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A comparative study of the effects of chronic kidney disease on sonographic arterial stiffness parameters in geriatric and normal population

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ABSTRACT

Aim: Due to its growing incidence rate worldwide, chronic kidney disease is a crucial public health problem which is strongly associated with cardiovascular disease. Cardiovascular disease in chronic kidney disease patients is characterized by arteriosclerosis and increased arterial stiffness, and is the leading cause of morbidity and mortality. A correlation was reported between an increased arterial stiffness and cardiovascular disease in high risk groups such as chronic kidney disease or hypertension as well as general undiagnosed population. Our aim was to show the changes in arterial stiffness parameters in patients with chronic kidney disease in the geriatric population.

Material and Method: 44 chronic kidney disease patients and 44 control group cases of the same age were included in the study. There were 20 female and 24 male cases in each group. Systolic and diastolic diameter were measured for all cases. Intima-media thickness was measured in carotid and femoral arteries. Arterial stiffness parameters were calculated using formulas. Systolic and diastolic arterial blood pressure and body mass index were measured. Their urea and creatinine values were recorded.

Results: There were no differences between two groups in terms of age and sex ($p=0.069$). Body mass index in the patient group was significantly lower compared to the control group ($p=0.025$). Systolic arterial blood pressure was higher in the patient group ($p<0.001$). Arterial stiffness parameters in both arterial systems, particularly in femoral artery, were significantly ($p<0.05$) worse in the patient group compared to the control group.

Conclusion: Intima-media thickness was measured higher, which overlaps with the existing literature. Femoral parameters were more effective in the prediction of atherosclerosis. Chronic kidney disease affects cardiovascular system negatively, and increases atherosclerosis significantly compared to the normal population.

Keywords Arterial stiffness, chronic kidney disease, geriatrics, compliance, diastolic wall stress

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INTRODUCTION

Chronic kidney disease (CKD) is a crucial public health problem due to its growing incidence rate worldwide and is strongly associated with cardiovascular disease (CVD) (1). CVD in CKD patients is characterized by arteriosclerosis and increased arterial stiffness (AS), and is the leading cause of morbidity and mortality. In fact, the risk of death from CVD is higher for CKD patients compared to progression towards end-stage renal disease (ESRD) or risk of death from renal failure (2). More than half of deaths in patients with ESRD is associated with cardiovascular causes (3). Apart from ESRD, patients with low-grade kidney diseases are more prone to cardiovascular events. Based on potential population-based studies, it is reported that mild-to-moderate kidney disease can predict cardiovascular morbidity and mortality. However, the increased cardiovascular risk cannot be explained by traditional atherosclerotic risk factors, and it probably results from non-atherosclerotic arterial and heart diseases processes (4).

The evaluation of AS parameters is a replicable, reliable and non-invasive method for the diagnosis of subclinical atherosclerosis. IMT measured in main carotid artery and the degree of subclinical atherosclerosis are associated with cardiovascular

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events and mortality in both general population and CKD patients. Sectional studies on groups without CKD indicated the correlation between carotid IMT and cardiovascular risk factors and presence of CVD (5). Several large observational studies also reported that carotid IMT was a precursor to coronary heart disease events for which it remained statistically significant following the adjustment of traditional risk factors. The correlation between IMT and cardiovascular event risk was also analyzed in terms of a dominant risk factor such as CKD (6).

Even though patient populations in previous studies included geriatric population samples, no studies have so far been carried out on peer patient groups. To this end, the present study analyzes the difference between CKD patients and a geriatric control group of the same age in order to evaluate the correlation between subclinical atherosclerosis and negative clinical results.

Similarly, although existing studies in the literature dealt with arterial stiffness in CKD, they partially focused on functional and quantitative markers such as compliance, diastolic wall stress, distensibility and elastic modulus. The present study concentrates more on these parameters.

MATERIAL AND METHOD

Ethics Approval

The study was carried out with the permission of Elazığ Training and Research Hospital, Noninvasive Clinical Researches Ethics Committee (Date: 18/01/2008 Decision No: Bl04ISM04230045 /21). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki.

Patient Population

After obtaining an ethical committee approval, the present study was conducted on geriatric individuals. It was a monocentral, prospective and observational cohort study on CKD patients and a control group. While the patient group included 20 female and 24 male patients, the control group, similarly, included the same number of males and females. The average age was 70.09 in the patient group, whereas it was 67.98 in the control group.

Measurement List

The following parameters were determined and defined before the study: BMI, systolic and diastolic arterial blood pressure levels, urea and creatinine values, carotid and femoral artery systolic and diastolic diameters, and AS values were calculated using IMT. US measurements were performed by the same radiologist on the same US device. AS values (compliance, diastolic wall stress, distensibility and elastic modulus) were calculated using relevant formulas.

Body mass index was calculated by dividing body weight (kilogram; kg) by the square (m^2) of height (meter; m).

Blood pressure was measured using a sphygmomanometer three times with an interval of 5 minutes. The mean value obtained from three different measurements was calculated unless their difference was higher than 10 mmHg, and, if so, the mean value of two closest measurements was used.

IMT Measurement

A high resolution broadband linear array (multiple frequency: 4-12 MHz) B-mode ultrasound transduser was used to evaluate right main carotid artery, carotid bulbus and internal carotid artery for carotid system and right main femoral artery for femoral system. Main carotid artery located about 1 cm in front of bulbus was standardized for measurement in the carotid system, while main femoral artery located about 1 cm in front of bifurcation was selected for the femoral system. The screen image was enlarged to increase measurement accuracy. Electronic calipers were used for IMT measurement. It was ensured that caliper lines were in parallel with arterial walls. Three different measurements were recorded, and a mean value was calculated for each group.

Systolic and Diastolic Diameter Measurement

For IMT, systolic and diastolic diameters were measured on standardized locations in both systems using the same US device and M-mode US. For a healthier measurement process, a screen image on which the same ultrasonic waves could be monitored without any artifacts was selected. In addition, the image was enlarged for a higher accuracy.

Exclusion Criteria

Smokers and diabetic patients were not included in the study. In addition, cases with a radiological kidney pathology was not included in the control group even if their clinical and laboratory results were not evaluated.

Statistical Analysis

Mean±standard deviation was used to explain the obtained data. An IBM SPSS for Windows (IBM statistics for Windows version 25, IBM Corporation, Armonk, New York, United States) was used or statistical analysis. Student T test was used to compare the parameters.

RESULTS

There were not any differences between two sexes in each group.

No statistically significant differences can be found between two geriatric populations in terms of their age.

Body mass index was calculated as 26.48±3.89 in the patient group, whereas it was 28.46±4.19 in the control group. BMI was significantly lower in CKD patient group compared to the control group.

Arterial blood pressure levels were measured as 162.55±25.60 and 86.64±17.12 mm/hg for systolic and diastolic blood pressure in the patient group, respectively. However, the same values were 125.25±6.30 and 77.50±6.04 mm/hg for systolic and diastolic blood pressure in the control group. As a result, it was found that both systolic and diastolic arterial blood pressure levels were higher in the patient group compared to the control group.

Carotid artery IMT (**Figure 1**) was 0.66±0.11 mm and 0.52±0.14 mm in the patient and control group, respectively. Similarly, femoral artery IMT (**Figure 2**) was 0.65±0.13 and 0.44±0.19 mm in the patient and control group, respectively. Being more apparent in femoral artery, IMT values in both carotid and femoral arterial system were higher (worse) in the patient group compared to the control group.

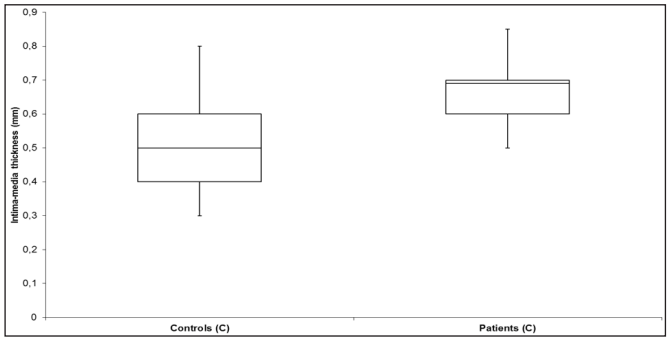

Figure 1. The distribution of carotid artery IMT values in both groups

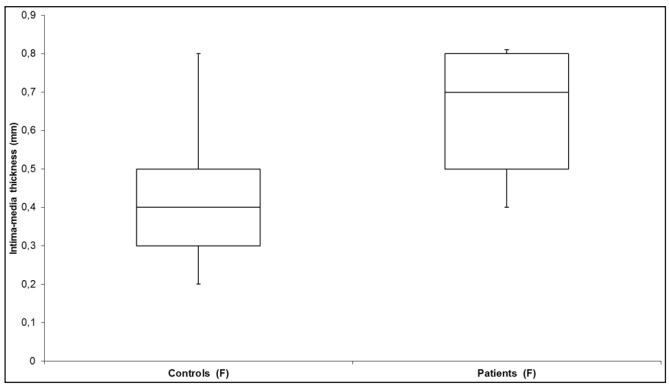

Figure 2. The distribution of femoral artery IMT values in both groups

Compliance: Carotid artery compliance values were statistically higher in the patient group compared to the control group. Although femoral artery compliance values were lower in the patient group compared to the control group, they were statistically insignificant.

Diastolic wall stress: In both carotid and femoral system (albeit being more apparent in femoral system), diastolic wall stress was higher in the patient group compared to the control group, it was still statistically insignificant.

Distensibility: Carotid artery distensibility values were statistically lower in the patient group compared to the control group. However, femoral artery distensibility values were lower and statistically insignificant in the patient group compared to the control group.

Elastic modulus: Carotid artery elastic modulus values (**Figure 3**) were lower in the patient group compared to the control group; however, they were statistically insignificant. On the other hand, femoral artery elastic modulus values (**Figure 4**) were statistically higher in the patient group compared to the control group.

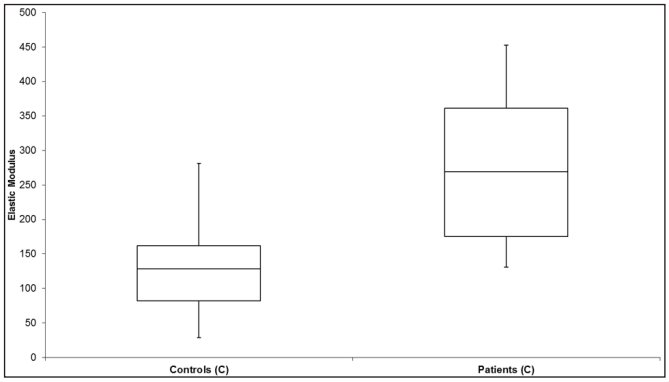

Figure 3. The distribution of carotid artery elastic modulus values in both groups

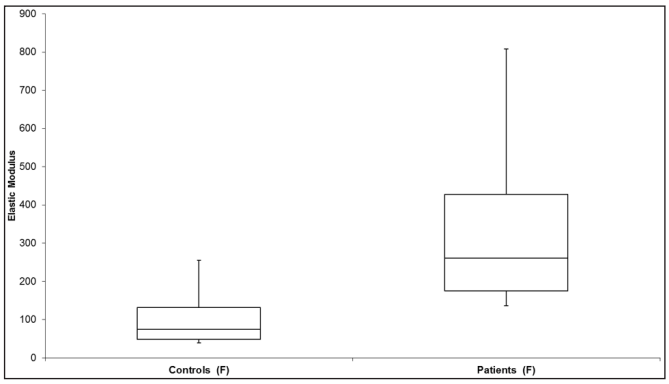

Figure 4. The distribution of femoral artery elastic modulus values in both groups

Urea and creatinine values in the patient group were 95.545±36.575 and 2.393±0.964, respectively.

The results are presented in **Table.**

Table. Collective representation of our findings

	Control		Patient		p
	Mean	Standard deviation	Mean	Standard deviation	
Age	67.982	5.190	70.091	5.531	0.069
Body-mass index	28.455	4.193	26.484	3.890	0.025
Systolic blood pressure	125.250	6.298	162.545	25.596	<0.001
Diastolic blood pressure	77.500	6.044	86.636	17.119	0.042
Pulse	67.500	12.404	74.091	14.079	0.104
Carotid artery intima-media thickness	0.518	0.135	0.664	0.108	<0.001
Carotid artery compliance	0.135	0.249	0.155	0.066	<0.001
Carotid artery diastolic wall stress	663.620	180.102	724.603	204.350	0.614
Carotid artery distensibility	0.004	0.010	0.004	0.002	<0.001
Carotid artery elastic modulus	130.718	96.807	274.069	105.981	0.591
Femoral intima-media thickness	0.436	0.189	0.645	0.132	0.141
Femoral artery compliance	0.249	0.130	0.137	0.097	0.015
Femoral artery diastolic wall stress	752.206	258.070	718.812	184.427	0.013
Femoral artery distensibility	0.009	0.005	0.003	0.002	0.163
Femoral artery elastic modulus	105.188	82.713	379.192	282.456	<0.001
Urea			95.545	36.575	
Creatinine			2.393	0.964	

DISCUSSION

The main innovation of the present study is to include a specific geriatric population and to focus on functional, local and quantitative AS markers, namely compliance, diastolic wall stress, distensibility and elastic modulus.

AS is a term which describes viscoelastic properties of blood vessel wall (8). The elastic structure of large- and medium-sized arteries is a critical factor in determining general cardiovascular health (9). Pulsatile blood flow decreases depending on the elasticity of these arteries. It thus ensures the fixed continuity of bloodstream from the heart at capillary level and its fixed perfusion into vital organs (10). Just as a decreased elasticity leads to such effect in the peripheral system, it may also reduce pulse wave reflection, which results in left ventricular hypertrophy (11). On the other hand, AS, which was defined in the first half of the twentieth century, is an inverse pathological process against this elastic structure (12).

AS measurement is performed non-invasively, and related measurement methods are divided into two groups. The first group benefits from different techniques such as arterial waveform analysis and diameter measurement for qualitative stiffness prediction, while the second group relies on quantitative calculation parameters such as compliance, diastolic wall stress, distensibility and elastic modulus. Compliance is the absolute diameter change based on the increased blood pressure. Diastolic wall stress is the force to which blood vessel wall is exposed during diastole. Distensibility is the proportional change in diameter based on the increased pressure. Elastic modulus offers information about the properties of wall material independently of arterial geometry. Intima-media thickness (IMT) is a structural property. However, compliance, distensibility, diastolic wall stress, elastic modulus and pulse wave velocity (PWV) are functional properties (13). PWV is a local marker of arterial stiffness along an artery. On the other hand, compliance, distensibility, diastolic wall stress and elastic modulus are local markers of arterial elasticity (14).

Increased AS occurs prior to atherosclerosis and is considered as an early marker of systemic atherosclerosis. AS is an independent factor in the prediction of morbidity and mortality in CVD. A correlation was reported between an increased AS and CVD in high risk groups (such as CKD or hypertension) as well as general undiagnosed population (15).

The correlation between CKD and AS is complex. In the field of pathophysiology, many mechanisms including traditional and non-traditional risk factors have been proposed so far. The very first studies demonstrated that an increased AS in CKD was caused by traditional risk factors (hypertension). Pulsatile wall stress increases during hypertension, which leads to the development of elastin degeneration and vascular remodeling. In addition, AS is a vascular biomarker and increases in CKD patients, and it may even become higher in patients with mild kidney disease independently of cardiovascular risk (16). An increased AS in CKD patients cannot be fully explained by traditional risk factors, since many different traditional and non-traditional risk factors such as inflammation, endothelial dysfunction, ageing, vascular calcification, hypertension, uremic toxins and bone-mineral disorders play a certain role in the development of AS in CKD. An increased AS is an important cause for the development of CVD in CKD patients, and it is acknowledged as a non-traditional risk factor for CVD in CKD patients. Additionally, some studies reported that AS itself was likely to contribute to the progress of CKD (17). However, other studies focusing on the correlation between AS and CKD reported contradictory results (18). The prevalence, pathogenesis and clinical importance of AS in patients with early-stage CKD are still unknown (19). On the other hand, it is described as a critical risk factor for all-cause mortality in progressed CKD (20). An increased AS points to an arterial ageing process. Early vascular ageing is already known to occur in early-

stage and progression of CKD. In parallel with increased cardiovascular risk and left ventricular abnormalities, AS is inversely proportional to renal function. Large vessel arteriopathy in CKD causes AS and, consequently, vascular compliance and loss of distensibility (21).

It was reported in the current literature that IMT was higher compared to the normal population at different stages of CKD (22, 23). In a similar vein, it was found in the present study that IMT was measured higher in geriatric age group compared to the normal population in terms of both carotid and femoral arterial system.

Various studies have so far dealt with changes in functional, local and quantitative AS markers in different patient groups such as diabetes (24), schizophrenia (25), and peripherial artery disease (26). In addition, different recovery factors such as treatment and aerobic exercise were analyzed for these parameters (7). Unlike previous studies on arterial stiff in CKD, the present study focuses more on functional, local and quantitative AS markers.

It is known that many different pathophysiological mechanisms contribute to an increased AS in CKD. In addition to a different pathophysiology, multiple and quantitative measurement methods for AS are likely to reveal their correlation in a clearer way. In this respect, similar to the present study, we recommend researchers to draw on functional quantitative parameters in AS studies.

In the present study, there were significant differences between the patient and control group in terms of all functional and quantitative parameters, and they were sometimes statistically significant. It can be thus argued that AS under different pathophysiological conditions may contribute to different parameters, a point which is particularly important for AS studies on CKD patients. Future studies may attempt to explore more correlations among pathophysiology, stiffness parameter and clinical picture.

Similar to the previous study (7), the defined stiffness parameters were more apparent in femoral system.

Limitations

The main limitation of the present study was its reliance on one-shot images, as the obtained data were collected once for the objectives of the present study without any detailed longitudinal evaluation. Additionally, our sectional analysis did not take into account the duration of exposure to risk factors. Even though carotid IMT is independently associated with a risk of cardiovascular event, it is a defective parameter for atherosclerosis and may not necessarily reflect the disease in other vascular beds. The present study aimed to overcome this problem by partially including femoral system in the analysis.

CONCLUSION

CKD affects cardiovascular system negatively and increases atherosclerosis remarkably compared to the normal population. Subclinical atherosclerosis can be diagnosed thanks to IMT and other parameters measured using US, which is a cost-effective, non-invasive and easily accessible imaging method. However, further studies are still needed to analyze clinical practices with IMT and other quantitative parameters for the clinical management and risk classification of CKD patients.

ETHICAL DECLARATIONS

Ethics Committee Approval: The study was carried out with the permission of Elazığ Training and Research Hospital, Noninvasive Clinical Researches Ethics Committee (Date: 18/01/2008 Decision No: Bl04ISM04230045 /21).

Informed Consent: All patients signed the free and informed consent form.

Referee Evaluation Process: Externally peer-reviewed.

Conflict of Interest Statement: The authors have no conflicts of interest to declare.

Financial Disclosure: The authors declared that this study has received no financial support.

Author Contributions: All of the authors declare that they have all participated in the design, execution, and analysis of the paper and that they have approved the final version.

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