)	28(58,4)	
Non diabetic	122 (62,2)	36 (34,6)		16(28,6)	20(41,7)	0,003
Average duration (years)	11,7 ± 7,8	11,03 ±9,11	*NSD*			
Diabetes encienty (years) ≥10	43(58,1)	35(51,5)	*NSD*			
Diabetes balance (n-%)						
Good balance	51(58,0)	15(27,8)	0,002			
Bad balance	26(29,5)	27(50,0)				
Tabacco (n-%)						
Smoker	108(55,1)	78(75)		41(73,2)	37(77,0)	*NSD*
Non-smoker	88(44,9)	26(25)	0,002	15(26,8)	11(22,9)	
Amount of smoking toxicity	28 ± 17,80	37,95 ± 19,36				
HT (n-%)						
HT	98(50,0)	78(75,0)	0,0001	41(73,2)	37(77,0)	*NSD*
No HT	98(50,0)	26(25,0)		15(26,8)	11(22,9)	
Average duration (years)	8,16± 6,134	8,18± 8,614	*NSD*			
HT encienty (years)≥10	40 (40,8)	26 (33,3)	*NSD*			
HT balance						
Good balance	42(42,1)	27(34,3)	0,003			
Bad balance	57(57,9)	51(65,7)				
Dyslipidimia(n-%)						
Dyslipidimia (LDLc < 0,7g/l)	101(51,5)	74(71,2)		39 (69,6)	35(72,9)	
			0,009			*NSD*
No dyslipidemia (LDLc≥0,7 g/l)	95(48,5)	30(28,8)		17 (30,4)	13 (27,0)	
Familial Coronaropathy (n-%)						
Coronaropathy F	51(26,0)	28(26,9)	*NSD*	16 (28,6)	12(25)	*NSD*
No coronaropathy F	145(74,0)	76(73,1)		40 (71,4)	36 (75)	
Severe renal failure	2(1,0)	5(4,8)	*NSD*	3 (5,4)	2(4,1)	*NSD*
Sedentarity (n-%)						
(+)sedentarity	102(52,0)	70(67,3)	0,015	47 (66,1)	33 (71,3)	*NSD*
(-)sedentarity	94(48,0)	34(32,7)		19 (33,9)	15 (28,7)	

(Table 1 continued)

Stroke (n-%)						
Stroke	2(1,0)	6(5,8)	0,0001	4(7,1)	2(4,1)	*NSD*
No stroke	194(99,0)	98(94,2)		52(92,9)	46(95,9)	
LVEF (n-%)						
LVEF altered	18(9,2)	32(30,77)	*NSD*	18 (32,1)	14 (29,1)	*NSD*
LVEF normal	178(90,8)	72(69,23)		38 (67,9)	34 (70,9)	
L VFP (n-%)						
HIGH LVFP	95(48,5)	68(65,4)	*NSD*	36(64,3)	32 (66,7)	*NSD*
Normal LVFP	101(51,5)	36(34,6)		20(35,7)	16 (33,3)	
LV mass (n-%)						
Normal LV mass	105(53,6)	33(31,7)	*NSD*	18(32,1)	15(31,6)	*NSD*
Increased LV mass	91(46,4)	71(68,3)		38(67,9)	33(68,4)	
Severe coronary artery disease (n-%)	19 (9,70)	64(61,53)	0,015	32(57,1)	32(66,7)	*NSD*

***NSD**: no significant difference; **HT**: arterial hypertension; **BMI**: body mass Index; **CVRF**: cardiovascular risk factors*
***LVEF**: left ventricular ejection fraction; **LVM**: left ventricular mass; **LVFP**: left ventricular filling pressures*

Tableau 2. Factors related to the occurrence of the PAD

Variables	adjusted odds ratio (aOR)	95% CI aOR	P
Male	0,53	0,172-1,654	0,277
Age ≥ 65 years	3,67	1,975-6,851	0,0001
Diabetes	3,48	1,843-6,589	0,0001
AHT	3,30	1,703-6,406	0,0001
Smoking	4,10	1,674-10,069	0,002
Dyslipidemia	2,32	1,234-4,381	0,009
Normal BMI	0,12	0,051-0,293	0,0001
Severe Renal failure	0,17	0,027-1,089	0,062
Sedentarity	2,14	1,159-3,971	0,015
Stroke	6,40	1,60-14,20	0,0001
Altered LVEF	0,58	0,164-2,025	0,390
Increased LVFP	0,90	0,422-1,948	0,801
Increased LVM	0,36	0,164-2,025	0,7
Severe coronary artery disease	2,36	1,159-3,822	0,015

DISCUSSION

Regardless of the stage of CAD, the presence of a PAD is a factor of bad prognosis and at least an aggravating factor [3]. The measure of ABI is the cornerstone of the lower arterial limb exploration strategy as an immediate complement to the clinical examination, not only to diagnose PAD in many cases, but also to help to identify a significant segment of the asymptomatic population, already at high cardiovascular risk. Studies show that there is no significant difference in risk of death and vascular events, at five years between symptomatic and asymptomatic patients [7]. The relative simplicity of this test and its high sensitivity seem to indicate this for the detection of PAD in pauci- or asymptomatic populations.

This led us to use it during our work to diagnose the PAD and then deduce the frequency of association with coronary artery disease especially since the contribution of questionnaires (Rose, Edinburgh etc.) and diagnostic clinical examination of PAD are reduced, as demonstrated by numerous epidemiological studies [8].

During our study, any symptomatic or asymptomatic patient with one of the following criteria was considered arteritic: an ABI ≤ 0.9 at rest, an ABI ≤ 0.9 after stress sensibilisation (positive Skinner Strandness test) or an ABI toe ≤ 0.7 in a patient with an ABI > 1.3. Based on these conditions, the frequency of the combination of coronary artery disease and PAD was 34.7%±5.3, 95% CI (29.3% - 40%). Various studies objectively target a high frequency of PAD in coronary patients; however, the prevalence figures remain heterogeneous [3]; this is naturally due to the recruitment method of coronary patients (population selected versus population and therefore average age) and the PAD diagnostic method. Our data on the prevalence of PAD is consistent with the most recent literature, and even appear to be superior to other studies; several explanations for this difference are possible:

- The diagnosis of PAD, in our study, was based on interrogation, clinical examination and measurement of the resting ABI (possibly supplemented by a measure of the stress ABI, in borderline cases, and measurement of the TBI, if mediacalcose.
- The ABI threshold used in our study to diagnose the PAD was an ABI ≤ 0.9, (0.9 included), which probably increased the number of detected patients with PAD compared to studies using an ABI < 0.9 as a criterion.
- The method of calculating ABI also influences the heterogeneity of PAD prevalence. Given the lack of consensus on the calculation of ABI. the use of the lowest ABI, in our study, provides a better sensitivity to a slight decrease in specificity [9] and more identification of patients with high cardiovascular risk, and consequently a better estimate of the frequency of PAD in patients with Coronary disease.
- Also noteworthy is the high prevalence of cardiovascular risk factors found in our study. Indeed, we have noted a high prevalence of arterial hypertension (AHT), diabetes,

tobacco, and dyslipidemia. These cardiovascular risk factors are associated with PAD in most of the conducted studies.

In our serie, the frequency of asymptomatic PAD diagnosed with ABI was higher than that of symptomatic intermittent claudication (IC) based PAD using the Edinburgh questionnaire, the ratio between the two frequencies was 2.97, in the literature. The prevalence of PAD determined by the ABI measurement is generally 2.5 higher than that determined by the CI [10-12]. This high frequency of asymptomatic PAD in our series can be explained by the fact that it is often underestimated in coronary scans. The various parameters predisposing to the installation of PAD in our coronary artery were personal antecedents of ischemic stroke, smoking, advanced age - 65 years, AHT, severe coronary impairment, dyslipidemia and sedentarity. However, some of the factors that were found to be significant in the bi-varied analysis no longer stood out in the multi-variance analysis such as sex or gender difference which disappeared after logistical regression and adjustment to confounding factors, such as age and CVRF mainly all-male tobacco in our study; a normal BMI was a rather protective factor, This seems to be related to the involvement of obesity in other risk factors of PAD such as hypertension, type II diabetes and dyslipidemia. This interaction may be responsible for decreasing the statistical power of the results [13].

LVM was significantly increased in the arteritic versus non-arteric group (P=0.0001); this finding is similar for LVFP (P=0.005), but these links disappear in multi-variance analysis. This loss of statistical power can be explained by the entanglement of several factors in the increase in LVM mainly AHT and diabetes, as well as for LVFP (AHT, diabetes, LVM, CAD). According to our analysis, LV dysfunction is significantly related to the occurrence of PAD in coronary patients in bi-varied analysis (P=0.03). After a multi-variate analysis, this link disappears (P =0.390), probably in relation to the decrease in the statistical power of this factor after adjusting to other factors essentially, the severe CAD often incriminated in the LV dysfunction.

CONCLUSION

Currently, the ABI is recognized by the majority of international recommendations as a rapid, low cost, non-invasive, and reproducible way to complete any clinical examination (any patient with at least one CVRF or in any subject with at least one atherothrombotic vascular disease). It must be available to any specialist practitioner or not, taking care of this type of patients and as part of a systematic vascular assessment, to establish or eliminate a PAD, symptomatic or asymptomatic.

CONFLICT OF INTEREST

The authors declare that they have no conflict of interests.

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