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Correlation Between Aortic Root Elastic Properties and Glomerular Filtration Rate in Patients With Chronic Kidney Disease

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Introduction. Aortic root stiffness is a highly prevalent condition in patients with chronic kidney disease (CKD), which independently associates with increased risk of mortality and morbidity in this group. This study aimed to investigate the relationship between glomerular filtration rate (GFR) level as a marker of kidney function and elastic properties of aortic root obtained with echocardiography.
Methods and Materials. Eighty-two patients (53 men and 29 women; mean age, 57.9 ± 15.0 years) with CKD stages 3 and 4 were enrolled in this study. Echocardiography and tissue Doppler imaging of the upper and lower aortic walls were done. Systolic wave (S wave) was obtained from each walls. Aortic distensibility and aortic root stiffness index were calculated using blood pressure measurement and aortic dimensions in systole and diastole by M-mode echocardiography.
Results. In all of the patients, aortic stiffness index (14.24 ± 9.82), aortic distensibility (0.018 ± 0.015), aortic upper wall S velocity (0.10 ± 0.03), and aortic lower wall S velocity (0.08 ± 0.02) were severely impaired. There was no correlation between GFR and aortic distensibility (r = -0.253, *P* = .20), aortic root stiffness index (r = 0.193, *P* = .09), aortic upper wall S velocity (r = -0.106, *P* = .17), and aortic lower wall S velocity (r = -0.150, *P* = .09).
Conclusions. Aortic stiffness was seen in all patients with kidney failure in stage 3 or 4 of CKD; however, we could not find any direct relationship between GFR and this phenomenon. Thus, aortic root stiffness may be a consequence of hypertension and other risk factors.

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INTRODUCTION

Cardiovascular diseases are highly prevalent among patients with chronic kidney disease (CKD) and currently are the biggest cause of death among these patients.[1-3] Three major effects of CKD on cardiovascular system are left ventricular hypertrophy, atherosclerosis, and arterial and aortic stiffness.[4] Recent studies show the independent effect of aortic stiffness on mortality and morbidity in patients with CKD.[5]

Brawmwell and colleagues first measured aortic stiffness using the pulse wave velocity (PWV) propagation in the arterial tree, which now is accepted as the gold standard method in most studies.[6] Incorporation in routine clinical practice needed availability and ease of use. Thus, echocardiographic-based methods to quantify aortic stiffness were described and its accuracy

was confirmed in many studies.[7-10]

Aortic elastic properties and stiffness are determined by 3 indexes in echocardiograghy: aortic distensibility, aortic stiffness index, and tissue Doppler imaging of aortic root by aortic upper wall S velocity (the bigger upper wall S velocity, the less aortic root stiffness).[7] Although the relationship between kidney failure and PWV was previously established,[11] but yet this correlation is not defined between levels of glomerular filtration rate (GFR) and aortic root stiffness achieved with direct echocardiographic based methods. The purpose of this study was to investigate the relationship between GFR levels and aortic root elastic properties and stiffness by means of echocardiography and also probability of prediction of aortic elastic properties with the level of GFR.

METHODS AND MATERIALS

We enrolled 82 hospitalized patients with CKD referred to perform echocardiographic assessment with any reason in 3 cardiovascular centers. The definition of CKD was a GFR of 60 mL/min/1.73 m² or less, lasting for at least 3 months. The estimated GFR was calculated according to the serum creatinine using the Cockroft-Gualt formula. The GFRs of patients on hemodialysis were assumed to be 10 mL/min/1.73 m². Patients with a history of moderate to severe valvular heart disease, congenital heart disease, cardiomyopathy (ejection fraction, < 45%), atrial fibrillation, hypothyroidism, previous open heart surgery, tamponade, and poor view on echocardiography were excluded from the study.

All of the patients were investigated for cardiovascular risk factors including diabetes mellitus (DM), hypertension, smoking, hyperlipidemia, and coronary artery disease (CAD). Echocardiographic examination was conducted using a General Electric vivid 3 echocardiographic system and 2.5 MHZ probe by one cardiologist. Valvular assessment, systolic function, and diastolic function were determined. Left ventricular ejection fraction was determined using M mode. The diameters of aortic root were measured 3 cm above the aortic valve between the lower edge of the upper wall and the upper edge of the lower wall in systole and diastole by M-mode echocardiography in the parasternal long axis view. The diastolic aortic root diameters were assessed at the point corresponding to the peak of QRS in electrocardiography tracing, and diastolic and systolic diameters were measured at the point of aortic valve opening. These values were adjusted by dividing by the body surface area. Then aortic root distensibility and stiffness index were measured using the following formula:

Aortic distensibility = 2 × (aortic diameter in systole - aortic diameter in diastole)/pulse pressure × aortic diameter in diastole

Aortic stiffness index = ln(systolic blood pressure/ diastolic blood pressure)/(aortic diameter in systole - aortic diameter in diastole)/aortic diameter in diastole

The velocities of the upper and lower walls of aortic root were measured with conventional tissue Doppler imaging at the same point as in M-mode measurement. Two diastolic (E and A) and one systolic (S) waves velocity was measured. The difference of S waves velocities of the upper and lower aortic root walls were calculated. All values were averaged from 6 consecutive cardiac cycles.

RESULTS

Clinical characteristics of the study population are presented in Table 1. Men's population was predominant and the average age was 57.9 ± 15.0 years. There were high prevalence rates of DM, smoking, hyperlipidemia, hypertension, and CAD among the study population (Table 1). Aortic stiffness index (14.24 ± 9.82), aortic distensibility (0.018 ± 0.015), aortic upper wall S velocity (0.10 ± 0.03), and aortic lower wall S velocity (0.08 ± 0.02) were significantly impaired.

The Pearson correlation coefficient showed that there was no correlation between GFR and aortic distensibility, aortic stiffness index, aortic upper wall S velocity, or aortic lower wall S velocity (Table 2). A significant relationship was found between pulse pressure and GFR (r = 0.369, $P < .005$). Aortic distensibility correlated with DM (r = -0.193, $P = .04$), hyperlipidemia (r = -0.199, $P = .04$), and hypertension (r = -0.253, $P = .01$). Also, aortic stiffness index corrrelated with hyperlipidemia (r = 0.207, $P = .03$). To resolve the confounding effect of some variants such as DM, hypertension, smoking, age, hyperlipidemia, and CAD, partial correlation analysis also was done, which showed no significant changes in the final results after adjustment of these variants.

Table 1. Characteristics of Study Population

Characteristic	Value
Age, y	57.90 ± 15.00 (20 to 70)
Male sex (%)	53 (64.6)
Weight, kg	71.50 ± 12.00 (32 to 105)
Height, cm	167.00 ± 7.00 (147 to 180)
Ideal body weight, kg	61.60 ± 6.70 (45.5 to 75)
Body surface area, m^2	1.79 ± 0.16 (1.17 to 2.15)
Systolic blood pressure, mm Hg	145.00 ± 29.00 (70 to 190)
Diastolic blood pressure, mm Hg	84.00 ± 21.00 (45 to 150)
Diabetes mellitus (%)	46 (56.1)
Smoking (%)	33 (40.2)
Hyperlipidemia (%)	39 (47.6)
Hypertension (%)	65 (79.3)
Coronary artery disease (%)	34 (41.5)
Aortic upper wall S velocity, m/sec	0.10 ± 0.03 (0.05 to 0.16)
Aortic lower wall S velocity, m/sec	0.08 ± 0.02 (0.04 to 0.14)
Serum creatinine, mg/dL	4.20 ± 2.90 (1.1 to 12.2)
Glomerular filtration rate, mL/min/1.73 m^2	23.70 ± 14.50 (4.9 to 66.9)
Pulse pressure, mm Hg	61.00 ± 18.00 (20 to 95)
Difference of upper and lower wall S velocity, m/sec	0.02 ± 0.02 (0 to 0.06)
Aortic systolic diameter, cm	3.08 ± 0.43 (2.15 to 3.99)
Aortic diastolic diameter, cm	2.90 ± 0.43 (1.97 to 3.83)
Aortic systolic index, cm/m^2	1.71 ± 0.25 (1.15 to 2.17)
Aortic diastolic index, cm/m^2	1.62 ± 0.24 (1.07 to 2.07)
Aortic distensibility, cm^2dynes^{-1}	0.02 ± 0.02 (0 to 0.0777)
Aortic stiffness index	14.24 ± 9.82 (1.94 to 48.66)

DISCUSSION

According to the results of this study, we did not find any relationship between GFR levels and elastic properties of the aortic root, namely aortic distensibility, aortic stiffness index, and velocity of S wave in tissue Doppler imaging. We also showed that there was no correlation between the findings of tissue Doppler imaging and aortic distensibility and aortic stiffness index. Although this issue may seem surprising at the first look, a review of patient's selection revealed all of our cases had a GFR below 60 mL/min/1.73m^2 matches to stage 3 or higher stages of CKD, and despite the absolute decrease in elastic properties of aorta, these properties did not change in correlation with GFR levels. It is perhaps because arterial stiffness is an early event in the progression of CKD. In a study of 102 patients with CKD, Wang and coworkers showed a stepwise increase in arterial stiffness from CKD stages 1 and 2 to the CKD stages 3 to 5.[11] They applied PWV to define the arteries stiffness and concluded that decrease in GFR and increases in systolic blood pressure were independently associated with arterial stiffness. In another study, Makita and colleagues demonstrated an increase in carotid artery stiffness in early stages of CKD.[12] Ix and colleagues defined the correlation between ankle-brachial index as a marker of arterial stiffness and even mild kidney dysfunction in a large cross sectional study of 4513 individuals from general population.[13]

These early changes in arterial properties are because the pathophysiologic process affecting the arteries start in early phases of CKD. For example, hypertension and hyperlipidemia develop in patients with only mild renal insufficiency.[13,14] Another limitation of our study was the small size of our sample of patients; applying a larger sample is suggested for future studies.

CONCLUSIONS

In this study, aortic stiffness was seen in all patients with CKD in stage 3 or 4; however, we could not find any direct relationship between GFR and

Table 2. Relationship Between Aortic Distensibility, Aortic Stiffness Index, Aortic Upper Wall S Velocity, and Aortic Lower Wall S Velocity, and Other Clinical Parameters

	Aortic Distensibility		Aortic Stiffness Index		Aortic Upper Wall S Velocity		Aortic Lower Wall S Velocity	
Parameter	r	*P*	r	*P*	r	*P*	r	*P*
Glomerular filtration rate, mL/min/1.73 m^2	-0.095	0.198	0.193	0.086	-0.106	0.170	-0.150	0.089
Hyperlipidemia	-0.199	0.037	0.089	0.431	0.044	0.347	-0.028	0.401
Hypertension	-0.253	0.011	0.210	0.061	-0.156	0.081	-0.129	0.124
Diabetes mellitus	-0.0193	0.041	0.111	0.328	0.088	0.217	0.007	0.474
Smoking	-0.113	0.156	0.080	0.478	0.054	0.314	0.058	0.303
Coronary artery disease	-0.027	0.405	-0.088	0.439	0.073	0.257	0.135	0.113
Pulse pressure, mm Hg	-0.386	0.000	0.268	0.016	0.001	0.498	0.001	0.495
Difference of upper and lower S velocity, cm	-0.121	0.139	0.19	0.864	0.666	0.000	0.150	0.090

this phenomenon. Thus, aortic root stiffness may be a consequent of early effects of hypertension, hyperlipidemia, DM, and other factors in CKD, such as volume overload, drug use, and impaired calcium metabolism. We should keep in mind that echocardiograghy is a reliable tool to estimate aortic stiffness in the hands of an expert, but its value reduces in high stages of CKD.

CONFLICT OF INTEREST

None declared.

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