

AORTIC COMPLIANCE AND STIFFNESS AMONG SEVERE LONGSTANDING HYPERTENSIVE AND NON-HYPERTENSIVE

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ABSTRACT

Introduction. Abnormal aortic function in hypertension is generally attributed to accelerated breakdown of elastin in the aorta, leading to dilatation of the lumen and stiffening of the wall as elastin is replaced with stiffer collagen. Aortic stiffness is an independent predictor of cardiovascular risk and all-cause and cardiovascular mortality. Vascular stiffening can activate endothelium which in turn may promote atherogenesis. Modulation of arterial stiffness

has been shown to be successfully managed via changes in lifestyle and put under control of hypertension pharmacologically with antihypertensive drugs and statins. **Methods.** Hundred and forty four patients have been enrolled in this study. They have been divided in two groups, with hypertension and group of control. Groups were with no age difference. **Results.** Group with hypertension were with reduced aortic strain, distensibility (compliance) and have higher stiffness than control group; GrHTA =9.3 compared to GC=5.4. After

successful treatment of hypertension with antihypertensives and statins, for two years, these parameters showed improvement, but still remain out of normal range compared to control group; 7.6 vs. 5.38. **Conclusions.** Hypertensive patients have reduced aortic elasticity and increased stiffness which can be stopped and improved after treatment with antihypertensive and statin.

Key words: Aortic stiffness, Aortic elasticity, Hypertension.

1. INTRODUCTION

Aortic stiffness is an independent predictor of all-cause and cardiovascular mortality in patients with essential hypertension (1, 2, 3). Furthermore, aortic stiffness constant is the best single predictor of acute coronary syndromes (3, 4). Aortic stiffness may predict sustained hypertension; in patients with hypertension and hypothyroidism and in patients with repaired coarctation of aorta, sustained hypertension is caused by the increased aortic stiffness (5, 6). It is concluded that in a population of non-hypertensive subjects with no overt cardiovascular disease or symptoms at baseline, aortic elastic properties measured through trans-thoracic echocardiography predicted the increase in systolic BP, diastolic BP, and pulse pressure beyond the prediction provided by risk factors including initial level of BP, assessed through a multivariate model (7). From the he-

modynamic factors that influence PP, 2 have been shown to independently predict CV risk: aortic stiffness, measured from aortic PWV (1, 8) and early return of reflected waves to the heart, evaluated from pulse wave analysis (9).

Vascular stiffening is associated with abnormalities in central aortic flow that can activate endothelium (10). Activation of the endothelium and increased pulsatile stress on the arterial wall may promote atherogenesis (11). Abnormal aortic function in hypertension is generally attributed to accelerated breakdown of elastin in the aorta, leading to dilatation of the lumen and stiffening of the wall as elastin is replaced with stiffer collagen (12) primary hyperparathyroidism (pHPT), pHPT is associated with increased aortic stiffness, which improves after parathyroidectomy. Data demonstrate that aortic stiffness may improve upon removal of hyper-parathyroid

stimuli (13). Based on the evidence that subjects with many chronic diseases have increased arterial stiffness when compared to a healthy control population, and that subjects such as athletes or the physically active elderly have decreased arterial stiffness when compared to a normally active control population (14, 15). The only study of this sort revealed by literature search was carried out in patients with end-stage renal disease, and thus is not applicable to the general population (16). However no decrease in arterial stiffness was found in trials of aerobic exercise in subjects with systolic hypertension (17). The main drug class acting on the rennin-angiotensin-aldosterone system (RAAS) are angiotensin converting enzyme inhibitors (ACE-Is). As well as being recognized as effective anti-hypertensive agents, they are of great interest in the treatment of atherosclerosis as they have been shown to protect against sec-

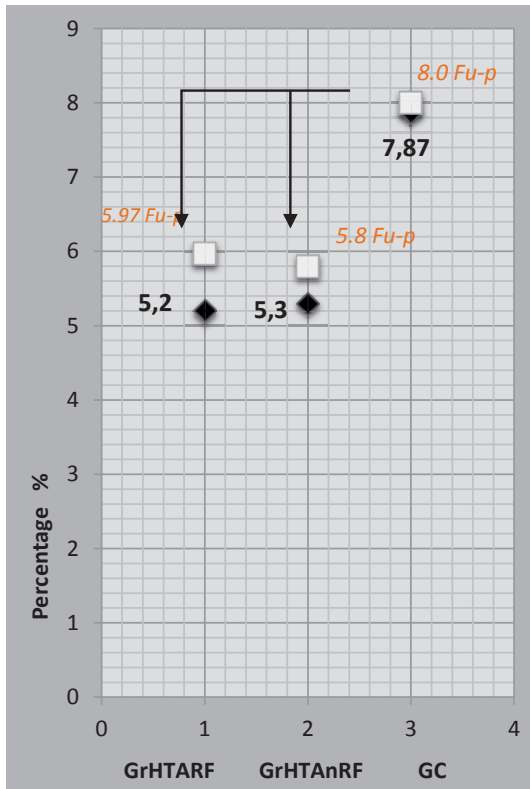


Diagram 1. Aortic strain: GrHTA (nRF and RF) vs. GC; $p < 0.001$

ondary coronary events in subjects with cardiovascular disease (18). In summary Antihypertensive therapy has a different effect on arterial stiffness. According to arterial stiffness, diuretics have no activity; beta blockers have different effects with some beta blockers increasing it and some others decreasing it; calcium channel blockers reduce arterial stiffness as well as ACE inhibitors and angiotensin receptor blocking agents; effect of aldosterone antagonist is that of decreasing arterial stiffness (19).

2. METHODS

The study has been approved by the Ethic Committee and written informed consent was obtained from all participants. Patients with severe and long-standing hypertension (SLH) were included in the study. As severe hypertension we considered to be those with systolic blood pressure >180 mmHg and/or diastolic blood pressure of >100 mmHg. Long-standing hypertension was considered HTA lasting for more than one year and not treated or not treated correctly for the same period. Hundred and forty patients were enrolled in the study. Number of patients

with severe long-standing hypertension was ninety-six and forty-four pts. serves as a control group-GC. Hypertensive patients were divided into two groups, one group with no risk factors (GrHTAnRF, and another group with risk factors (GrHTARF); all of them have been treated with ACE-inhibitors, Hydrochlorothiazide and beta-blockers. Patients have been follow-up for 24 months. BP was measured and recorded three to four times at home following the recommendations of the American Heart Association (20). Predefined exclusion criteria were: terminal illness, dementia, significant disability, or esophageal disease precluding TEE), and refusal to participate in the study. Trans-thoracic echo-

cardiography (using machine iE33 Phillips and Siemens accuson CV 70 Siemens) examination of the aorta is a routine part of the standard echocardiographic examination. We have respect all of the techniques (left and right parasternal long-axis views, basal short-axis views, and apical long-axis as well as modified apical five chamber views) most used to measure proximal aorta. Our TTE we have accomplish using the supra-sternal view which allow us to depict the aortic arch and the three major supra-aortic vessels (innominate, left carotid, and left subclavian arteries).

Aortic Stiffness Measurement. Aortic systolic (AoS) diameter was measured at the time of full opening of the aortic valve and diastolic (AoD) diameter was measured as min. diameter. Three to five consecutive beats were measured routinely and averaged. Measurements were performed by the same investigator. The percentage change of the aortic root was calculated as:

$$\Delta Ao(\%) = 100 * (AoS - AoD) / AoD$$

to obtain the aortic strain. Aortic distensibility was calculated from the formula: $\Delta A: (A * PP) = \pi * [(AoS/2)^2 - (AoD/2)^2] : [\pi (AoD/2)^2 * PP]$, with A being the cross-sectional lumen area and PP being pulse pressure. A was estimated as the product of π by r^2 ; where r was the AoS/2 or AoD/2. The aortic stiffness index (β) was calculated: $\beta = \ln(SBP/DBP) / (AoS - AoD) / AoD$ (pure number), where SBP is systolic BP and DBP is diastolic BP (6, 21, 22, 23).

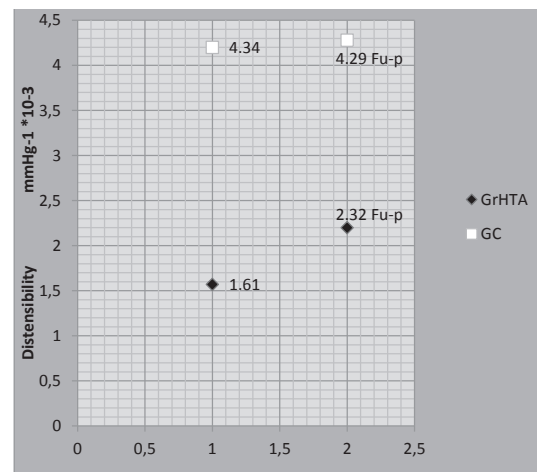
The results were analyzed by a standard method of descriptive statistics using Pivot Table of Excel Office 2007, MedCalc, Simple Interactive Statistical Analysis (SISA), Sigma Stat and Sigma Plot programs.

3. RESULTS.

GrHTAnRF-Group with hypertension with no risk factors; Fu-p-follow-up;

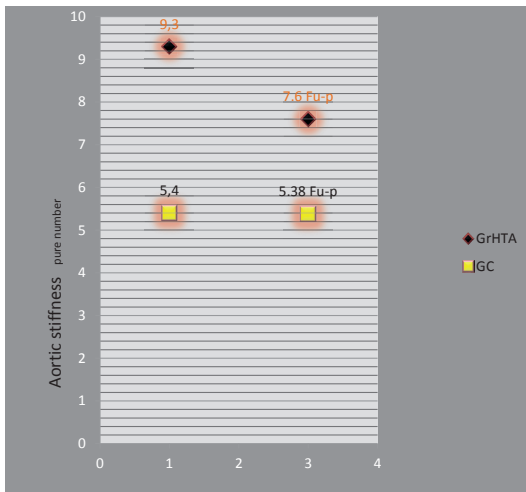
GrHTARF- Group with hypertension with risk factors; GC-Group of control.

Diagram 1. Shows aortic strain of GrHTA (RF and nRF; $5.2\% \pm 0.9$ and $5.3\% \pm 1.1$ respectively)-compared to GC ($7.87\% \pm 1.2$) and follow-up; GrHTA(RF and nRF; $5.97\% \pm 0.8$ and $5.8\% \pm 1.3$ respectively), vs. GC ($8.0\% \pm 1.24$). Aortic strain has significant difference between groups, with higher strain of control group. Some improvement of strain happened during follow-up period but still the difference remain significant between GrHTA (nRF and RF) and GC.



GrHTA-group with hypertension; GC-group of control; Fu-p-follow-up.

Diagram 2. Aortic distensibility: GrHTA vs. GC; and (on the right) follow-up ($p < 0.001$)



GrHTA-group with hypertension; FU-P-follow-up; GC-group of control.

Diagram 3. Aortic stiffness index (B): GrHTA vs. GC and (on the right) follow-up ($p=0.001$)

Diagram 2. Shows aortic distensibility of GrHTA ($1.61 \pm 0.4 \text{ mmHg}^{-1} \times 10^{-3}$) compared to GC ($2.32 \pm 0.6 \text{ mmHg}^{-1} \times 10^{-3}$) and follow-up. Aortic strain has significant difference between groups, with higher distensibility of control group. Some improvement of distensibility happened during follow-up but still the difference remain significant between GrHTA and GC; ($2.32 \pm 0.5 \text{ mmHg}^{-1} \times 10^{-3}$ vs. GC $4.29 \pm 0.7 \text{ mmHg}^{-1} \times 10^{-3}$ respectively).

Diagram 3. Shows aortic stiffness of GrHTA (9.3 ± 1.0) compared to GC (5.4 ± 0.9) and follow-up. Aortic stiffness has significant difference between groups, with higher stiffness of hypertensive group. Improvement of aortic stiffness happened during follow-up but, difference remain significant between GrHTA and GC ; (7.6 ± 1.1 vs. 5.38 ± 0.8 respectively).

4. DISCUSSION

Aortic strain of the three groups (Diagram 1) was with no significant difference between hypertensive groups (group with RF and without RF) but the difference was very significant between GrHTA (RF and nRF) compared to GC ($p < 0.001$).

Calculated **aortic distensibility** of our patients shows no difference between groups with hypertension (RF and nRF group) but difference was very significant between GrHTA and GC ($p < 0.001$) (Diagram 2).

Aortic stiffness has no difference between group with hyperten-

sion (non-RF and RF) but, difference was very significant between GrHTA and GC ($p < 0.001$) (Diagram 3). All parameters of elasticity (strain and distensibility) were compromised in aorta of the severe long-standing hypertension group compared to control group. These parameters were not related to age as in many trials has been proved (24, 25, 26) since control group and SLH group were with no age difference statistically; we consider that these changes are due to atherosclerosis as it is reported in many studies that atherosclerosis reduce elasticity of big arteries (27, 28, 29), atherosclerosis have been often found in our hypertensive patients (30). These data are in concordance with data of reported from Vitarelli A. et. al. (31) Analyzing these data we conclude that hypertension significantly reduce “elasticity” (distensibility and strain), and increase stiffness of the aortic wall. As it is well known these usually, if left untreated, leads to refractory hypertension especially isolated systolic hypertension, but also diastolic hypertension and pulse pressure (4). In group with hypertension (GrHTARF and GrHTAnRF) during follow-up, aortic distensibility and strain (compliance), increased or have been improved (Diagram 1 and Diagram 2) and stiffness, decreased (Diagram 3). We conclude that meticulous treatment of hypertension will improve compliance of the aorta which is very important in stopping rigidity of the aorta, remodeling of thoracic aorta (progressive passive dilatation, thickening of its wall and lowering of amplitude of systolic excursion)(29), (which will improve ISH, and other pathologies caused from this, mentioned above (22, 32, 33, 34, 35) This is achieved due to reduced atherosclerosis in thoracic aorta after successful treatment with anti-hypertensive and with statins.

5. CONCLUSIONS.
Meticulous treatment of hypertension and atherosclerosis is necessary, among others proved benefits,

also to reduce stiffness of the aorta and to improve compliance of it, but it seems that this will be realized after long time period.

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