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# Evaluation of Proximal Aortic Elastic Properties in Non-Ischemic Dilated Cardiomyopathy by Trans-Thoracic Echocardiography: A Case-Control Study

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ABSTRACT

***Background:*** Stiffening of the large vessels, especially aorta, plays a significant role in increasing the left ventricular work and aggravating the cardiovascular diseases by attenuating the vascular wall distensibility and its buffering effect.

***Objectives:*** This study aimed to compare the stiffness of proximal aorta in the patients with established diagnosis of Non-Ischemic Dilated Cardiomyopathy (NIDC) and the normal population.

***Patients and Methods:*** This case-control study aimed to compare 50 patients with established diagnosis of NIDC and 50 individuals with no history of significant cardiovascular diseases in the outpatient echocardiography clinics affiliated to Shiraz University of Medical Sciences, Shiraz, Iran during a three-month period in 2011. The patients with aortic valve disorders, coronary artery disease, congenital heart disease, diabetes mellitus, hypertension, and renal failure were excluded from the study. Stiffness indices were determined using the data gathered via echocardiography (left ventricular ejection fraction, end-systolic and end-diastolic volumes, and internal aortic diameter) and blood pressure measurement. Ordinal and quantitative data were analyzed by Chi-square and independent T-test, respectively using the SPSS statistical software, version 16.0. Besides, $P < 0.05$ was considered as statistically significant.

***Results:*** The results of this study revealed significantly lower aortic strain ($0.05 \pm 0.02$ in the NIDC patients versus $0.20 \pm 0.46$ in the controls, $P < 0.001$) and brachial pulse pressure ($40.50 \pm 9.00$ in the NIDC patients versus $45.90 \pm 8.08$ in the controls, $P < 0.001$) in the NIDC patients.

***Conclusions:*** Aortic stiffness is capable of deteriorating the cardiovascular function by augmenting the afterload. Thus, it should be seriously considered as an issue while approaching NIDC patients since they demonstrate lower aortic distensibility.

►*Implication for health policy/practice/research/medical education:*
The presence of higher aortic stiffness in patients with non-ischemic dilated cardiomyopathy underscores large arteries' distensibility as a critical issue in determining the cardiac afterload. It seems that evaluating the distensibility of the proximal part of aorta would be a key element in predicting systolic and diastolic performance of the cardiac muscle.

## 1. Background

Cardiovascular performance is highly reliant on collaboration of heart and large vessels (1). The large arteries possess elastic characteristics that facilitate proper cardiac function by buffering pulsatile blood flow and diminishing cardiac afterload (2-6). Furthermore, the Windkessel model presented by Westerhof et al. demonstrated that aortic resistance is the main determining factor of Left Ventricular (LV) load among diverse arterial characteristics contributing to cardiac load (7). Thus, stiffening of the large vessels, especially aorta, plays a significant role in intensification of LV work and aggravation

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of cardiovascular diseases by means of attenuating the vascular wall distensibility and its buffering effect (2, 8-10).

Previous studies demonstrated participation of multiple factors, including aging, diabetes mellitus, and hypertension, in aortic elasticity (1). However, it has been shown that stiffening of aorta in diastolic Heart Failure (HF) is independent of age and/or hypertension.

Besides, evaluations of abdominal aorta and carotid artery in HF patients proposed that large arteries are stiffer and their distensibility influences LV diastolic function indices (11, 12). Considering what was mentioned above, evaluation of aortic distensibility is of significant importance in patients with HF since it is able to exacerbate the failure by delivering augmented resistance on the cardiac muscle (2, 5, 13).

## 2. Objectives

Considering the fact that proximal aorta is responsible for approximately half of the total arterial compliance (4) and limited comprehensive data is available about proximal aorta stiffness in Iranian patients, the present study aims to investigate stiffness of proximal aorta in HF patients due to Non-Ischemic Dilated Cardiomyopathy (NIDC) by means of M-mode transthoracic echocardiography since it provides meticulous measurements of aortic strain and distensibility, the factors determining aortic stiffness (14).

## 3. Patients and Methods

The current case-control study was approved by Institutional Ethics Committee of Shiraz University of Medical Sciences (SUMS). The study was performed on 100 participants in the echocardiography clinics affiliated to SUMS in a three-month period in 2011.

The study sample size was calculated according to confidence interval of 95% and margin of error of 0.5. Then, 50 patients with NIDC who were under follow-up were selected through convenience sampling and were then randomly assigned to the case group based on the following inclusion criteria: presence of established echocardiographic diagnosis of dilated cardiomyopathy; i.e., presence of LV end-diastolic dimension > 55 mm, LV Ejection Fraction (LVEF) < 40%, and New York Heart Association (NYHA) Class II or III heart failure, being diagnosed at least six months earlier, and being under standard therapeutic regimen. Thereafter, 50 individuals with no significant cardiovascular diseases in their past medical history who were sex- and age-matched with the case group were enrolled into the control group. Written informed consents for taking part in the study were obtained from all the participants.

The exclusion criteria of the study were suffering from major coronary artery disease (lumen stenosis > 50% of any coronary artery or previous myocardial infarction), bicuspid aortic valve, aortic valve stenosis or regurgitation, congenital heart disease, diabetes mellitus (> 1 year), arterial hypertension, and renal failure (glomerular filtration rate < 50%). In order to measure LVEF and end-systolic and end-diastolic volumes, standard two-dimensional and M-mode echocardiography was performed by GE vivid 7 system through biplane Simpson method while all the subjects were placed in left lateral decubitus position. Simultaneously, the internal diameter of ascending aorta was measured at a level 3 centimeters above the aortic valve through parasternal long axis view at the end of systole and diastole in 3 consecutive beats and their average was considered for calculation of aortic strain (Figure 1). Moreover, the participants' brachial blood pressure was measured by a mercury sphygmomanometer in supine position.

The data derived from echocardiography and clinical measurements of blood pressure were used to determine the parameters of aortic elasticity, including aortic strain and aortic distensibility. The subsequent formulas were applied to calculate the mentioned indices:

$$\text{aortic strain} = \frac{\text{end systolic aortic diameter(ESD) - end diastolic aortic diameter(EDD)}}{\text{end diastolic aortic diameter(EDD)}}$$

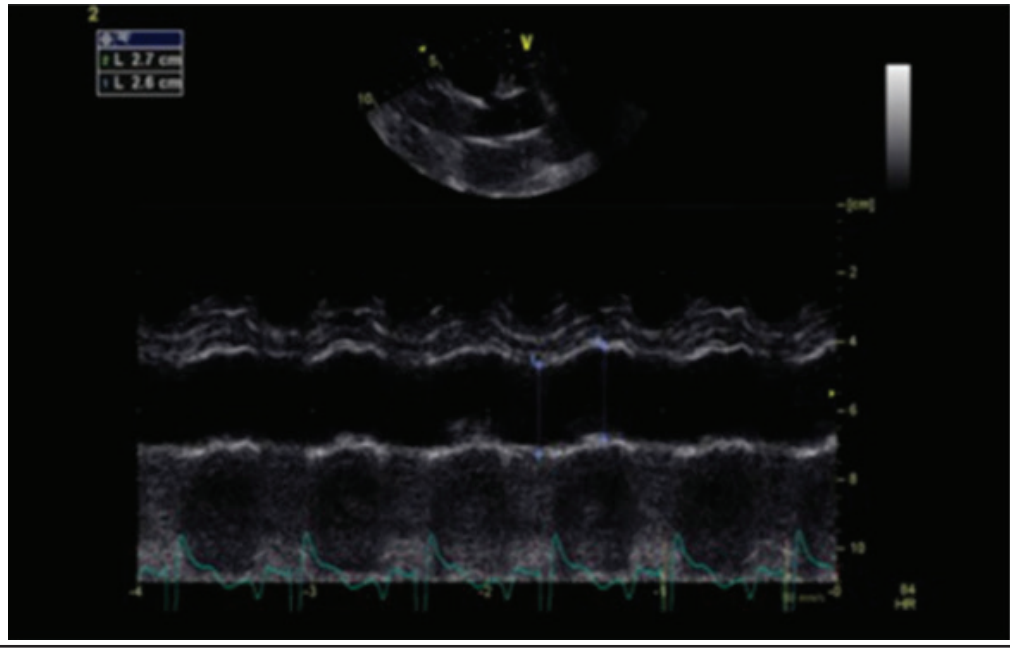

**Figure 1.** Standard Two-Dimensional and M-Mode Echocardiography Performed by GE Vivid 7 System

$$\text{Aortic distensibility} = \frac{2 \times \text{aortic strain}}{\text{Brachial pulse pressure}}$$

*3.1. Statistical Analysis*

All the statistical analyses were performed using the SPSS statistical software (v. 16.0). The ordinal data were analyzed by Chi-square test, while independent T-test was used to evaluate the quantitative data which were reported as mean ± SD. $P < 0.05$ was considered as statistically significant.

## 4. Results

The current case-control study was conducted on two groups each containing 50 members (NIDC patients and controls). Age and sex distributions were similar between the patients and controls. The mean age of the patients and the controls was 40.20 ± 9.72 and 37.84 ± 8.07 years, respectively ($P = 0.19$).

Moreover, LVEF was > 50% in the control group and < 40% in the patients. Among the patients, 46% had LVEF ≤ 30% and 54% had LVEF = 30% - 40%. The characteristics of the study participants have been presented in Table 1.

Considering the echocardiographic evaluations, the patients demonstrated decreased aortic strain and distensibility compared to the controls. The mean aortic strain was 0.05 ± 0.02 and 0.20 ± 0.46 in the patients and controls, respectively and the difference was statistically significant ($P < 0.001$). It should be mentioned that the aortic distensibility values were multiplied by 1000 to facilitate the comparison (Table 1). Furthermore, the results showed that the measured brachial pulse pressure was significantly lower in the patients compared to the controls (40.50 ± 9.00 in the NIDC cases versus 45.90 ± 8.08 in the controls, $P < 0.002$).

## 5. Discussion

Aorta, especially its proximal part, plays an important role in the LV afterload. Thus, investigation of its elastic characteristics is of great importance, especially in diseased heart muscle. In the present study, the proximal aorta properties were evaluated by means of echocardiography in the patients with NIDC. In other studies, however, Pulse Wave Velocity (PWV) was evaluated. The study results indicated that aortic strain and distensibility were significantly lower in the patients with HF due to NIDC compared to the healthy individuals. Although multiple factors have been proposed to affect the elastic characteristics of the proximal part of aorta, including diabetes mellitus, aging, and hypertension, it has been demonstrated that this phenomenon independently takes place in diastolic HF (12).

In accordance with our results, intensification of proximal aortic stiffness and decline in distensibility and exercise tolerance were reported among the patients with NIDC in a study performed by Patrianakos et al. based on measurement of PWV. They also reported a correlation between reduced distensibility and systolic and diastolic functions of the left ventricle (1).

In another study performed by Patrianakos et al. on the patients with end stage renal disease, PWV measures showed that increase in aortic stiffness influenced LV function by increasing the LV afterload (15). In addition, evaluation of the abdominal aorta and carotid artery in patients suffering from HF determined the presence of high-grade stiffness in large arteries and revealed a correlation between their distensibility and LV diastolic function. Nonetheless, such a relationship was absent for radial arteries (11).

Moreover, Mitchell et al. reported abnormalities in the proximal aorta properties, indicating increased functional stiffness of the central conduits in congestive HF in contrast to less stiff distal (muscular) conduit vessels (16).

Considering what was mentioned above, it seems that distensibility of the proximal part of aorta is of significant importance in determining the cardiac afterload. Prior investigations have also reported that it influences the systolic and diastolic functions of the cardiac muscle, modifying oxygen consumption and coronary perfusion which are of specific importance in diseased myocardium. Likewise, it has been established that the imbalances resulting from decreased aortic distensibility accentuates the afterload, thus affecting relaxation (1, 17).

The main underlying reasons for the mentioned changes in aortic stiffness are not clear. Yet, it might be due to the disease process itself or might act as an aggravating element. The findings of the study performed by Bonapace et al. demonstrated that alterations of arterial stiffness were primarily proportionate to propeptide tissue III collagen, providing a probable clarification of the increased aortic stiffness present in NIDC patients (18).

Furthermore, numerous mechanisms, including abnormalities of baroreceptors located in aorta and carotid, diverse neuro-humoral pathways such as the renin angiotensin system, and increased plasma norepinephrine that causes vasoconstriction and sodium retention in vasculature wall, have been considered as contributing to reduced arterial distensibility in HF (2, 19, 20).

**Table 1.** Characteristics of 50 Patients with Established Diagnosis of Non-Ischemic Dilated Cardiomyopathy (NIDC) and 50 Individuals without History of Significant Cardiovascular Diseases

| Variables | NIDC (N = 50) | Control (N = 50) | P value |
|---|---|---|---|
| **Age (Mean ± SD)** | 40.20 ± 9.72 | 37.84 ± 8.07 | 0.191 |
| **Sex (male/female)** | 26/24 | 25/25 | 0.842 |
| **EDD (Mean ± SD)** | 3.01 ± 0.34 | 2.51 ± 0.34 | 0.001 [b] |
| **ESD (Mean ± SD)** | 3.14 ± 0.34 | 3.01 ± 0.34 | 0.592 |
| **BPP (Mean ± SD)** | 40.5 ± 9.00 | 45.90 ± 8.08 | 0.001 [b] |
| **Strain (Mean ± SD)** | 0.05 ± 0.02 | 0.20 ± 0.46 | 0.001 [b] |
| **Distensibility [a] (Mean ± SD)** | 2.40 ± 1.04 | 8.87 ± 1.86 | 0.001 [b] |

Abbreviations: NIDC, non ischemic dilated cardiomyopathy; EDD, end diastolic diameter; ESD, end systolic diameter; BPP, Brachial pulse pressure; SD, standard deviation, [a]: values are multiplied by 1000 to facilitate comparison, [b]: $P < 0.05$ is significant

The results of the current study were in line with those of the previous studies about deterioration of aortic distensibility in patients with cardiovascular disorders, underscoring the importance of administration of pharmacologic agents aimed at improving cardiac function via reducing the aortic stiffness in management of the aforementioned condition. Similar to other observational studies, our study was subjected to selection bias and was inefficient for rare exposures. Besides, information on exposure was subjected to observational bias and did not allow calculation of incidence (absolute risk).

In brief, it seems that large arteries' distensibility, which can actually influence cardiovascular function adversely by augmenting the afterload, should be considered as a critical issue in approaching the patients with NIDC since they have higher aortic stiffness in comparison to the normal population. Nonetheless, more studies should be performed in order to assess proper medications for preventing or at least decreasing the amount of stiffening.

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**Authors' Contribution**

Study concept and design: Alireza Moaref, Mohammad Hossein Nikoo. Analysis and interpretation of data: Fereshte Horree. Drafting of the manuscript: Sanam Javid Anbardan. Critical revision of the manuscript for important intellectual content: Alireza Moaref, Mohammad Hossein Nikoo. Statistical analysis: Fereshte Horree.

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