THE RELATIONSHIP BETWEEN AGE, GENDER AND VENTRICULAR ARTERIAL COUPLING IN PRIMARY HYPERTENSIVE PATIENTS WITHOUT HEART FAILURE

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Summary

Objectives: *To investigate the ventricular arterial coupling (VAC) and its components and their relation with sex and gender in primary hypertensive patients without heart failure, compared with people without cardiovascular dysfunction.*

Subjects and methods: *In a descriptive study at Military Hospital 103, Vietnam Military Medical University on 98 primary hypertensive patients without heart failure and 69 healthy adults without cardiovascular diseases, clinical data, Doppler echocardiography, electrocardiogram and blood pressure (BP) measurements were obtained. Ventricular - vascular coupling was defined as Ea/Ees ratio, in which, Ea was calculated from stroke volume and systolic BP and indexed to body size (EaI). Ees was calculated by the modified single-beat method using systolic and diastolic BP, stroke volume and tNd (ratio of pre-ejection period to total systolic period) and indexed to body surface area (BSA) (EesI).*

Results: *In patients with hypertension without heart failure, the mean value of VAC was 0.74 ± 0.13, Ea was 3.18 ± 1.03; Ees was 4.42 ± 1.57 mmHg/mL; EaI was 2.02 ± 0.74; EesI was 2.80 ± 1.15 mmHg/mL.m2. Ea, EaI, Ees, EesI were higher, while VAC was lower than people without cardiovascular disease (with p < 0.05). Ea, EaI, Ees, EesI all increased with age in women (p < 0.01). EaI, Ees, EesI in women were higher than in men. VAC was significantly lower in women than in men. VAC and its components were not correlated with age in men.*

Conclusion*s: In patients with primary hypertension and without heart failure, the arterial elastance and the ventricular elastance are higher than those in healthy adults, and tend to increase with advancing age, higher in females than in males. Meanwhile, VAC is lower in females than in males, and is not related with aging. VAC in hypertension patients is not different from healthy people.*

**** Keywords:*** *Ventricular-arterial coupling; Arterial elastance; Ventricular elastance; Hypertensive.*

INTRODUCTION

Aging is one of the main risk factors of cardiovascular diseases. Age-dependent increases in vascular stiffening are well established with evidence from multiple large cross-sectional studies involving various ethnicities [2], accompanied with changes of left ventricle, leading to increase of end-systolic left ventricular stiffness [3]. The mechanism of this problem is due to the interaction between heart and arterial load, and is exacerbated by many common disorders such as hypertension, diabetes,

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and renal disease... The consequence of this process is heart failure [4]. This change influences the phasic mechanical stresses imposed on the blood vessels that in turn is important to regulate smooth muscle tone, endothelial function, and vascular health. In addition, the heart typically adapts to confront higher and later systolic loads by both hypertrophy and ventricular systolic stiffening. This creates altered coupling between heart and vessel that importantly affects. Meanwhile, epidemiology studies report that 40 - 50% of patients with heart failure (HF) have preserved ejection fraction (EF). Indeed, the prevalence of heart failure with preserved ejection fraction increases more sharply with age than systolic HF, especially in women [5]. One hypothesis proposed for this discrepancy is based on sex differences in ventricular - arterial mechanics. Understanding the coupling between the left ventricle (LV) and arterial system, termed ventricular- arterial coupling (VAC), provides important mechanistic insights into the complex cardio vascular system and its changes with aging in the absence and presence of disease. VAC can be *defined* as the ratio of *the arterial elastance (Ea) to the ventricular* elastance (Ees). In Vietnam, no report of this issue in hypertensive patients has been published. The aim of this study is: *To investigate the VAC, its components and its relation between sex and gender with VAC in primary hypertensive patients without heart failure, compared with people without cardiovascular dysfunction.*

SUBJECTS AND METHODS

1. Subjects

The study was comprised of 2 groups: the control group and the patient group. The former consisted of 69 adults aged over 40 including the normal health individuals working in the Military Medical University, and the patients treated in 103 Military Hospital with no cardiovascular diseases or other co-morbidities which could influence the cardiovascular functions. The latter including 98 hypertensive patients without heart failure were treated in the Department of Cardiovascular Diseases of 103 Military Hospital.

- *Exclusion criteria:* Patients suffered from acute heart failure, heart valve stenosis, coarctation of the aorta, left ventricular outflow tract obstruction, and refused to participate in the study.

2. Methods

A descriptive study was performed in 2 groups from 10/2014 to 12/2020.

All the subjects were obtained clinical and laboratory test data. The blood pressure was measured from the arm and echocardiography were performed simultaneously, in which Ps was systolic and Pd was diastolic pressure. The diagnosis criteria was based on the 2008 Guidelines of Vietnam National Heart Association [1]. End-systolic pressure (ESP) was estimated as systolic pressure (Pd) x 0.9/ stroke volume (SV). SV was measured from the LV outflow tract diameter and the pulse wave Doppler signal. The arterial elastance (Ea) was

calculated from stroke volume and systolic blood pressure and indexed to body size (EaI). Ees was calculated by the modified single-beat method of Chel et al., using systolic and diastolic BP, stroke volume and tNd (*ratio of pre-ejection period to total systolic period*) and indexed to body surface area (BSA) (EesI). The unit of Ea and Ees is mmHg/ml, and of EaI and EesI is mmHg/ml.m^2. The ventricular arterial coupling (VAC) is the ratio of Ea/Ees. Systemic vascular resistance index (SVRi) was estimated as [(mean arterial pressure/cardiac index)×80]. End systolic wall stress (ESWS, g/cm2) was estimated as [(Pes)×(Des)×(1.35)]/[4×(hes)×(1+hes/Des)], where Des is the end-systolic LV dimension and hes is the average of the septal and posterior wall end-systolic wall thickness. The ratio of FS to ESWS (stress-corrected FS) was used as a load-independent measure of systolic performance [7].

**Data analysis:* Using SPSS 17.0.1. A *p* value of less than 0.05 was considered to be significant.

RESULTS

The baseline characteristics of study subjects showed the similarity of mean age, male/female ratio, height, weight and body surface area (BSA) in both groups. Only one difference was seen in the body mass index (BMI), which was higher in the hypertensive group.

Table 1: The values of ventricular - arterial coupling and its components in both genders.

	Control (n = 69)	**Hypertension (n = 98)**	**p**	**Hypertension**		**p**
				Males (n = 52)	**Females (n = 46)**	
Ea (mmHg/mL)	2.71 ± 0.74	3.18 ± 1.03	< 0.05	3.10 ± 0.93	3.28 ± 1,15	> 0.05
EaI (mmHg/mL.m^2)	1.75 ± 0.59	2.02 ± 0.74	< 0.05	1.86 ± 0.63	2.19 ± 0.82	< 0.05
Ees (mmHg/mL)	3.54 ± 1.13	4.42 ± 1.57	< 0.05	3.99 ± 1.25	4.90 ± 1.76	< 0.05
EesI (mmHg/mL.m^2)	2.27 ± 0.81	2.80 ± 1.15	< 0.05	2.38 ± 0.80	3.28 ± 1.29	< 0.001
VAC	0.80 ± 0.20	0.74 ± 0.13	< 0.05	0.79 ± 0.12	0.68 ± 0.11	< 0.001

The Ea, EaI, Ees, EesI in the hypertensive patients were significantly higher than those in the control group. EaI, Ees, EesI in females were higher than males. Meanwhile, the VAC in the hypertensive group was lower than the control, and VAC in females was also lower than males, showing the absolute increase of Ees was higher than that of Ea.

Table 2: The values of ventricular - arterial coupling and its components with age in men and women hypertensive without heart failure.

		Hypertension (n=98)	
		Males (n = 52)	**Females (n = 46)**
Ea (mmHg/mL)	40 - 49	3.04 ± 0.52	2.61 ± 0.54
	50 - 59	2.56 ± 0.61	2.70 ± 0.36
	60 - 69	3.27 ± 1.09	3.52 ± 1.17
	> 70	3.30 ± 1.03	4.15 ± 1.44
	p	> 0.05	< 0.05
EaI (mmHg/mL.m2)	40 - 49	1.72 ± 0.30	1.65 ± 0.34
	50 - 59	1.47 ± 0.31	1.78 ± 0.15*
	60 - 69	1.92 ± 0.71	2.35 ± 0.73
	> 70	2.14 ± 0.74	2.90 ± 1.09
	p	< 0.05	< 0.05
Ees (mmHg/mL)	40 - 49	3.84 ± 0.78	3.72 ± 0.81
	50 - 59	3.28 ± 0.91	4.28 ± 0.98*
	60 - 69	4.50 ± 1.35	5.12 ± 1.65
	> 70	3.99 ± 1.41	6.36 ± 2.22*
	p	> 0.05	< 0.05
EesI (mmHg/mL.m2)	40 - 49	2.16 ± 0.39	2.34 ± 0.47
	50 - 59	1.89 ± 0.48	2.81 ± 0.55*
	60 - 69	2.63 ± 0.86	3.43 ± 1.09*
	> 70	2.58 ± 0.96	4.45 ± 1.74*
	p	> 0.05	< 0.05
VAC	40 - 49	0.80 ± 0.12	0.71 ± 0.10
	50 - 59	0.79 ± 0.12	0.65 ± 0.09*
	60 - 69	0.73 ± 0.11	0.69 ± 0.10
	> 70	0.84 ± 0.10	0.67 ± 0.16*
	p	> 0.05	> 0.05

: p < 0.05 between men and women

Ea, EaI, Ees, EesI in the female hypertensive patients increased with advancing age, but this increase of EaI was not seen in males.

Table 3: The correlation of VAC and its components with age and gender in hypertensive patients without heart failure.

	Age					
	Whole group		Males		Females	
	r	p	r	p	r	p
Ea (mmHg/ml)	0.310	< 0.05	0.102	> 0.05	0.510	< 0.001
EaI (mmHg/ml.m2)	0.401	< 0.001	0.245	> 0.05	0.581	< 0.001
Ees (mmHg/ml)	0.319	< 0.05	0.075	> 0.05	0.571	< 0.001
EesI (mmHg/ml.m2)	0.394	< 0.001	0.218	> 0.05	0.628	< 0.001
VAC	0.002	> 0.05	0.054	> 0.05	-0.112	> 0.05

Ea, EaI, Ees and SVRi in the hypertensive patients without heart failure increased with age, but the correlation of these parameters with age were mainly seen in women, not in men. SVRi had a positive correlation with age in both genders.

Regarding to the relation of age and gender with left ventricular geometry and function, Ees, EesI and LVMI were also higher with advanced age, and mostly associated with age in females and not in males. Sc-Fs also increased with age just in females. No change was observed in VAC in both men and women.

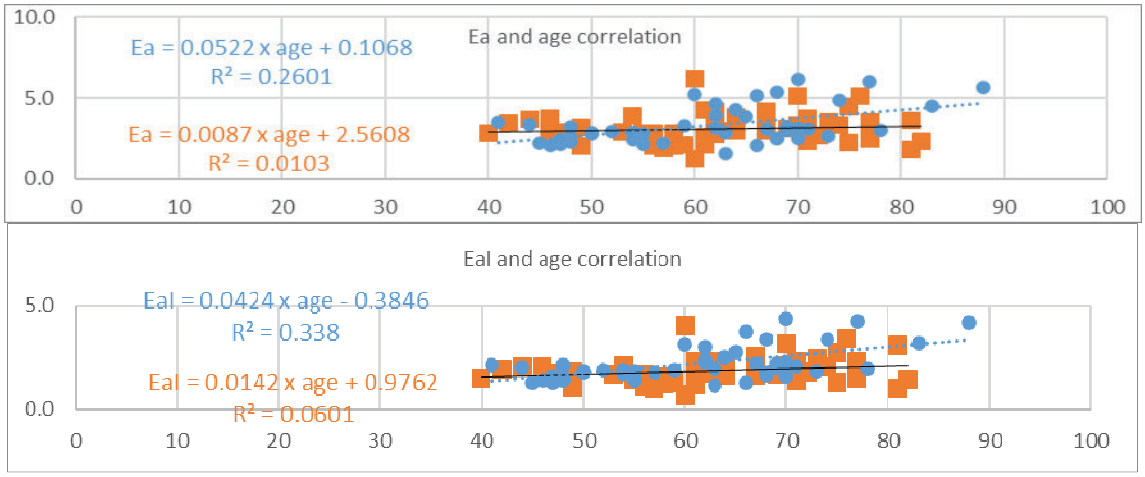

Figure 1: The correlation of age and Ea, EaI in men and women with hypertension and without heart failure

(Blue: Female; Orange: Male)

Ea, EaI and SVRi in females increased with age and were higher than in men. The calculation of these correlations were as follows:

Ea = 0.0522 x age + 0.1068; R = 0.51, p < 0.001 in women

EaI = 0.0424 x age - 0.3846; R = 0.581, p < 0.001 in women

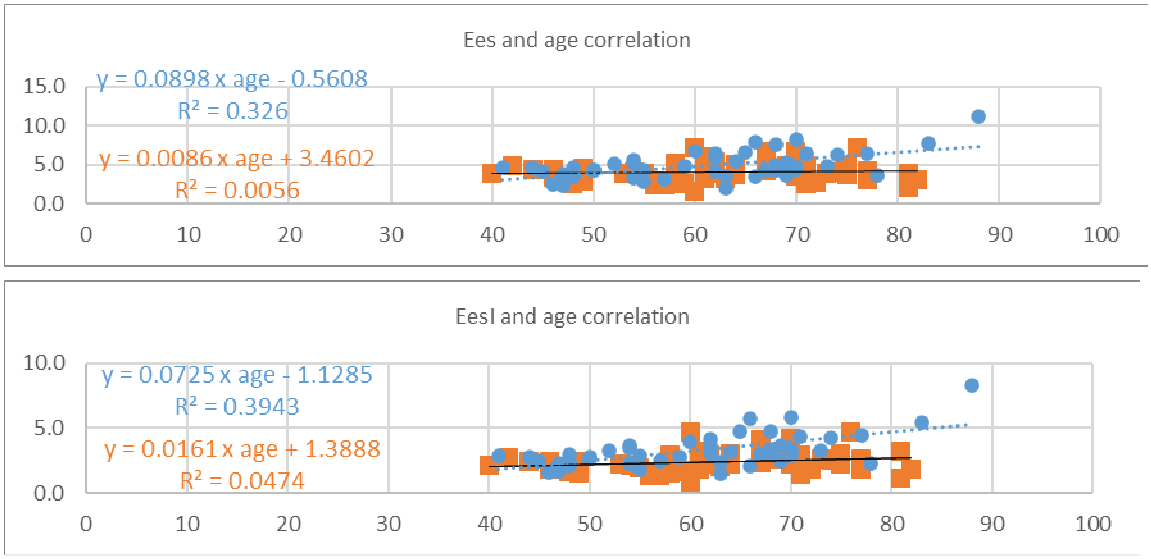

Figure 2: The correlation of age and Ees, EesI in men and women with hypertension and without heart failure

(Blue: Female; Orange: Male)

Ees, EesI, Sc-Fs and LVMI in women increased with age and higher than in men. The calculation of these correlations were as follows:

Ees = 0.0898 x age - 0.5608; R = 0.57, p < 0.001 in women

EesI = 0.0725 x age - 1.1285; R = 0.394, p < 0.001 in women

DISCUSSION

Our results showed that there was an increase in arterial and left ventricular stiffness in primary hypertensive patients without heart failure, demonstrated by the increase in arterial and left ventricular elastance (Ea, EaI, Ees, EesI), which was 1.15 - 1.17 higher than the individuals with normal cardiovascular function; and the mean value of Ea was 3.18, of Ees was 4.42 (mmHg/mL). These figures were higher than Luca Faconti's finding on 102 hypertensive patients (Ea 1.13 ± 0.38, Ees 1.45 ± 0.42 mmHg/mL) [8]. In another study by Melenovsky (2007) on 40 patients with hypertension and left ventricular hypertrophy, the value of Ea was 1.78 ± 0.5, of Ees was 3.72 ± 1.4 mmHg/mL [9]. However, our VAC was 0.80 ± 0.20, similar to Faconti's study (0.78 ± 0.10). The difference among those studies was mainly due to lower BMI of Vietnamese people compared to that of Westerners like Italians, and the stroke volume is the same, which leads to a higher Ea and Ees. On the other hand, the application of different calculating methods of VAC also influenced the results.

We also saw an increase in Ea with age and higher in women than men. This result was similar to Redfield và Faconti's finding [7, 8]. Previous studies using a variety of indices have established that large-artery stiffness increases with age

even in the absence of vascular disease or risk factors, higher in women. Multiple mechanisms have been proposed to explain age-dependent vascular stiffening, including alterations in endothelial function, structural protein composition, collagen cross-linking, geometric changes, and neurohumoral signaling. The cause of gender differences in vascular stiffening is unclear, although both the present and earlier data indicate that this is not simply a matter of differences in body size and vasculature length [7].

In this regard, both the findings that Ees was increased in women and that Ees increased more steeply with age in women than in men are novel and are supported by similar findings with an additional index of systolic performance, stress-corrected FS [3]. Hearts coupled to a stiffer vascular system are subjected to higher systolic stresses as well as wider pulse pressures that can adversely influence the regulation of coronary flow and contribute to microvasculature and end organ damage. Hearts coupled to a stiffer vascular system are subjected to higher systolic stresses as well as wider pulse pressures that can adversely influence the regulation of coronary flow and contribute to microvasculature and end organ damage. Interestingly, the present analysis found concordant changes in the stress-corrected FS [3, 7].

Because increases in arterial stiffness with age and females may stimulate left ventricular remodeling and because structural changes may contribute to the increases in Ees and Ed, we examined the relationship between age and gender and chamber geometry. left ventricular volume indexed to BSA increased modestly with age in men in the entire population but was not associated with age in women or in men without cardiovascular disease. As previously reported, left ventricular mass index increased with age in the community and in those without cardiovascular disease. This appeared to represent concentric remodeling, because relative wall thickness increased with age, most dramatically in women [7]. We speculate that other aspects of remodeling, such as left ventricular fibrosis, may vary in age and between genders and contribute to the changes in systolic and diastolic elastance. The similarity was seen in our results that LVMI increased with age and was related to females, but there was no relation between RWT with age and gender. This may be due to the small sample size of our study.

CONCLUSIONS

In patients with primary hypertension and without heart failure, the arterial elastance and the ventricular elastance are higher than those in healthy adults and tend to increase with advancing age, higher in females than in males. Meanwhile, VAC is lower in females than in males, and is not associated with aging. VAC in hypertension patients is not different from healthy people.

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