Anxiety a possible peripheral artery disease risk factor among older Africans: The EPIDEMCA study.

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Abstract

Objective During the past ten years considerable progress has been made in research on cardiac effects of anxiety. On the other hand, epidemiological research on the implication of this psychosocial factor in the development of peripheral artery disease (PAD) is lacking. The present study sought to examine the association of anxiety and PAD in elderly individuals in two sub-Saharan countries in Africa.

Methods This cross-sectional study, was performed in urban and rural population in Central Africa: Republic of Congo and Central African Republic. All individuals ≥ 65 years living in these areas were invited to participate. Socio-demographic data, medical history, medication, clinical and biological data were collected. Anxiety symptoms were assessed with the Geriatric Mental State version B3. Peripheral artery disease was defined as ankle brachial index (ABI) ≤ 0.90 .

Results A total of 1662 subjects composed our study population (age 72.9 ± 6.5 years, 59.3% females). Overall, the prevalence of anxiety was 7.2%, significantly higher in women (9.2% vs. 4.3% in men, $p < 0.001$). Independently of all confounding factors, anxiety was strongly associated with PAD in both countries (OR: 2.56, 99%CI: .52-4.20) and more frequently associated with PAD in women than in men (OR: 3.37, 95%CI: 1.22-4.10 vs. OR: 2.34, 95%CI: 1.13-5.06).

Conclusion Our study underlines the high prevalence of anxiety in African general population in the elderly, as well as a significant association with the peripheral artery disease, independently of all possible confounding factors. The higher rates of anxiety in women and stronger association with PAD as compared to men might explain the higher rates of PAD in African women.

Introduction

Anxiety, a sustained mental health disorder, can be triggered by stress when the adaptive capacities of individuals to their environment are perceived as strained or exceeded. In contrast to stress, once the threat is mediated, anxiety does not fade into time and cause significant impairment in daily life and organism physiology.

Many studies have shown an interaction between anxiety and hypertension, coronary artery disease (CAD), and even outcomes after cardiac surgery¹⁻⁴. Considerable progress has been made during the past decade in research on effects of this psychosocial factor, but data are still limited to CAD, stroke and hypertension. The pooled relative risk of acute coronary syndrome in case of prior anxiety is 3.1 in cross sectional studies⁵. In the Whitehall II study, anxiety was also associated with components of metabolic syndrome, such as higher waist circumference (central obesity), obesity, and dyslipidaemia⁶. Peripheral artery disease (PAD) is a frequent presentation of atherosclerotic disease and shares the same major risk factors as CAD. Nevertheless, no specific information is available regarding the relationship between anxiety and PAD. Furthermore, the prevalence of PAD seems to be different according to ethnicity., Individuals of African descent in the United States are at up to 3-fold higher risk of PAD as compared to

non-Hispanic Whites⁷ and recent studies highlighted the higher prevalence of PAD in native African populations^{8–10}. The Global Burden Disease project highlighted the burden of PAD in low-and-middle income countries, especially Africa, with higher prevalence of this condition among women, without a clear explanation on why this sex disparity is more pronounced in these countries than high-income ones¹¹.

As findings from previous studies have shown that psychosocial factors such as anxiety may be associated with the development of cardiovascular disease, the present study sought to examine the association of anxiety and PAD in a cohort of elderly individuals in two sub-Saharan countries in Africa.

Material And Methods

Study Design and Population

The EPIDEMCA study (Epidemiology of Dementia in Central Africa) is a cross-sectional population-based study in rural and urban areas of two countries of Central Africa: Central African Republic (CAR) and Republic of Congo (ROC), focused on cardiovascular diseases and risk factors, cognitive disorders and their interrelation.

The study population included all people aged ≥ 65 years. Exclusion criterion was refusal to participate. Written consent was obtained or confirmed by fingerprint marks for illiterate subjects. In case of severe cognitive impairment, the purpose of the study was verbally explained to the person and his family. Sampling was proportional to the size of the main subdivisions in the urban areas (Brazzaville in ROC, Bangui in CAR) and an exhaustive door-to-door sampling was applied in two rural areas (Gamboma in ROC, Nola in CAR). Additional details pertaining to study design have been published elsewhere¹².

Ethical committees in CAR and ROC approved the study protocol, as well as the “Comité de la Protection des Personnes Sud-Ouest Outre-Mer” in France (SOOM4-CE–3).

Data collection

Psychosocial and cognitive measurements

As anxiety symptoms may span the cognitive and behavioural fields, assessment of cognitive status was achieved using the Community Screening Interview for Dementia (CSI-D)¹³ adapted, back-translated and pretested in the local languages (Sango in CAR, Lari, Lingala, and Kituba in Congo).

Symptoms of anxiety and depression were studied for their potential role as CV risk factors. The psychosocial status of each participant was self-reported by a coordinator-administered questionnaire.

Depressive and anxiety symptoms were assessed with the Geriatric Mental State version B3¹⁴. Neurologists have performed neurological examination during which history of stroke and depressive disorders were sought.

Peripheral artery disease assessment

Peripheral artery disease was defined as $ABI \leq 0.90$. The ABI was measured using a manual cuff and a hand-held Doppler device (Super Dopplex II, Huntleigh Technology PLC, Luton, UK) to determine systolic blood pressure in the posterior tibial and dorsal pedis arteries and humeral arteris bilaterally.

Measurements followed the protocol used in our core laboratory in France, in accordance to the American Heart Association guidelines^{15,16}

Covariates

Epidemiological data were collected following a standardized questionnaire.

Participants' systolic blood pressure (SBP), hypertension medication use (yes/no), current smoking behaviour (never, past - former smoker who quit smoking more than one year prior to the survey/ current smoking), body-mass index (BMI), diabetes (yes/no), dyslipidaemia, and physical activity were included as covariates in the multivariable analyses. Physical activity was measured in minutes per week using the Typical Week's Physical Activity Questionnaire¹⁸. Definitions and measurements methods have been detailed in a previous publication⁸.

Alcohol drinking was assessed based on the frequency and amount of alcohol intake in a typical drinking week, and was categorized as never, occasional (less than 5 days/week) and regular (more than 5 days/week).

Marital status data, education (school cycles completion) and occupation were collected. Covariates were selected because of their role as potential confounders in the association between psychosocial factors and PAD¹⁹. These same covariates were used in the study by Ohira et al., which studied the association between anger, anxiety, and depression on subclinical atherosclerosis in non-Hispanic Whites, African American, Hispanic, and Chinese populations in the MESA study¹⁹.

Statistical Analysis

Descriptive statistics (chi-square, t-test) were used to compare baseline demographic data, and to compare differences between PAD and non-PAD subjects for all psychosocial measures, and covariates, in both countries. Linear regression analysis was performed to determine the relationship between psychosocial variables and PAD. The multivariate model was adjusted for age, sex, country, urban and rural areas, traditional CV risk factors (hypertension, smoking, BMI, diabetes, cholesterol, physical activity), socioeconomic factors (education, marital status, occupation), cognitive status and depression.

Statistical analyses were carried out using Statview 5.0 software (SAS Institute, Cary, USA).

Results

Among 1871 participants (939 in CAR and 932 in ROC), cognitive and psychological data were lacking for 209 subjects. A total of 1662 subjects (832 in CAR and 830 in ROC) composed our study population; 59.3 % were females (Table 1). The mean age of the 209 excluded subjects was 74.9 ± 7.1 years (vs 72.9 ± 6.5 years in those included in this study). The rates of female sex were also comparable (58.2% vs 59.3% in our study population). Among patients excluded from the current analysis, the prevalence of hypertension, diabetes, dyslipidaemia and obesity did not differ as compared to those included in this study.

Mean age of the study population was significantly higher in PAD subjects but no difference was observed between CAR and ROC. The prevalence of hypertension, diabetes and obesity in our study population was higher in ROC, while subjects in CAR smoked tobacco and drank alcohol more. The general characteristics of the total population, in both countries as well as comparisons between PAD and no-PAD subjects are presented in Table 1. The prevalence of PAD in women and men was 16% and 11.7%, respectively. Female sex, hypertension, dyslipidaemia, lower education, cognitive disorders, anxiety but not depression were more frequently associated with PAD. Overall, the prevalence of anxiety was 7.2%, significantly higher in women (9.2% vs. 4.3% in men, $p < 0.001$). Prevalence of PAD and anxiety in each country and gender are presented in Figure 1. Anxiety was more frequently associated with PAD in women than in men (Figure 2).

In multivariate analysis, adjusted to age, sex, country, urban or rural areas, all traditional CV risk factors, socioeconomic status and associated cognitive disorders, PAD was significantly associated with anxiety but not depression. (Figure 3).

Discussion

In this population study composed of older Africans living in two sub-Saharan countries, we found a high prevalence of anxiety, especially in women and underlined the strong association between anxiety and PAD independently of age, country, all traditional CV risk factors, socioeconomic status and associated cognitive disorders.

Anxiety is known to be one of the most common mental health disorders worldwide. Data suggest that its prevalence is higher in western countries and particularly in the United States, affecting 9% of the elderly population²⁰. A recent systematic review on the prevalence of anxiety disorders in adult populations²¹ found the lowest prevalence in East Asia (2.8%, 95% CI: 2.2–3.4) and the highest in North America (7.7%, 95% CI: 6.8–8.8). It also analysed data in North African/Middle Eastern region (7.7%, 95% CI: 6.0–10), Switzerland, Korea, Pakistan and Germany but no data were available in Sub-Saharan countries. Our study underlines the high prevalence of this disorder in general elderly African population, higher than in western countries and particularly high in women.

The association between anxiety and cardiovascular diseases, especially CAD is demonstrated in cross-sectional, longitudinal, and prognostic studies with an estimated prevalence of anxiety substantially

greater in CAD populations (7.9%) than in general population (3.1%)²². Our study also confirms the higher prevalence of anxiety in PAD patients compared to the general population (13.4% vs. 6.2%). No geographical difference for the association of anxiety with PAD was found between in CAR or ROC.

Importantly, while previous studies described a similar prevalence of depression and anxiety in population with acute coronary syndrome^{23,24} and after coronary artery bypass graft surgery²⁵, depression disorders seem to be less common than anxiety in our PAD population. Anxiety disorders are comorbid with depression disorders in approximately 50 % of CAD cases^{5,26}. In our study only 9.2% of PAD subjects had concomitant anxiety and depression.

Evidence is mixed on possible sex differences in CV risk though anxiety and depression are more commonly reported among females than males. Results are still controversial: studies report incident rate of CAD consistent among both males and females²⁷ while others found a significant association between anxiety and CV disease occurrence in men (OR = 1.10, 95 % CI 1.05–1.15) but not women²⁸. In our study, interactions of PAD with anxiety were significant in both sexes but higher in women. This might explain the highest prevalence of PAD in female African population.

Pathways explaining the association between anxiety and cardiovascular disorders are less known than for depression. Findings from previous studies suggested that psychosocial factors such as anxiety and depression may be associated with the development of CV disease through unhealthy coping behaviours such as smoking, sedentary lifestyle and caloric intake^{29,30}. Adverse metabolic changes are also one of the underlying plausible mechanisms, such as abdominal obesity and dyslipidaemia, that are related to psychiatric disorders³¹. Nevertheless, our study demonstrates a strong association between anxiety and PAD, independently of all CV risk factors or lifestyle behaviours and suggests a possible causal relationship.

One hypothesis that might explain this association suggests that sympathetic nervous overactivity in depressed and anxious persons can mediate the association with atherosclerosis, e.g., through elevated resting and 24-hour heart rate and reduced heart rate variability³². A major challenge over the next years is to incorporate anxiety processes into the mainstream of cardiovascular pathophysiological research.

Our study has several limitations. The first is related to its cross-sectional design which might lead to the assumption that anxiety was triggered by PAD. It is however not plausible that PAD induces anxiety as most participants were not aware of their condition and had PAD diagnosed through the measurement of ABI. Second, 209 subjects were excluded of the study. Nevertheless, as described above, no different characteristics were found between the study population and the subjects excluded from these analyses. A “selection bias” must also be considered in studies of older persons as those with severe atherosclerosis might not live to older age and women have a higher life expectancy.

The strengths of our study are the large sample of participants (the largest population-based study in Central Africa), the rigours sampling covering rural and urban zones, the exhaustive data collection and

particularly the mental state assessment allowing an accurate diagnosis of the psychosocial factors.

Conclusions

Our study underlines the high prevalence of anxiety in African general population in the elderly, as well as a significant association with the peripheral artery disease, independently of all possible confounding factors. The higher rates of anxiety in women and stronger association with PAD as compared to men might explain the higher rates of PAD in African women. Further studies in other low- and middle- income countries are necessary to confirm the burden of PAD in this setting, in part related to increased levels of anxiety.

Abbreviations

ABI: ankle brachial index, BMI: body mass index, CAD: coronary artery disease, CAR: Central African Republic, CSI-D: Community Screening Interview for Dementia, CV: cardiovascular, EPIDEMCA: Epidemiology of Dementia in Central Africa, PAD: Peripheral artery disease, ROC: Republic of Congo, SBP: systolic blood pressure.

Declarations

Ethics approval and consent to participate

The study protocol conforms to the ethical guidelines of the 1975 Declaration of Helsinki. Informed consent (written or thumbprint for illiterate people) prior to inclusion in the study was given by all participants and/or their families.

The study protocol and its consentment method had prior approval of the Ethical committees in CAR and ROC, as well as the “Comité de la Protection des Personnes Sud-Ouest Outre-Mer” in France.

Consent for publication

Not applicable

Availability of data and material

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request

Competing interests

The authors declare that they have no competing interests

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Authors' contributions

Authors I.D, Ph.L, M.G, B.M, A. T., P.M.P, V. A. designed the study, directed its implementation, including quality assurance and control, and prepared its analytic strategy. Authors B. N. B. and P.M. helped conduct the literature review and prepare the Methods and the Discussion sections of the text. Authors I.D and M.G conducted the investigations. Author I. D. did the statistical analysis and drafted the manuscript. Author V.A was a major contributor in writing the manuscript. All authors read and approved the final manuscript.

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Authors' information

All authors are members of the Research team INSERM 1094 actively implicated in epidemiological research of non-communicable diseases in tropical countries, with a particular focus on cardiovascular risk factors in Africa.

Authors I.D and V.A actively participated at the 2017 European Society of Cardiology/European Society of Vascular Surgery for the management of the peripheral artery disease, as members of the ESC/ESH Task Force.

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Tables

Table 1. Characteristics of study population

	Study population		CAR	ROC	<i>p</i>	no PAD	PAD	<i>p</i>
	N (%)	M±SD	N (%)	N (%)	<i>CAR vs ROC</i>	N (%)	N (%)	<i>no-PAD vs PAD</i>
			M±SD	M±SD		M±SD	M±SD	
Participants	1662 (100)		832 (50.1)	830 (49.9)		1424	238	
Age (years)	72.9 (6.5)		72.4 (6.4)	73.5 (6.7)	0.013	72.7 (6.4)	74.6 (7.1)	<0.001
Women	986 (59.3)		498 (59.9)	488 (58.8)	0.659	828 (58.1)	158 (66.4)	0.017
Hypertension	1003 (61.0)		436 (52.4)	567 (68.3)	<0.001	842 (59.1)	161 (67.6)	0.008
Diabetes	128 (7.8)		36 (4.3)	92 (11.1)	<0.001	106 (7.4)	22 (9.2)	0.361
Dyslipidaemia	157 (11.1)		71 (8.5)	86 (10.4)	0.118	120 (0.8)	37 (15.5)	<0.001
Tobacco					<0.001			0.7252
Past	115 (6.9)		66 (7.9)	49 (5.9)		100 (0.1)	15 (6.3)	
Active	368 (22.2)		257 (30.9)	111 (13.4)		311 (21.8)	57 (23.9)	
BMI (kg/m ²)	21.0 (4.7)		20.5 (4.2)	21.6 (5.0)	<0.001	20.9 (4.7)	21.7 (5.3)	0.617
Alcohol					<0.001			0.041
Occasionally	90 (5.4)		52 (6.3)	38 (4.6)		76 (5.3)	14 (5.9)	
Regularly	347 (21.0)		241 (28.9)	106 (12.8)		312 (21.9)	35 (14.7)	
Sedentary lifestyle	690(41.5)		331(40.1)	160 (19.3)	<0.001	567 (39.8)	123 (51.7)	<0.001
Profession					<0.001			0.566
Employed	330 (19.9)		156 (18.8)	174 (20.9)		290 (20.4)	40 (16.8)	
Storekeeper	407 (24.5)		194 (23.4)	213 (25.7)		340 (23.9)	67 (28.1)	

Farmer	801 (48.3)	399 (48.1)	402 (48.5)		87 (48.2)	114 (47.9)	
No activity	81 (4.9)	49 (5.9)	32 (3.8)		69 (4.8)	12 (5.0)	
Primary education or higher	256 (15.4)	111 (13.3)	145 (17.5)	0.019	232 (16.3)	24 (10.1)	0.014
Marital status				0.263			0.313
Single	44 (2.6)	21 (2.5)	23 (2.8)		39 (2.7)	5 (2.1)	
Married	650 (39.2)	310 (37.3)	340 (40.9)		574 (40.3)	76 (31.9)	
Widow /Divorced	968 (58.2)	501 (60.2)	467 (56.3)		811 (56.9)	157 (65.9)	
Cognitive impairment				0.014			0.003
MCI	112 (6.7)	60 (7.2)	52 (6.3)		87 (6.1)	25 (10.5)	
Dementia	110 (6.6)	69 (8.3)	41 (4.9)		87 (6.1)	23 (9.7)	
Depression	609 (36.6)	260 (31.3)	349 (42.0)	<0.001	514 (36.1)	95 (39.9)	0.257
Anxiety	120 (7.2)	27 (3.2)	93 (11.2)	<0.001	88 (6.2)	32 (13.4)	<0.001

BMI : body mass index, , CAR: Central African Republic, MCI : Mild cognitive impairment , PAD: Peripheral arterial disease; ROC: Republic of Congo,

Figures

Figure 1

Prevalence of Peripheral arterial disease (PAD) and anxiety in : Central African Republic (CAR) and ROC: Republic of Congo (ROC) in men and women

Figure 2

Prevalence of Peripheral arterial disease (PAD) and concomitant anxiety in men and women.

Figure 3

Association between anxiety and Peripheral arterial disease (PAD) *Multivariate analysis MODEL 1: adjusted to age, country, rural/urban region; MODEL 2: MODEL 1 + cardiovascular risk factors (hypertension, diabetes, dyslipidaemia, tobacco, body mass index, sedentary lifestyle); MODEL 3: MODEL 2 + sociodemographic characteristics (profession, education, marital status); MODEL 4: MODEL 3 + cognitive impairment and depression.