

## ORIGINAL ARTICLES

# Left ventricular hypertrophy and linked cardiovascular risk factors among Congolese licensed civilian aircrew

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## ABSTRACT

**Objective:** To assess the prevalence of left ventricular hypertrophy (LVH) and linked cardiovascular risk factors in civilian aircrew.

**Methods:** Cardiovascular risk factors were assessed among flight and cabin crew undergoing routine clinical and biological evaluation for initial or renewal of aeromedical license. The evaluation also included a standard 12-lead ECG and echocardiography. Echo-based LVH was LVM  $\geq 49$  g/m<sup>2.7</sup> (men) or  $\geq 45$  g/m<sup>2.7</sup> (women). LVH was categorized as mild (men: 49-55 g/m<sup>2.7</sup>; women: 45-51 g/m<sup>2.7</sup>), moderate (men: 56-63 g/m<sup>2.7</sup>; women: 52-58 g/m<sup>2.7</sup>), or severe (men:  $\geq 64$  g/m<sup>2.7</sup>; women:  $\geq 59$ g/m<sup>2.7</sup>) according to Lang's report.

**Results:** Among the 379 aircrew members (70.4% men; 23% Caucasians; 62.5% flight crew; mean age 40.6  $\pm$  12.8 years), LVH was present in 36 individuals (9.5%) with mild, moderate and severe pattern observed respectively in 19.4%, 33.3% and 47.2% of the cases. The rate of LVH amounted to 16.7% in normotensive subjects, 25.0% in those with prehypertension, and 58.3% among hypertensive individuals. In addition to age of 40-59y (OR: 8.48; 95% CI: [2.23-12.23];  $p = .002$ ) or more (4.22 [1.57-11.35];  $p = .004$ ), hypertension (3.55 [1.50 - 8.41];  $p = .004$ ), overweight/obesity (5.33 [1.14 - 25.05];  $p = .034$ ) and hyperuricemia (5.05 [2.11 - 12.09];  $p = .001$ ), all well-known constituents of the metabolic syndrome, were the main factors significantly associated with LVH.

**Conclusion:** The frequency and link of LVH to the components of the metabolic syndrome highlights the need for a comprehensive approach to the management of cardiovascular risk factors in civilian aircrew.

**Key Words:** Left ventricular hypertrophy, Associated factors, Civilian aircrew

## 1. INTRODUCTION

Left ventricular (LV) hypertrophy (LVH) is a well-established predictor of cardiovascular (CV) morbi-mortality

in the general population.<sup>[1,2]</sup> Indeed, LVH is the strongest risk factor for sudden death and ventricular arrhythmias as well as myocardial ischemia, coronary heart disease, and con-

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gestive heart failure.<sup>[3-5]</sup> Abnormal LV geometry in hypertensive individuals is often linked with diastolic dysfunction that can be assessed by performing transmitral flow in tandem with tissue Doppler techniques.<sup>[6]</sup> Various antihypertensive drugs induce LVH regression.<sup>[7]</sup> Therefore in high-risk individuals the management of LVH and its correlates could help lessening the burden of CV morbi-mortality.<sup>[8]</sup>

In the Democratic Republic of the Congo (DRC), the prevalence of hypertension, although fragmentary, is estimated to exceed 30% of adult population leading to increased high blood pressure (BP) related CV events.<sup>[9,10]</sup> The correlates of LVH as well as its geometric patterns have already been assessed in the general population and in some high-risk groups such as hypertensive individuals, and those with type-2 diabetes mellitus (T2DM) or chronic kidney disease,<sup>[11]</sup> but not among Civilian Aircrew with a rather high reported CV disease risk.<sup>[12]</sup> We, therefore, explored the correlates of LVH and its geometric patterns among hypertensive Civilian Aircrew attending the accredited Aeronautical Medical Centers at Kinshasa for their initial or routine medical check-up.

## 2. METHODS

Aircrew personnel attending Congolese certified Aeromedical Centers to initiate or renew their medical license were invited to participate by informed consent in the present study. According to the CAA/DRC and the ICAO regulations aircrew comprised of flight crew (pilots: class I and flight Engineers (FE): class II) and cabin crew (class II). The participants underwent routine clinical and biological assessment including standard 12-leads ECG and echocardiography. A trained nurse allotted a questionnaire to summon details on medical background (known hypertension, T2DM, and current drug use), and lifestyle habits (alcohol and tobacco consumption, and physical activity). Sedentary lifestyle was defined as a less than 2h-weekly physical activity. Smoking and drinking habits were the self-reported notion of any amount of cigarettes or alcohol consumed at least once per week the previous year. Body weight was determined using a FAZZINI scale (Italy), the subject barefooted in light clothing. Height and waist circumference (WC) were measured with a tape measurer. Body mass index (BMI) was the ratio of weight (kg) to the square of height (m<sup>2</sup>). Overweight and obesity were defined as BMI  $\geq 25$  Kg/m<sup>2</sup> and BMI  $\geq 30$  Kg/m<sup>2</sup>, respectively;<sup>[13]</sup> abdominal obesity as WC > 94 cm (men) or > 80 cm (women) in the Africans, or WC > 10<sup>2</sup> cm (men) in Caucasians.<sup>[14]</sup> After a 5-minute rest in a calm room, three BP measurements were obtained using an OMRON HEM 7001 monitor with appropriate size cuff secured on the non-dominant arm. The average of these

measurements was used in data analysis. Hypertension was defined as BP  $\geq 140/90$  mmHg or current use of high BP lowering drugs.<sup>[15]</sup> Pulse pressure (PP) was obtained by subtracting diastolic from systolic BP and values > 60 mmHg defined subclinical atherosclerosis.<sup>[15]</sup> A standard 12-lead ECG was used to compute heart rate. A 2D-guided (GE Logic 5) M-mode in the short view or a linear 2D parasternal long axis view was used to assess left atrium (LA), aortic, and LV internal (LVIDd) diameters at ending diastole as well as posterior wall (PWTd), and interventricular septum (STd) thickness. LV mass (LVM) was calculated using appropriate formula<sup>[16]</sup> and was indexed (LVMi) to height<sup>2.7</sup>.<sup>[17]</sup> The relative wall thickness (RWT) was 2-fold PWTd divided by LVIDd. Pulsed-wave Doppler technique was performed to obtain E- and A- wave as well as deceleration time (DcT) of E. E/A ratio in tandem with DcT was used to assess diastolic dysfunction.<sup>[16]</sup> We defined Echo-based LVH as LVM  $\geq 49$  g/m<sup>2.7</sup> in men or  $\geq 45$  g/m<sup>2.7</sup> in women. We listed LVH as mild (men: 49-55; women: 45-51 g/m<sup>2.7</sup>), moderate (men: 56-63; women: 52-58 g/m<sup>2.7</sup>) or severe (men:  $\geq 64$  g/m<sup>2.7</sup>; women:  $\geq 59$ g/m<sup>2.7</sup>) according to Lang's report.<sup>[18]</sup> RWT  $\geq 0.42$  or < 0.42 with increased LVM indicates concentric or eccentric LVH, respectively. RWT  $\geq 0.42$  with normal LVM identifies concentric remodeling.<sup>[19]</sup>

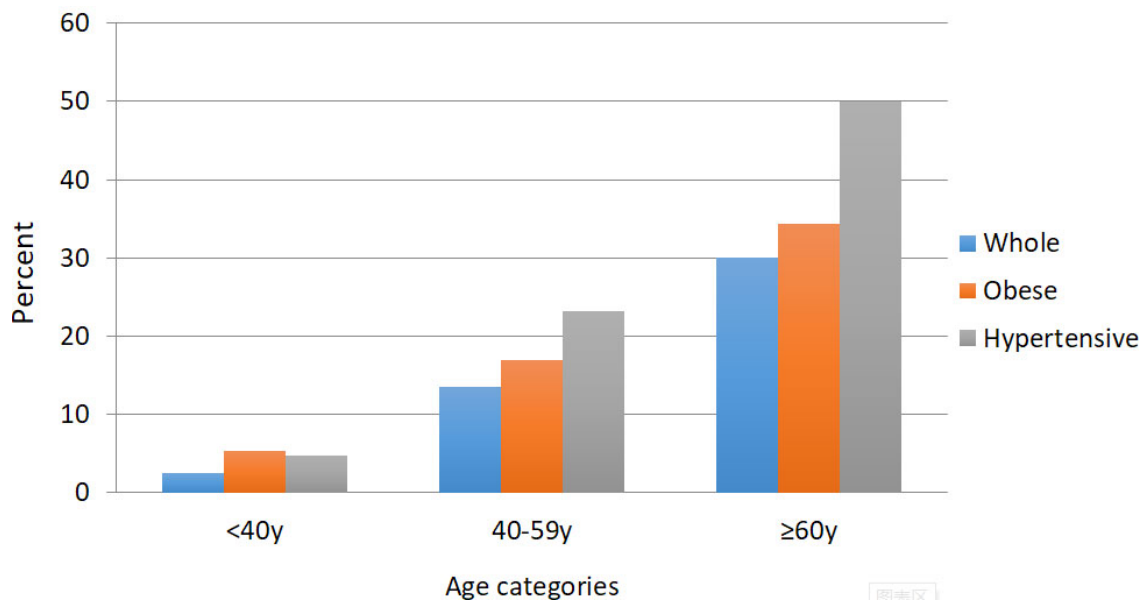
Fasting serum glucose (FSG), total cholesterol (TC), high-density lipoprotein cholesterol (HDL-c), triglycerides (TG), urea, creatinine, and uric acid (UA) were measured from a half-a-day starving oneself venous blood sample. Low-density lipoprotein cholesterol (LDL-c) was determined using appropriate procedures.<sup>[20]</sup> T2DM was a FSG > 126 mg/dl, a self-disclosed diagnosis, or the use of glycemic lowering medications.<sup>[21]</sup> TC > 200 mg/dl, LDL-c  $\geq 100$  mg/dl-, and/or HDL-c < 50 mg/dl (in women) or 40 mg/dl (in men) represent dyslipidemia.<sup>[22]</sup> Abdominal adiposity linked with at least two of the subsequent attributes: BP > 130/85 mmHg and/or use of high BP lowering drugs, FSG > 100 mg/dl and/or self-disclosed T2DM diagnosis, TG > 150 mg/dl or use of lipid lowering medications, HDL-c < 50 mg/dl in women or < 40 mg.dL<sup>-1</sup> in men represent metabolic syndrome (MetS).<sup>[22]</sup> Microscopic examination of urine was performed on centrifuged urinary sediment to assess positive semi-quantitative proteinuria.

Absolute CV risk was assessed according to 2018 ESC/ISH recommendations, which take into account BP levels, CV risk factors, hypertension target organ damage, and comorbidities.<sup>[23]</sup> It was classified as low, medium, high, and very high according to 2018 ESC/ESH guidelines. The ethical committee (School of Public Health; University of Kinshasa) approved the present protocol.

**Table 1.** Socio-demographic characteristics of licensed civilian aircrew as a whole and according to LVH status

Characteristics	All	LVH	No LVH	p
	(n = 379)	(n = 36)	(n = 343)	
Age, years	40.6 ± 12.8	51.9 ± 10.5	39.5 ± 12.4	< .001
Age's categories, years				< .002
< 40, n(%)	199 (52.5)	5 (2.5)	194 (97.5)	
40-59, n(%)	140 (36.9)	19 (13.6)	12 (86.4)	
≥ 60, n(%)	40 (10.6)	12 (30)	28 (70)	
Category, n(%)				< .001
Flight crew	237 (62.5)	32 (88.9)	205 (59.8)	
Cabin crew	142 (37.5)	4 (11.1)	138 (40.2)	
Gender, n(%)				.006
Men	267 (70.4)	32 (88.9)	235 (68.5)	
Women	112 (29.6)	4 (11.1)	108 (31.5)	
Ethnicity, n(%)				.093
African black	291 (77.0)	24 (66.7)	267 (78.1)	
Caucasian	87 (23.0)	12 (33.3)	75 (21.9)	
Marital Status, n(%)				.018
Single	153 (44.6)	5 (18.5)	148 (46.8)	
Married	179 (52.2)	21 (77.8)	158 (50.0)	
Widow/	11 (3.2)	1 (3.7)	10 (3.2)	
Total flight time, hours				.035
< 5000	81 (46.3)	5 (25.0)	76 (49.0)	
≥ 5000	94 (53.7)	15 (75.0)	79 (51.0)	

Note. Data are expressed as mean ±SD, relative frequency (percent). Abbreviations: LVH: Left Ventricular Hypertrophy



**Figure 1.** Prevalence of LVH by age group in the whole study population, in obese and hypertensive subjects

**Table 2.** Clinical and biological characteristics of licensed civilian aircrew

Characteristics	All	LVH	No LVH	P
	(n = 379)	(n = 36)	(n = 343)	
Age	41 ± 13	52 ± 11	39 ± 12	.001
SBP, mmHg	121.7 ± 17.9	138.5 ± 27.9	119.9 ± 15.6	< .001
DBP, mmHg	77.3 ± 10.9	87.4 ± 13.6	76.3 ± 10.1	< .001
BMI, kg/m <sup>2</sup>	26.5 ± 4.5	30.3 ± 4.8	26.1 ± 4.3	< .001
WC, cm	92.7 ± 11.3	102.1 ± 11.1	91.7 ± 10.9	< .001
Creatinine, mg/dl	1 ± 0.2	1 ± 0.2	1 ± 0.3	.4
MDRD-eGFR, ml/min/1.73 m <sup>2</sup>	97 ± 25	88 ± 20	97 ± 26	.039
FPG mg/dl	86 ± 19	87 ± 25	86 ± 18	.764
TC, mg/dl	172 ± 43	171 ± 48	172 ± 43	.059
HDL-C, mg/dl	63 ± 22	60 ± 20	63 ± 23	.401
Uric acid, mg/dl	6 ± 2	7 ± 2	6 ± 2	.002
LDL-C, mg/dl	87 ± 48	91 ± 38	86 ± 49	.538
Vldl-C, mg/dl	45 ± 33	53 ± 47	45 ± 32	.18
Triglycerides	101 ± 76	110 ± 103	101 ± 72	.479

Note. Data are expressed as mean ± SD, or relative frequency (percent). Abbreviations: SBP: Systolic blood pressure, DBP: Diastolic blood pressure, BMI: Body mass index, WC: Waist Circumference MDRD-eGFR: Modified of Diet in Renal Disease estimated Glomerular Ratio, Ht: Hematocrit, Hb: Hemoglobin, RBC: Red blood cells, FBG: Fasting Plasma Glucose, TC: total cholesterol, LDL-c: low-density lipoprotein cholesterol, HDL-c: high-density lipoprotein cholesterol TG, triglycerides, MetS.: Metabolic syndrome, T2DM: Type-2 Diabetes, CVR: Cardiovascular Risk.

**Table 3.** The rates of various CVRF with and without LVH

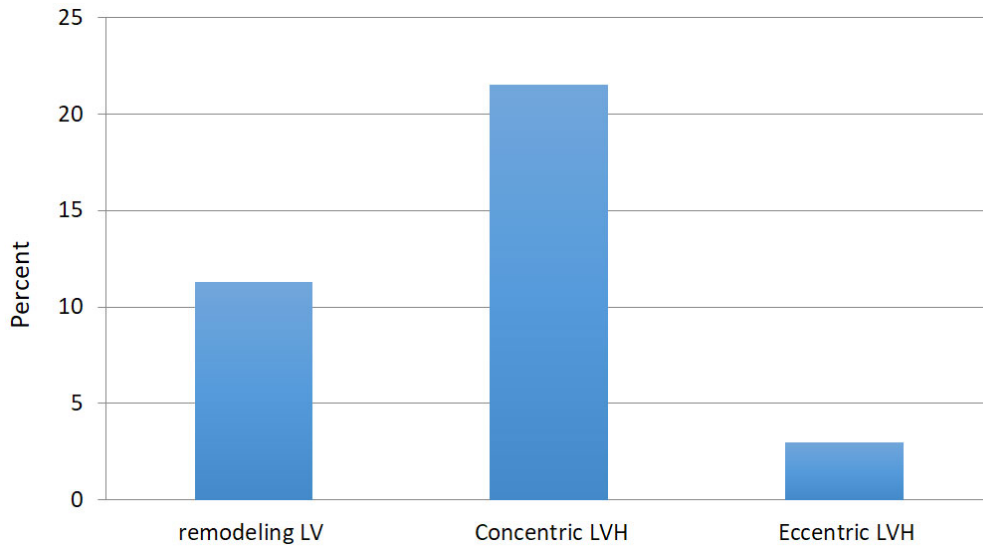
Characteristics	All	LVH	No LVH	p
	(n = 379)	(n = 36)	(n = 343)	
Hypertension, n(%)	97 (25.6)	24 (66.7)	73 (21.3)	< .001
T2DM, n(%)	10 (2.6)	4 (11.1)	6 (1.7)	.01
Subclinical atherosclerosis, n(%)	40 (10.6)	9 (25.0)	31 (9.0)	.007
Abdominal obesity, n(%)	224 (59.1)	30 (83.3)	194 (56.6)	.001
Overweight/obesity, n(%)	233 (61.5)	34 (94.4)	199 (58.0)	< .001
Tachycardia, n(%)	23 (6.1)	6 (16.7)	17 (5.0)	.031
Hyperuricemia, n(%)	50 (16.7)	15 (45.5)	35 (13.1)	< .001
MetS, n(%)	63 (16.6)	12 (33.3)	51 (14.9)	.008
Smoking, n(%)	80 (21.1)	9 (25.0)	71 (20.7)	.339
Alcohol, n(%)	259 (68.3)	28 (77.8)	231 (67.3)	.136
Physical Inactivity, n(%)	328 (86.5)	34 (94.4)	294 (85.7)	.108
CVR, n(%)				< .001
Low risk	238(63)	10(4)	228(96)	
Moderate risk	69(18)	9(13)	60(87)	
High/Very high risk	72(19)	17(24)	55(76)	

Note. Data are expressed as relative frequency (percent). Abbreviations: CVR: Cardiovascular risk; T2DM: Type 2 diabetes mellitus

## 2.1 Statistical Analysis

We expressed our data as absolute and relative frequencies or mean ± standard deviation as appropriate. We used Student's t-test and Pearson's Chi-squared or Fisher's exact test to compare means and proportions, respectively. We per-

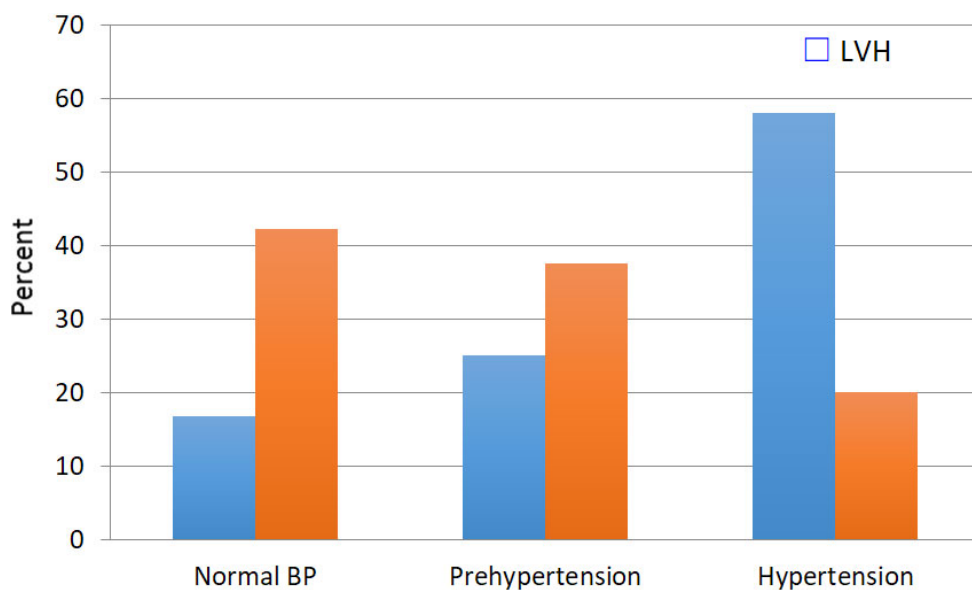
formed logistic regression analysis to assess independent determinants of LVH. We utilized the Statistical Package for Social Sciences (SPSS Inc., Chicago, IL, version 17.0) and set the significance level at  $p < .05$ .



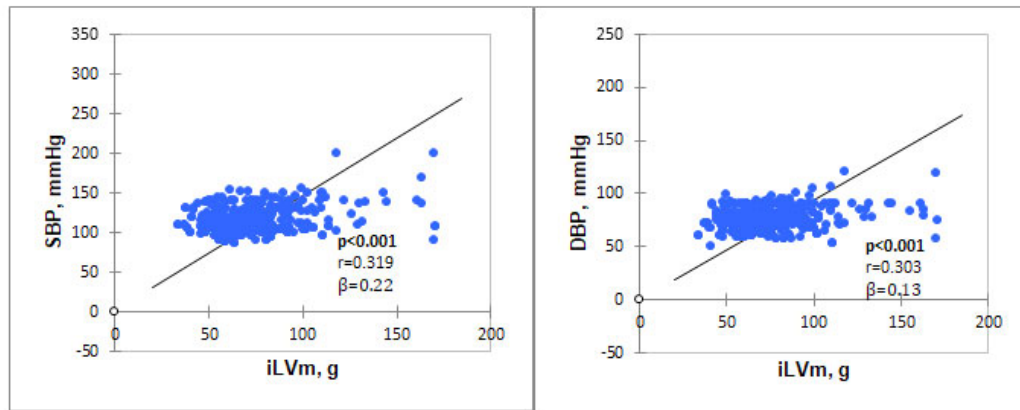
**Figure 2.** Patterns of LV geometry

**Table 4.** Determinants of LVH in univariate and multivariate analysis

Characteristics	Univariate analysis		Multivariate analysis	
	P	OR(95% CI)	P	aOR (95% CI)
Age, 40-59 y vs ≤ 40 y	< .001	16.63 (5.45-50.76)	.002	8.48 (2.23-12.23)
Age, ≥ 60 y vs ≤ 40 y	.018	2.73 (1.19-6.27)	.004	4.22 (1.57-11.35)
Hypertension	< .001	7.40 (3.53-15.50)	.004	3.55 (1.50-8.41)
Subclinical atherosclerosis	.005	3.36 (1.46-7.77)	.285	1.80 (0.61-5.32)
Abdominal obesity	.003	3.84 (1.56-9.47)	.428	1.56 (0.52-4.63)
Overweight/Obesity	.001	12.30 (2.91-52.03)	.034	5.33 (1.14-25.05)
Hyperuricemia	< .001	2.06 (0.85-5.00)	.001	5.05 (2.11-12.09)



**Figure 3.** Relationship between categories of BP and LVH



**Figure 4.** depicts the simple linear correlation of LVMI to SBP (left) and DBP(right) and shows LVMI to increase positively with BP. As expected, we found that LVMI was significantly positively correlated to both SBP and DBP;  $p < .001$ .

### 3. RESULTS

Of the 379 aircrew members (African blacks 77%; men 70.4%) enrolled in the present study 237 (62.5%) were flight crew, the majority of whom ( $n = 94$ ; 53.7%) having a total flight time  $\geq 5000$  hours. Echo-LVH was present in 36 aircrew members (9.5%) with mild, moderate and severe subtypes observed respectively in 19.4%, 33.3%, and 47.2%. With regard to socio-demographic characteristics (see Table 1), LVH predominated among men than women, among flight than cabin crew, and among those with flight time  $\geq 5000$  h. The observed difference between Africans and Non-Africans was not significant. Clinical and biological features of the study population and per LVH status are depicted in Table 2. Aircrew members with LVH were older with significantly higher BP, BMI and serum UA, but lower eGFR than those without LVH. The proportions of study participants with various CV risk factors are shown in Table 3. The rate of LVH was significantly higher in most conditions except smoking, alcohol drinking and physical inactivity. LVH was observed in 24.7% of hypertensive and 14.6% of obese aircrew. The rate increased with age for the whole study population (see Figure 1) and amounted to 2.5% ( $< 40$  y), 13.6% (40-59 y), and 30% ( $\geq 60$  y) ( $p$  trend  $< .001$ ). The respective rates were 4.8%, 23.2%, and 50.0% ( $p$  trend = .003) for hypertensive subjects and 5.3%, 17%, and 34.4% ( $p$  trend  $< .001$ ) for the obese ones. Normal LVM, LV remodeling, concentric and eccentric LVH were present in 63.9%, 11.3%, 21.6% and 3.1% of subjects, respectively (see Figure 2). Figure 3 depicts the positive correlation linking the stage of hypertension and the prevalence of LVH ( $p < .001$ ). In fact, normal BP, prehypertension, and hypertension were respectively involved in 6 (16.7%), 9(25.0%), and 21(58.3%) individuals with LVH, suggesting the higher category of BP, the greater the proportion of

LVH. As shown in Figure 4 LVMI was positively correlated to both SBP and DBP ( $p < .001$ ). In univariate regression model, the probability to have LVH was lower in subjects  $< 40$  y old compared to those 40-59 y (16.63 [5.45-50.76];  $p < .001$ ) or  $\geq 60$  y (2.73 [1.19-6.27];  $p < .018$ ); it was higher in the presence of hypertension (7.40[3.53-15.50];  $p < .001$ ), subclinical atherosclerosis (3.42[1.26-9.25];  $p = .15$ ), abdominal adiposity (3.84[1.56-9.47];  $p = .003$ ), overweight/obese (12.30[2.91-52.03];  $p = .001$ ) or hyperuricemia (5.05[0.85-5.00];  $p < .001$ ). In multivariate stepwise regression analysis, subclinical atherosclerosis as well as abdominal adiposity were no longer associated with LVH. Having 40-59 y (8.48[2.23-12.23];  $p = .002$ ) or more (4.22 [1.57-11.35];  $p = .004$ ) exhibited a weighty impact on LVH. Similarly, the likelihood of LVH was significantly higher in overweight/obese (5.33[1.14-25.05];  $p = .034$ ) and hypertensive individuals (3.55[1.50-8.41];  $p = .004$ ), and those with hyperuricemia (5.05[2.11-12.09];  $p = .001$ ).

### 4. DISCUSSION

Our data indicate that Echo-LVH was found in one out of four hypertensive aircrew members with moderate to severe and concentric geometry pattern being more prevalent. Echo-based LVH predominates among aircrew with moderate to high global CV risk whilst increasing age, subclinical atherosclerosis and components of metabolic syndrome emerged as its main correlates.

Echo-based LVH appears to be a common feature among our hypertensive aircrew members. To the best of our knowledge, no survey reporting on LVH among hypertensive aircrew personnel is available to which our results could be confronted. Nonetheless, the rate of LVH we report appears of similar magnitude as those found in primary care settings in Malaysia,<sup>[24]</sup> New York,<sup>[25]</sup> and Rome.<sup>[26]</sup> It is

however lower than the 41.1% reported among hypertensive patients<sup>[27]</sup> or the 91% among patients with reduced kidney function<sup>[28]</sup> at Kinshasa. Various factors might account for the observed disparities including differences in study methodology, cut-off points used to define LVH, socio economic characteristics of participants as well as possible concomitant co-morbidities.

LVH in the present study was predominantly of moderate to severe subtypes and of concentric geometry pattern suggesting the pressure overload could be the main pathogenic mechanism behind the cardiomyocytes remodeling.<sup>[29,30]</sup>

In keeping with previous reports, LVH was associated with ageing and subclinical atherosclerosis and was more prevalent in hypertensive and obese patients. The relationship between ageing, high BP and obesity on one hand, and LVH on the other side, has been shown in the general population as well as in hypertensive patients.<sup>[31,32]</sup> Ageing-associated vascular remodeling and insulin resistance in tandem with multiple CV risk factors can favor development of the LVH<sup>[33]</sup> and enhance worsening the 10-year global CV risk as observed in our aircrew.<sup>[12]</sup> Insulin resistance and subsequent hyperinsulinemia have been reported to activate the sympathetic nervous and the renin angiotensin systems resulting in endothelial dysfunction.<sup>[34,35]</sup> With reference to Laplace's law, high BP and obesity could trigger cardiac remodeling through hemodynamic and these humoral mechanisms and the thickening of cardiac wall may occur through collagen deposits.<sup>[36]</sup> Mehta et al. in the Dallas Heart Study found LVH to be an independent risk factor for subclinical atherosclerosis diagnosed by cardiac MRI, coronary artery calcium, and C-reactive protein measurements.<sup>[33]</sup> The postulated common denominator linking LVH and subclinical atherosclerosis was the oxidative stress and subsequent endothelial dysfunction and inflammation.<sup>[33]</sup>

In the present survey, LVH was also linked to raised serum UA levels. Such an observation appears consistent with reports by Cuspidi<sup>[37]</sup> and Bayauli et al.<sup>[11]</sup> of increased odds of having LVH with higher serum uric acid levels a relationship for which the underlying mechanism is not yet elucidated. Not only has serum UA been considered as a marker of insulin resistance and accepted as a component of the MetS, but also as a surrogate marker of oxidative stress and subsequent endothelial dysfunction.<sup>[38]</sup>

Our data might be considered enclosed by the flaws of the current study. Indeed, the use of 2D transthoracic echocardiography (TTE) that is less reliable and reproducible in assessing LVM than 3D TTE or cardiac MRI may have resulted in under or overestimation of the frequency of LVH. Furthermore, the cross-sectional design of the survey inhibits the foundation of any causal link between variables of interest. Finally, the small sample size does not allow adequate power to identify further links between variables of interest and the generalization of our findings to all the aircrew.

## 5. CONCLUSION

Our results indicate that moderate to severe LVH, of mainly concentric geometric subtype is a common finding among aircrew with age, subclinical atherosclerosis and components of the MetS as its main associated CV risk factors. A study with a comprehensive sample of aircrew is awaited.

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## CONFLICTS OF INTEREST DISCLOSURE

The authors declare no conflict of interest.

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