



## Original Article

# Prevalence of Aortic Regurgitation and Associated Factors in Patients with Severe Hypertension in Sub-Saharan Africa: A Cross Sectional Echocardiographic Study

*Fréquence de la régurgitation aortique et facteurs associés chez les patients hypertendus sévères en Afrique subsaharienne : Une étude transversale échocardiographique*

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### ABSTRACT

Arterial hypertension is one of the main cardiovascular risk factors affecting about a third of subjects in low- and middle-income countries. During its course, there are many damages on the heart including aortic regurgitation. We aimed to determine the prevalence of aortic regurgitation and associated factors in patients presenting with severe hypertension. **Methods.** This was a cross-sectional study including patients with severe hypertension recruited at the cardiology outpatient consultation in two tertiary hospitals of Yaounde, Cameroon. Clinical data were recorded and transthoracic echocardiography was performed to evaluate cardiac function and describe aortic valve. Associated factors were assessed with Chi Square test or Fisher Exact test. **Results.** We included 92 patients with a mean age of  $60.8 \pm 13.1$  years. The median blood pressure values were 189 (IQR 180 – 207) for systolic and 114 (103 – 123) for diastolic. Sixteen patients (17.4%) had aortic regurgitation, with moderate severity for more than half of them. Age above 70 years, systolic blood pressure greater than 200 mmHg and diastolic blood pressure greater than 130 mmHg were significantly associated with aortic regurgitation. **Conclusion.** Aortic regurgitation is found in about one fifth of patients with severe hypertension, and is associated to aging and higher values of blood pressure. Special attention should be paid to the diagnosis of aortic regurgitation in patients with these factors.

### RÉSUMÉ

**Introduction.** L'hypertension artérielle est l'un des principaux facteurs de risque cardiovasculaire affectant environ un tiers des sujets dans les pays à revenus faibles et/ou intermédiaires. Elle entraîne de nombreux dommages sur le cœur, y compris la régurgitation aortique. Le but de notre travail était de déterminer la fréquence de la régurgitation aortique et les facteurs associés chez les patients ayant une hypertension sévère. **Méthodologie.** Il s'agissait d'une étude transversale incluant des patients souffrant d'hypertension sévère recrutés lors de la consultation ambulatoire de cardiologie dans les hôpitaux central et général de Yaoundé. Des données cliniques ont été enregistrées et l'échocardiographie transthoracique a été réalisée afin d'évaluer la fonction cardiaque et l'éventuelle valvulopathie aortique. Les facteurs associés ont été évalués avec le test du Chi Carré ou le test exact de Fisher. **Résultats.** Nous avons inclus 92 patients présentant un âge moyen de  $60,8 \pm 13,1$  ans. Les valeurs médianes de pression artérielle étaient 189 (IQR 180 – 207) pour systolique et 114 (103 – 123) pour diastolique. Seize patients (17,4 %) ont eu la régurgitation aortique, avec la sévérité modérée pour plus de la moitié d'entre eux. L'âge au-dessus de 70 ans, la tension artérielle systolique plus grande que 200mmHg et la tension artérielle diastolique plus grande que 130mmHg ont été sensiblement associés à la régurgitation aortique. **Conclusion.** La régurgitation aortique est retrouvée chez environ 1/5<sup>ème</sup> des patients ayant une hypertension sévère, et est associée au vieillissement et à des valeurs plus élevées de la pression artérielle. Une attention particulière doit être accordée au diagnostic de régurgitation aortique chez les patients présentant ces facteurs.

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**Mots clés:** Hypertension artérielle sévère; Régurgitation aortique; Facteurs associés; Cameroun

### INTRODUCTION

Hypertension (HTN) – or elevated blood pressure – is a major cardiovascular risk factor; it affects more than 1 billion people worldwide, with about two-thirds living in low- and middle-income countries. The World Health

Organization African Region has the highest prevalence of hypertension (27%) [1]. It affects about 29.7% of adults in Cameroon, and this prevalence is predicted to increase to 35.5% by 2025 – this represents a 40% increase in 10 years. About one patient in ten is aware of the disease, thus many patients are diagnosed at a stage

of severe hypertension [2,3]. HTN significantly increases the risk of heart diseases, including aortic regurgitation (AR) which is characterized by reflux of blood from the aorta into the left ventricle during diastole. HTN is a common cause of abnormalities of the aortic root, thus of secondary AR. Furthermore, several risk factors are common to HTN and AR, including aging and dyslipidemia [4].

AR worsen the prognosis of patients with hypertension by causing left ventricular volume overload, then a dilation and eccentric hypertrophy of the left ventricle, which overtime result in a decline in ventricular systolic function and ejection fraction, and finally in heart failure [5]. However, few studies have been conducted to estimate the real burden of this complication of hypertension in low income settings, especially in the group of patients with severe hypertension which is at higher risk of congestive heart failure [6]. We aimed to determine the prevalence of AR in a group of Cameroonian patients with severe hypertension, and to identify factors associated to AR in this population. These data will help to identify the subgroups of patients with severe hypertension who need special care and monitoring in order to reduce the risk of AR, especially in our context where resources are limited.

## MATERIALS AND METHODS

### Study population and data collection

This was a cross sectional study done in the cardiology outpatient units of the Yaoundé Central Hospital (YCH) and the Yaoundé Central General Hospital (YGH), during a period of eight months (October 2018 to May 2019). Patients presenting with severe hypertension or who were diagnosed with severe hypertension (define as systolic blood pressure  $\geq 180$  and / or a diastolic blood pressure  $\geq 110$ ) within the past three months were included in the study. We excluded patients with past history of heart's structural abnormality. At inclusion, sociodemographic and clinical were collected, and the transthoracic echocardiography was performed.

### Echocardiography

Doppler transthoracic echocardiography was performed for all patients according to the American Society of Echocardiography recommendations with a Hitachi Arietta V70 (made by Hitachi-Aloka in 2014) machine in YGH and a Sonoscape S50 (made in China in 2017 by Guangzhou Yueshen Medical Equipment Corporation) machine in YCH [7]. The left ventricular ejection fraction (LVEF) was measured with the biplane Simpson's method. Doppler ultrasound was used to evaluate the valves and to characterize the AR when it was diagnosed.

### Data analysis

The data were analyzed with the Statistical Package for Social Science (SPSS) version 23.0 for Windows (IBM SPSS, Chicago, Illinois, USA). Categorical variables were described using frequencies and percentages. Continuous variables were described using mean and standard deviation or median and interquartile range (IQR) as appropriate. The Chi square and the Fisher tests were used to assess the association between

categorical variables and the aortic regurgitation. A  $p$  value  $< 0.05$  was considered statistically significant.

### Ethical consideration

We conducted the study in accordance with the Declaration of Helsinki and the Harmonized Tripartite Guideline for Good Clinical Practice from the International Conference on Harmonization. An ethical clearance was obtained from the Institutional Ethics and Research Committee of the Faculty of Medicine and Biomedical Sciences of the University of Yaoundé I and informed consent was taken from all the patients (N°183/UY1/FMSB/VDRC/CSD).

## RESULTS

### Demographic and clinical characteristics of the study population

A total of 92 patients were recruited, 85 from YCH and 7 from YGH. The mean age was  $60.8 \pm 13.1$  (range: 23 – 96) years and the median blood pressure values were 189 (IQR: 180 – 207) mmHg and 114 (IQR: 103 – 123) mmHg respectively for systolic and diastolic blood pressure. More than half of participants were physically inactive. Calcium channel blockers were the most used antihypertensive medication (Table 1).

**Table 1: Description of the study population**

Characteristics	n (%)
<b>Age range (years)</b>	
< 40	5 (5.5)
[40 – 50[	14 (15.2)
[50 – 60[	28 (30.4)
[60 – 70[	24 (26.1)
$\geq 70$	21 (22.8)
<b>Sex</b>	
Male	43 (46.7)
Female	49 (53.3)
<b>Cardiovascular risk factors</b>	
Physical inactivity	51 (55.4)
Obesity*	33 (35.9)
Diabetes	13 (14.1)
Smoking	4 (4.3)
<b>Anti-hypertensive medications used</b>	
ACEi	22 (23.9)
ARBs	7 (9.7)
Calcium channel blockers	59 (64.1)
Beta blockers	8 (8.7)
Thiazide diuretics	33 (35.9)
Central acting antihypertensive	1 (1.1)
Self-medication with herbal medicine	8 (8.7)
None	20 (21.7)
<b>SBP (mmHg)</b>	
< 180	20 (21.7)
[180 – 200[	42 (45.7)
[200 – 220[	20 (21.7)
$\geq 220$	10 (10.9)
<b>DBP (mmHg)</b>	
< 110	30 (32.6)
[110 – 120[	31 (33.7)
[120 – 130[	18 (19.6)
$\geq 130$	13 (14.1)
<b>Left ventricular systolic dysfunction</b>	54 (58.7)

SBP: Systolic blood pressure; DBP: Diastolic blood pressure;

ACEi: Angiotensin converting enzyme inhibitors;

ARBs: Angiotensin II receptor blockers;

\*Obesity was defined as BMI  $\geq 30$  Kg/m<sup>2</sup>.

**Characteristics of aortic regurgitation**

The prevalence of aortic regurgitation was 17.4% (95% CI: 10.9 – 26.1), with 62.5% of moderate severity and 87.5% with calcifications (Table 2). The Tele diastolic flux velocity was less than 18 cm/s for more than 80 % of the participants with AR.

**Table 2: Characteristics of aortic regurgitation (n = 16)**

Characteristics	n (%)
<b>Flux cartography (mm<sup>2</sup>)</b>	
Grade 1: <10	11 (68.8)
Grade 2: 10 – 20	5 (31.3)
<b>Valve aspect</b>	
Normal	1 (6.3)
Thickened	1 (6.3)
Calcified	14 (87.5)
<b>Vena contracta (cm)</b>	
< 3	5 (31.2)
3- 6	11 (68.8)

**Table 2: Characteristics of aortic regurgitation (n = 16)**

<b>Pressure half time (ms)</b>	
200- 500	12 (75)
>500	4 (25)
<b>Tele diastolic flux velocity (cm/s)</b>	
<18	13 (81.3)
18- 20	2 (12.5)
>20	1 (6.3)
<b>Aortic regurgitation severity</b>	
Mild	6 (37.5)
Moderate	10 (62.5)

**Factors associated with aortic regurgitation**

AR was more frequent in patients aged 70 years and above ( $p = 0.046$ ) and those with herbal medicine self-medication ( $p = 0.011$ ). Similarly, higher systolic and diastolic blood pressure were significantly associated with AR (Table 3). Patients with obesity had a lower frequency of AR compared to those with BMI less than 30 Kg/m<sup>2</sup> ( $p = 0.007$ ).

**Table 3: Factors associated with aortic regurgitation**

Characteristics	Aortic regurgitation		OR (95 % CI)	p value
	Yes (n = 16)	No (n = 76)		
<b>Sex</b>				
Male	8 (18.6)	35 (81.4)	1.2 (0.4- 3.4)	0.774
Female	8 (16.3)	41 (83.7)		
<b>Age range (years)</b>				
< 40	1 (20)	4 (80)	1.2 (0.1 – 11.5)	1.000
[40 – 50[	2 (14.3)	12 (85.7)	0.8 (0.2 – 3.8)	1.000
[50 – 60[	4 (14.3)	24 (85.7)	0.7 (0.2 - 2.5)	0.768
[60 – 70[	2 (8.3)	22 (91.7)	0.4 (0.1 – 1.7)	0.222
≥70	7 (33.3)	14 (66.7)	3.4 (1.1 - 10.8)	0.046
<b>Anti-hypertensive medications used</b>				
ACEi	4 (18.2)	18 (81.8)	1.1 (0.3 – 3.7)	1.000
ARBs	0 (0)	7 (100)	n/a	0.348
Calcium channel blockers	8 (13.6)	51 (86.4)	0.5 (0.2– 1.5)	0.195
Beta blockers	2 (25)	6 (75)	1.7 (0.3 – 9.1)	0.624
Thiazide diuretics	6 (18.2)	27 (81.8)	1.1 (0.4 – 3.3)	0.881
Central acting antihypertensive	0 (0)	1 (100)	n/a	1.000
Self-medication with herbal medicine	4 (50)	4 (50)	6 (1.4 – 27.3)	0.011
None	5 (25)	15 (75)	1.8 (0.6 - 6.1)	0.327
<b>Cardiovascular risk factors</b>				
Diabetes	1 (7.7)	12 (92.3)	0.4 (0.04 – 2.9)	0.453
Tobacco	0 (0)	4 (100)	n/a	1.000
Alcohol	6 (16.2)	31 (83.8)	0.9 (0.3 – 2.6)	0.807
Physical inactivity	10 (19.6)	41 (80.4)	1.4 (0.5 – 4.3)	0.532
<b>SBP (mmHg)</b>				
< 180	4 (20)	16 (80)	1.3 (0.3 – 4.4)	0.744
[180 – 200[	1 (2.4)	41 (97.6)	0.06 (0.007 – 0.5)	< 0.001
[200 – 220[	8 (40)	16 (60)	5.3 (1.7 – 16.9)	0.006
≥ 220	3 (30)	7 (70)	2.3 (0.5 – 9.9)	0.370
<b>DBP (mmHg)</b>				
< 110	4 (13.3)	26 (86.7)	0.6 (0.2 – 2.2)	0.475
[110 – 120[	5 (16.1)	26 (83.9)	0.9 (0.3 – 2.8)	0.820
[120 – 130[	2 (11.1)	16 (88.9)	0.5 (0.1 – 2.6)	0.729
≥ 130	5 (38.5)	8 (61.5)	3.9 (1.1 – 14)	0.046
<b>BMI (Kg/m<sup>2</sup>)</b>				
< 18.5	0 (0)	1 (100)	n/a	1.000
[18.5 – 25[	10 (32.3)	21 (67.7)	4.4 (1.4 – 13.5)	0.007
[25 – 30[	5 (18.5)	22 (81.5)	1.1 (0.3 – 3.5)	1.000
≥ 30	1 (3)	32 (97)	0.09 (0.01 – 0.7)	0.007
<b>LV systolic dysfunction</b>	7 (13)	47 (87)	0.5 (0.2 – 1.4)	0.182

ACEi: Angiotensin converting enzyme inhibitors; ARAs: Angiotensin II receptor blockers; BMI: Body mass index; DBP: D

## DISCUSSION

We found that AR is present in about one fifth of patients with severe HTN in our setting, with more than 60% of moderately severe cases. Aging and higher blood pressure values were significantly associated to AR in this population while obesity appears to be a protective factor against AR. We didn't find any significant association of AR with left ventricular systolic dysfunction.

The prevalence of AR in our population was lower to the prevalence reported by Vríz et al. (34.8%), in a group of hypertensive patients in Italy, while they included patients with mild and moderate hypertension [8]. This difference can be explained by the longer duration of hypertension in their population. They recruited patient who were aware of their status since up to one year, while our patients were diagnosed during the past three months. This difference shows that the impact of HTN on aortic valves may be related to the duration of HTN, as it was suggested by other authors [9]. In fact, one of the mechanisms which explain the relation between HTN and AR is a degenerative process which leads to aortic root enlargement. There was no significant effect of AR on left ventricular systolic dysfunction in our population. It suggests that HTN didn't last enough to impact the heart structure and function. This emphasizes the need of long-term control of blood pressure, and sensitization of patient with longer duration of HTN about their risk of AR.

Similarly to previous study, we found a significant association of aging with AR; patients above 70 years were significantly at higher risk [8,10]. Age related abnormalities have been described for both the aortic valve and the aortic root, with respectively calcific and degenerative lesions [4]. Thus, hypertension may act here as a potentiator of these lesions, and increases the risk of AR in older patients. Practitioners should therefore give special care and counselling to older patients, in order to reduce the probability of developing AR. The early diagnosis of this complication through standard transthoracic echocardiography can also be considered as a priority in the management of these patients.

Our results show that among patients with severe HTN, those with higher values of SBP or DBP are significantly at higher risk of AR. Vríz et al. also found a significantly higher systolic blood pressure in hypertensive patient with AR compared to hypertensive patients without AR after adjustment with age [8]. Although other studies didn't find a significant relation between aortic root diameter and severity of HTN, our results suggest that there may be other pathophysiological pathways which explain the occurrence of AR in patients with hypertension.

This study has some limitation. Firstly, our small sample size may hide some significant factors associated to AR, due to the low power of the study; we didn't perform a multivariate analysis to address potential confounders because of the low sample size. Nevertheless, these

results -which are among the few rare data available in low and middle incomes countries - can serve as basis to design more powerful studies. Another limitation is that office BP was used to diagnose severe HTN, which has a less reproducible index of the BP load than the ambulatory blood pressure monitoring.

Aortic regurgitation is a complication of severe hypertension found in about one fifth of the patients. Most of the cases are of moderate severity with calcification. Aging and higher blood pressure significantly increases the risk of AR in patients with severe hypertension. Therefore, AR can be considered as a priority in the management of older patient with high values of blood pressure. Further studies should also be undertaken to better understand the impact of high values of blood pressure on aortic valve.

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