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Cardiovascular Anomalies during Chronic Inflammatory Rheumatic Disease in Yaoundé: A Cross-Sectional Study

Complications cardiovasculaires au cours des rhumatismes inflammatoires chroniques à Yaoundé: une étude transversale

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Mots-clés. Rhumatisme inflammatoire chronique, complications cardiovasculaires, risque cardiovasculaire.

ABSTRACT

Background and rationale. Chronic inflammatory rheumatic disease (CIRD) represent a heterogeneous group of diseases associated to a high inflammatory state. They are associated to a huge morbidity mainly due to cardiovascular complications. Although cardiovascular risk factors associated to CIRD are well described, the major cardiovascular anomalies are largely unknown in our milieu. **Aim**. To identify the major cardiovascular anomalies in a population of Cameroonian patients with chronic inflammatory rheumatic disease. **Methodology**. We carried out a cross sectional study which included CIRD patients followed at the rheumatology unit of the Yaoundé Central Hospital. The cardiovascular complications were diagnosed by determining ankle to brachial systolic arterial pressure index (ABPI) and performing electrocardiogram (ECG), transthoracic echocardiography (TTE) and supra aortic trunk ultrasound (SATU). Blood samples were collected for lipid profile evaluation and cardiovascular risk were assessed by using the Framingham criteria. **Results**. Fifty two patients with CIRD were included. The age range was 14-82 years; There were 71.15% of women. Determination of ABPI showed that 1.92% had obliterans arteriopathy of lower limb and 5.76% had mediacalcosis. On ECG, we found 13 cases of branch block (25%) and one case of left ventricular hypertrophy (1.92%). TTE revealed 4.08% of pericarditis and 44.9% of valvulopathies. Among patients who did SATU, we found three cases of atheromatous plaques (7.89%) and five patients with calcification (13.15%). We found no factor associated to cardiovascular complications through univariate statistical analysis and the assessment of cardiovascular risk showed a globally low risk among the majority of our population. **Conclusion**. Cardiovascular anomalies in CIRD are present in Cameroonian patients with CIRD. However, the assessment of the cardiovascular risk using Framingham shows low risk for the majority of them. We can therefore conclude that these tools underestimate the risk among CIRD.

RÉSUMÉ

Contexte et justification. Les rhumatismes inflammatoires chroniques (RIC) représentent un groupe hétérogène de pathologies associées à un processus inflammatoire important. Elles sont la cause d'une grande morbidité chez ces patients par l'intermédiaire des complications cardiovasculaires (CCV) qu'elles entrainent. Bien que les facteurs de risque cardiovasculaires (FDRCV) dans les RIC aient été étudiés dans notre contexte, des zones d'ombres subsistent quant aux CCV majeurs retrouvées dans cette population. **Objectifs**. Identifier les CCV majeures retrouvées chez les patients atteints de RIC. **Méthodologie**. Nous avons mené une étude transversale descriptive chez des patients suivis pour RIC au sein du service de Rhumatologie de l'Hôpital Central de Yaoundé. Les pathologies cardiovasculaires ont été recherchées à travers la détermination de l'index de pression systolique par la mesure automatique, la réalisation de l'électrocardiogramme (ECG), l'échographie transthoracique (ETT), et de l'échographie des troncs supra aortiques (ETSA). Les prélèvements sanguins ont permis la détermination du profil lipidique et le risque cardiovasculaire a été évalué en utilisant les critères de Framingham. **Résultats**. Au total, notre population était constituée 52 patients. Le sexe féminin était majoritairement représenté (71,15%) et les extrêmes d'âges étaient 14 et 84 ans. L'artériopathie des membres inférieurs et la médiacalcose étaient présentes chez respectivement 1, 92% et 5,76% des patients. À l'ECG, nous avons observé 13 cas d'anomalies de la conduction (25%) et un cas d'hypertrophie ventriculaire gauche (1,92%). L'ETT a détecté des cas de péricardites (4,08%) et de valvulopathies (44,9%). Parmi les patients ayant réalisé l'ETSA, nous avons retrouvé trois cas de plaques athéromateuses (7,89%) et cinq cas de calcification artérielle (13,15%). Nous n'avons pas trouvé de facteurs associés aux CCV et notre population avait majoritairement un risque cardiovasculaire faible. **Conclusion**. Les CCV dans les RIC sont présentes et variées dans notre population malgré le faible risque cardiovasculaire retrouvé. L'utilisation des critères de Framingham aurait donc sous-évalué ce risque dans notre population.

INTRODUCTION

Chronic inflammatory rheumatic disease (CIRD) are a heterogenous group of disorders characterized by humoral or cell-mediated immune responses against diverse autoantigens, with prominent involvement of synovial joins [1]. IRD, including rheumatoid arthritis, ankylosing spondylitis and psoriasis arthritis are prevalent worldwide with a considerable burden in healthcare systems [2]. In fact, the prevalence of systemic auto immune diseases is estimated to 3.2 % and 9.4% respectively in USA and in Denmark [3,4]. In Sub-Saharan Africa we found a hospital prevalence of 8.2% and 28.85% respectively in Cameroon and in Togo [5,6]. Moreover, standardized mortality ratio in patients with IRD are higher than dose in the general population (1.3-2.3 in RA, 1.6-1.9 in AS, and 0.8-1.6 in PsA respectively) this increased mortality in mainly due to cardiovascular events [2].

Cardiovascular diseases are very frequent in patients with IRD. Intima media thickness was increased in patients with rheumatoid arthritis in France [7]. Arrhythmia and thromboembolic manifestations were prevalent in the evolution of scleroderma [8]. In Africa, we found a prevalence of 46% of cardiovascular events on 50 patients with Systemic Erythematous Lupus. The main complications found were auricular and ventricular hypertrophy (36%), pulmonary hypertension (22%) and repolarization abnormalities (16.3%) [9]. The pathogenesis of cardiovascular disease in patient with CIRD is mainly due to the underlying inflammation which impaired the function of apolipoprotein A1 and HDL particle and therefore increase the cardiovascular risk [10]. Even though there is a huge burden of both chronic inflammatory rheumatic disease and cardiovascular disease in Sub-Saharan Africa, no published study in our knowledge exist on the major cardiovascular anomalies found in patients with chronic inflammatory disease in Cameroon. Then we carried out this study to find out the cardiovascular complication of CIRD in patients seen in Rheumatology unit in Centre Hospital.

MATERIALS AND METHODS

We carried out a cross sectional study in a period of four months in the cardiology and rheumatology unit of the Yaoundé Central Hospital. For the recruitment, we looked for all patients seen in rheumatology unit and treated for chronic inflammatory rheumatic disease and with complete medical file. Then, we included in our study all CIRD patients which diagnosis is based on 2010 ACR/EULAR criteria for the RA [11,12], 1997 and 1980 ACR criteria respectively for lupus and sclerodermia [13,14], Amor and al. criteria for spondylarthritis [15], Hoogendjick and al. criteria for auto-immune Dermatopolymyositis [16]and Alarcon-Sergovia and Villareal for auto-immune connective tissue disease. Sjogren disease was diagnosed considering euro-american consensus [17]. We excluded any incomplete medical files and patients which did not give written consent.

The demographic, clinical and paraclinical information were recorded in two visits. At the first visits, we recorded sociodemographic, clinicals and we performed blood samples. Body Mass Index was calculated using Quetelet's indices and excess adiposity was defined by BMI $\geq$ 25 kg/m^2 [18]. Blood pressure was measured using a validated electronic devices (OMRON). Ankle to brachial systolic arterial pressure index (ABPI) was obtain using an automatic device (ABPI MD) and obliterans arteriopathy was diagnosed when ABPI < 0.90 and mediacalcose when ABPI > 1.30 [19]. We determined lipid profile using a spectrophotometric method and dyslipidemia were defined with the presence of at least one of the following criteria: Total cholesterol $\geq$ 2g/l, LDLc $\geq$ 1.3 g/l, HDLc $\leq$ 0.4g/l or triglyceride $\geq$ 1.5 g/l [20]. The cardiovascular risk was evaluated using the Framingham criteria. This score assesses the risk of developing cardiovascular disease in the next 10 years[21].

At the second visit, a cardiologist and a radiologist respectively realized and interpreted Electrocardiogram (ECG), transthoracic echocardiography (TTE) and supra aortic trunk ultrasound (SATU). During SATU an intima media thickness > 1 mm was considering to be pathologic.

Ethics Approval and consent to Participate

The research protocol was in accordance with the Declaration of Helsinski. An ethical clearance was obtained from the Institutional Ethics Committee of the Faculty of Medicine and Biomedical Sciences of the University of Yaoundé I and the Regional Ethics Committee in charge of Human Research. Administrative authorizations to recruit and manipulate blood samples were obtained from the Yaoundé Central Hospital and National Center of obesity of Yaoundé Central Hospital respectively.

RESULTS

General characteristics of the population

Table 1 summarizes the demographic and clinical characteristics of participants. In a total of 64 patients with CIRD seen, 52 were included in our study. The range of age was 14-82 years. The female (71.15%) were more represent than men (28.85%). The main chronic inflammatory rheumatic disease found including systemic erythematous lupus (34.62%), ankylosing spondylitis arthritis (17.31%), juvenile arthritis (15.38%) and rheumatoid arthritis (11.54%). The mean duration of the disease was 6.85 ± 5.19 years.

Concerning the anthropometric parameters, 55.77% of participants has a normal BMI. The overweight was found in 23.08% and obesity in 21.26 of all cases. The main cardiovascular risk factors registered were dyslipidemia (59.62%), BMI $\geq$ 25 Kg/m^2, family history of cardiovascular events (42.30%), menopause (13.46%) and advanced age (13.46%).

In our population, there was no glycemia disturbances. Among the 18 cases of Lupus, 27.78% has anti DNA antibodies and 44.44% Anti Sm antibodies. All cases of rheumatoid arthritis have anti-CCP and Rheumatoid factor antibodies. We also found Anti-RNP in all cases of mixed connective tissue disease.

Among our patients, 96.15% patient have disease modifying antirheumatic drugs (DMARDs). The other main drugs found in the specific treatment was hydroxychloroquine (51.92%), methotrexate (32.69%) and azathioprine (23.08%). Drugs found in the symptomatic treatment were corticoids (59.62%) and NSAID (26.92%).

Table 1. Demographics and clinical characteristics of the study population

Characteristics		
	Mean	SD
Age, year	36.19%	±14,42
Duration, year	6,85	± 5,19
	Number	%
Sex		
Female	37	71.15
Male	15	28.85
CIRD		
SLE	18	34.62
Ankylosing spondylitis	9	17.31
Juvenile spondylitis	8	15.38
Rheumatoid arthritis	6	11.54
MCTD	4	7.69
Sclerodermia	2	3.85
Polymyositis	2	3.85
Vascularitis	1	1.92
Gougerot-Sjogren Syndrome	1	1.92
Reactive arthritis	1	1.92
Cardiovascular risk factors		
Dyslipidemia	31	59.62
BMI ≥ 25 Kg/m^2	23	44.23
Familial history of CVD	22	42.30
Menopause	7	13.46
Advanced age	7	13.46
Hypertension	5	9.62
Physical inactivity	5	9.62
Treatment		
Specific treatment		
DMARDS	50	96.15
HCQ	27	51.92
MTX	17	32.69
AZT	12	23.08
SSZ	9	17.31
Symptomatic treatment		
Corticoids	31	59.62
NSAIDS	14	26.92

CIRD : chronic inflammatory rheumatic diseases;
SLE: systemic lupus erythematous;
MCTD : : mixed connective tissue diseases; BMI: body mass index;
CVD : Cardiovascular disease ;
DMARDS : disease-modifying antirheumati drugs ;
HCQ : hydroxychloroquine MTX : methotrexate ;
AZT : azathioprine ; SSZ: sulfasalazine ;
NSAIDS: non- steroidal anti-inflammatory drugs.

Cardiovascular complications

Ankle to brachial systolic arterial pressure index detect one case of obliterans arteriopathy of lower limb (1.92%) and 03 cases of mediacalcosis. We found at ECG 13 cases of branch block (25%) and 01 case of left ventricular hypertrophy (1.92%). The various type of branch block was incomplete right bundle branch block (02 cases) , complete right bundle branch block (03 cases) , incomplete left bundle branch block (06 cases) and complete left bundle branch block (02 cases) Transthoracic echocardiophy showed 02 cases of pericarditis (4,08%) and 22 cases of valvulopathies (44.9%). The main valvulopathies found were tricuspid incompetence (20.41%) and mitral incompetence (18.37%). These anomalies were mainly found in SEL and in sclerodermia. Among the 52 patients with CIRD, 38 had done Supra aortic trunk ultrasound (SATU). We observed 05 cases of atheromatic plaques (7.89%) and 05 patients with calcification (13.15%). Table 2 summarizes the main cardiovascular anomalies in our study population.

Table 2. Cardiovascular anomalies in our study population

Investigations	Anomalies	N	%
ABPI measurement	Obliterans arteriopathy	1	1.92
	Mediacalcosis	3	5.76
ECG (n=52)	Conduction disorders: branch block	13	25
	Ventricular hypertrophy	1	5.55
	Prolonged QTc	8	21.62
TTE (n=49)	Pericarditis	2	4.08
	Valvulopathies	22	44.9
SATU (n=38)	IMT	8	21.05
	Plaques	3	7.89
	Calcifications	5	13.15

ABPI: Ankle to brachial systolic arterial pressure index;
ECG: electrocardiogram; TTE: Transthoracic echography;
SATU: supra aortic trunk ultrasound.

Risk factors to cardiovascular anomalies

In our study we did not detected any associated factors to cardiovascular complications through univariate statistical analysis

Evaluation of the cardiovascular risk considering the Framingham criteria

For the evaluation of the cardiovascular risk, we have taken in consideration patients with at least 20 years old. The cardiovascular risk of our population was resume in figure 1. On the 45 patients evaluated, we found that 97% had a low risk and 2.22% had a moderate risk. The elevated risk was not found in our study. Figure 1 represents the repartition of cardiovascular risk assessment in our population.

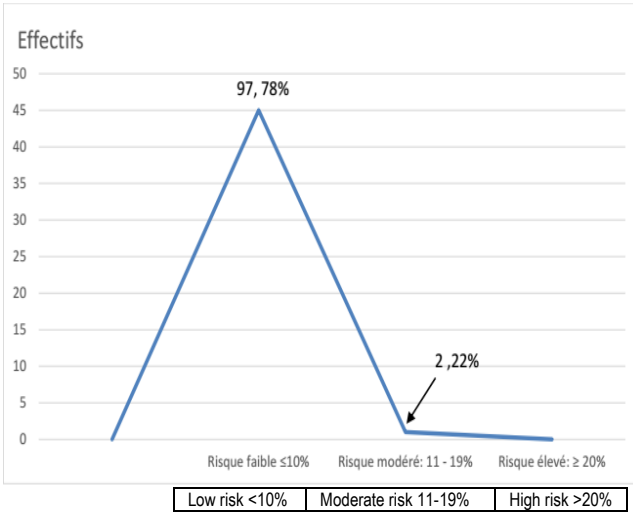

Figure 1. Cardiovascular risk assessment in our population

DISCUSSION

Chronic inflammatory rheumatic diseases are a group of heterogenous disorders characterized by autoimmune response [1]. They are associated to a great morbidity and mortality mainly due to cardiovascular complications [2]. Aim of our study was to describe the sociodemographic, clinic and paraclinical characteristics of CIRD patients seen in the rheumatology unit at the Yaoundé Centre Hospital, to list cardiovascular anomalies and to assess the cardiovascular risk based on the Framingham criteria. We therefore carried out cross sectional study on 50 patients with CIRD.

In our study, the mean age was 36 years and female were most represented than men (sex ratio: 0.41). The age range between 20-30 years and 30-40 years were most present in our population which was similar to the existing data. In fact, CIRD are most present in women in childbearing age and are triggering by pregnancy and ovulation-induction drug [22,23]. Thus, suggesting the implication of hormone in the pathogenesis of the pathology [24]. The predominance of female was also observed by study done by Singwe-Ngandeu and al. in which found mean age was 31 years and a sex ratio of 0.09[6]. Furthermore, 96.15% of patients have a DMARDs. Hydroxychloroquine (51.92%) and Methotrexate (36.69%) were the main drugs used. These results can be explained by the fact that DMARDs have down regulated the immune system in the evolution of CIRD [25]. The use of corticoid (59.62%) and NSAID (26.92%) was also associated to the treatment. In fact, these drugs are used for symptomatic treatment in a case of exacerbation[26].

Assessment of cardiovascular risk factor revealed that the prevalence of dyslipidemia was 59.62%. Data existed were quite different of our results. In fact, the presence of proinflammatory state currently leads to a decrease of total HDL and LDL cholesterol levels in [27] patients with CIRD [27]. Family history of cardiovascular diseases and obesity were respectively found on 21.16% and 9.62% of patients. Obesity is normally associated with elevated CRP levels and increased risk of cardiovascular events[29]. In pathology such as Rheumatoid arthritis and Psoriasis arthritis, abnormal body composition is also associated with higher inflammatory state and more severe disease[30].

Among patients who did SATU, 7.89% have atheromatic plaques and 13. 15% calcifications. Ankle to brachial systolic arterial pressure index detect one case of obliterans arteriopathy of lower limb and 03 cases of mediacalcosis. The mechanism explaining the proatherogenic effect of chronic inflammation are numerous including conformational changes in HDL, which transform it into a proinflammatory and proatherogenic molecule, the development of endothelial dysfunction, the activation of the coagulation cascade, the induction of secondary dyslipidemia, an increased atheromatous plaque vulnerability, and an increased extent of coronary artery calcification [31,32].

The assessment of the cardiovascular risk using Framingham criteria showed a low risk in 46 patients (97%) and a moderate risk in one patients (2.22%). This finding was also found by Singwe-Ngandeu and al. which also found a low cardiovascular risk in patients with CIRD using the WHO/ISH risk charts [6]. Moreover, many cardiovascular risk calculators appropriate for the general population have not been tested to the majority of CIRD.

Authors' contribution:

Designed the research: CNNG, MM, BH, MNS
Collected data: CNNG, MM, MG
Analysed data: MG, CNNG
Wrote the first draft of the paper: CNNG, DWA, FUN
Critically revised and adopted the manuscript: All the authors.
All the authors approved the final version of the manuscript.

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