Assessment of Cardiac Functions and Subclinical Cardiovascular Risk In Children with Urolithiasis: An Initial Study

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Abstract

Information on cardiovascular problems related to childhood urinary stone disease is limited. The aim of this study is to assess the ventricular functions and subclinical cardiovascular risk in children with urolithiasis using echocardiographic measurements. Children readily diagnosed with urolithiasis were enrolled in the study as well as children with no urinary stone disease confirmed via urinary ultrasonography. Body mass index (BMI) and blood pressures were noted as well as basic serum parameters. Carotid intima media thickness (cIMT), epicardial fat tissue (EFT) thickness and periaortic fat tissue (PFT) thickness were measured via transthoracic echocardiography in addition to pulsed and tissue Doppler imaging. Myocardial performance indexes were also calculated and correlation analyses were made. A total of 17 patients (10 boys) were enrolled in the study with a mean age of 8.57 ± 2.62 years. There were 17 children (12 boys) in the control group and their mean age was 9.53 ± 1.72 years. There was no statistically significant difference between the two groups in terms of demographic and laboratory variables. Tissue Doppler echocardiography revealed that Tei indexes of left ventricle, right ventricle and septum were significantly higher in the study group than in the controls ($p < 0.001$ for all). The cIMT (0.041 ± 0.012 vs. 0.025 ± 0.002), EFT (0.432 ± 0.083 vs. 0.325 ± 0.032) and PFT thicknesses (0.138 ± 0.029 vs. 0.113 ± 0.008) of the study group were statistically higher than the control group ($p < 0.001$, $p < 0.001$ and $p = 0.002$, respectively) indicating a higher CVD risk.

Conclusions:

Children with urolithiasis presented not only biventricular early systolic and diastolic dysfunction but also subclinical atherosclerosis in early ages. Cardiovascular complications should be considered in the follow-up and treatment of these patients.

What Is Known?

- Incidence of urolithiasis is increasing globally.

- Chronic inflammation is associated with subclinical atherosclerosis

What is new?

- Subclinical atherosclerosis in addition to early systolic and diastolic dysfunction is observed in children with urolithiasis.

Introduction

Urolithiasis is a global disease with an increasing prevalence in recent years and it causes significant morbidity for all ages. In the USA, 11% of men and 7% of women are diagnosed with urinary stone disease throughout their lives [1]. Further, recurrences may be observed in 30 to 50% of the cases in 5–10 years after the first stone incidence [2]. As a chronic disease, urolithiasis affects 3–5% of the population

whereas exact incidence in children is not known [3]. Pediatric emergency room (ER) visits due to urinary stone disease comprised 8 of 100,000 in 1996 while this increased to 18 of 100,000 in 2007 [4]. It is very-well documented that pediatric urolithiasis is strictly related to metabolic abnormalities [5]. Thus, it has higher risk for recurrence and morbidity in children [6]. Moreover, chronic kidney disease prevalence is 1.5 times higher and end stage kidney disease may be seen 2.4 times in pediatric kidney stone formers [7].

Chronic inflammation is an independent factor for subclinical atherosclerosis and thus, cardiovascular complications. It was shown that inflammatory cytokines have a role in the progression of atherosclerosis [8]. Studies in adult population indicated that urolithiasis is related to chronic inflammation such as hypertension, diabetes and metabolic syndrome. Also, it has been shown that myocardial infarction, stroke and coronary artery disease are more commonly found in patients with urinary stone disease [9]. A recent study that looked into adolescents with urolithiasis reported increased levels of urinary cytokines that point out presence of chronic inflammation [10].

Furthermore, studies showed oxidative stress and inflammation induces Randall's plaque which is the initial step in stone formation [11]. In CARDIA study, researchers revealed a positive correlation between urolithiasis and subclinical atherosclerosis in young adults [12]. To date, there is a single study that investigated atherosclerosis and cardiovascular complications in children. Carotid intima media thickness (cIMT) which is a sign of subclinical atherosclerosis was found to be increased in children with nephrolithiasis this study [13].

In current practice, cIMT is used as a marker to identify subclinical atherosclerosis as well as epicardial fat tissue (EFT) thickness and periaortic fat tissue (PFT) thickness. Several researchers demonstrated the use of these markers of subclinical atherosclerosis in different chronic diseases in pediatric population [14; 15]. The aim of this initial prospective case-control study is to assess the risk of subclinical cardiovascular risk in children with urolithiasis using cIMT, EFT and PFT thickness in addition to tissue Doppler imaging (TDI) echocardiographic evaluation of cardiac functions.

Material And Methods

Patients

After obtaining ethical board approval (Number: 419011325-050.99), patients were prospectively included for this study beginning from December 2019 - May 2020. Patients >5 years of age and had kidney stones (>3 mm) that were confirmed by two consecutive ultrasonographic images or a computed tomography and those had normal serum chemistries were included in the study. Those with congenital heart diseases, chronic kidney disease, inflammatory bowel disease, monogenic stone phenotypes, normal serum chemistries, urogenital malformations (vesicoureteral reflux, posterior urethral valves, neuropathic bladder etc.), obesity, hypertension, chronic diseases (i.e., diabetes mellitus) and patients who were passive smokers were excluded.

Blood pressures were measured from the left arm using age-appropriate manual sphygmomanometer cuffs after 5 minutes of resting and mean of 3 measurements were noted. All blood samples including urea, creatinine, glucose, uric acid, total cholesterol, triglyceride, high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C) were obtained a.m. after 8 hours of fasting. Glomerular Filtration Rate (GFR) was calculated by Schwartz formula [16].

Control group consisted of health children who have normal BMI and blood pressure (adjusted for age) with no known history of urolithiasis (confirmed by urinary ultrasonography).

Echocardiographic measurements

M-mode echocardiographic measurements

Echocardiographic investigations were performed using Philips Affiniti 50 (Philips Healthcare, Andover, Netherlands) with 2.0-4.0 MHz transducers. Echocardiograms were recorded on a half-inch VHS videotape. All measurements were performed according to the American Society of Echocardiography by the same observer blinded to the participant's clinical details [17]. The measurements were obtained during 3 consecutive cardiac cycles and the average values were computed. Ejection fraction and fractional shortening of the left ventricle (LV), interventricular septum systolic (IVSs) and diastolic thickness, LV end-systolic and end-diastolic dimensions, and LV posterior wall systolic and diastolic thicknesses were measured from M-mode echocardiographic tracings obtained at midchordal leveling the parasternal long axis view. The left ventricular mass (LVM) was estimated by using the anatomically validated formula of Devereux and Reichek [18]. The LVM index (LVMI) was calculated by dividing the LVM with the height $^{(2.7)}$.

Pulsed Doppler echocardiographic measurements

Ventricular functions were evaluated using the following pulse-wave Doppler (PWD) echocardiographic parameters: early (E) and late (A) mitral/tricuspid diastolic velocities, E/A ratio, and LV/right ventricle (RV) ejection times. Standard measurement techniques were used for evaluation [17]. We calculated the myocardial performance index (MPI) using the formula, the sum of isovolumic contraction and relaxation times divided by the ejection time [19].

Tissue Doppler echocardiographic measurements

Tissue Doppler velocities; peak early diastolic myocardial (e'), peak atrial systolic (a'), and peak systolic (s') myocardial velocities were measured by standard technique [17]. Also, e'/a' and E/e' ratios were calculated. The Tei index (MPI) was calculated as defined above.

Measurement of epicardial fat tissue thickness

The EFT thickness was identified as an echo-free space in the pericardial layers on 2-dimensional echocardiography, and its thickness was measured perpendicularly on the free wall of the RV at end

diastole from the parasternal long-axis views [20]. The mean EFT thickness was calculated from 3 consecutive measurements.

Measurement of common carotid artery intima-media thickness

Longitudinal images of the common carotid artery were obtained by combined 2-dimensional mode and color Doppler examinations. On a longitudinal echocardiographic image of the posterior wall of the carotid artery was displayed as 2 bright white lines separated by a hypoechogenic space [21]. The mean cIMT was calculated from the 3 consecutive measurements of the maximum far wall thickness obtained from 10 mm below the carotid bulb.

Measurements of periaortic fat thickness

Measurement of PFT thickness was done with conventional methods from the adventitia layer of the abdominal aorta and the adventitial layer of the aorta adjacent to the form of the measurement of the linear echogenic line. Periaortic fat tissue cannot be directly distinguished with echocardiographic and ultrasonographic images in deep tissue. Therefore, it should be measured with adventitia. Measurements were taken in the axial plane in the supine position at the L1–2 level (just above the umbilicus), proximal to the iliac bifurcation. Evaluation was repeated three times and the mean value was calculated.

Statistical Analysis

The compatibility of numerical variables to normal distribution was examined using the Shapiro-Wilk test. Descriptive findings were presented as number, percentage mean and standard deviation. Comparisons between groups were made by Chi-Square test for categorical variables, and t test for independent groups if assumptions were met for numerical variables, otherwise by Mann-Whitney U test. Statistical significance level was accepted as $p < 0.05$.

Results

A total of 17 patients, 10 boys and 7 girls (41% and 59%), were enrolled in the study. Mean age of the study group was 8.57 ± 2.62 years (range years). Eleven (64.7%) of the patients in the study group had positive family history for urolithiasis, 10 (58.8%) had multiple stones, 6 (35.3%) had bilateral stones. Mean stone size was 8.6 ± 4.3 mm and mean follow-up period was 16.2 ± 9.3 months. In terms of metabolic abnormality, 7 (41.2%) had hypocitraturia, 4 (23.5%) had hypercalciuria, 2 (11.8%) had hyperoxaluria while no abnormalities were detected in 4 (23.5%). At the time of enrollment, 8 (47.1%) children were on medical treatment (in the form of oral potassium citrate), 4 (23.5%) and 5 (29.4%) have underwent Extracorporeal Shock Wave Lithotripsy and surgical treatment (3 ureterorenoscopic intervention,2 percutaneous nephrolithotomy), respectively. There were 12 boys and 5 girls (71% and 29%) in the control group with mean age of 9.53 ± 1.72 years. There was no significant difference between the two groups in terms of age, gender, blood pressure, BMI, serum lipids, hemoglobin and GFR (Table 1).

There was no statistical difference between the M-mode echocardiography, LVM and LVMI results of study and control groups (Table 2). Pulsed Doppler echocardiographic evaluation revealed that; LV ejection time (261.71 ± 21.09 vs. 279.59 ± 28.51, p = 0.046) was significantly shorter in the study group. Additionally, while LV MPI (0.283 ± 0.27 vs. 0.166 ± 0.07, p = 0.013) was significantly higher in the study group, the tricuspid valve E/A ratio (1.13 ± 0.24 vs. 1.29 ± 0.19, p = 0.026) was statistically lower for the same group (Table 3).

Tissue Doppler echocardiography measurements revealed that; mitral valve lateral annulus e' (11.34 ± 2.08 vs. 16.23 ± 3.16, p < 0.001), a' (7.07 ± 1.11 vs. 8.49 ± 2.14, p = 0.021), tricuspid valve lateral annulus e' (11.67 ± 1.66 vs. 13.56 ± 1.94, p = 0.005), interventricular septum e' (9.26 ± 1.69 vs. 13.46 ± 2.34, p < 0.001) and a' velocities (5.39 ± 0.89 vs. 6.43 ± 1.17, p = 0.007) were significantly decreased in study group than in controls (Table 5). On the other hand, time intervals including IVCT (isovolumic contraction time) measured from tricuspid valve lateral annulus (53.12 ± 8.43 vs. 47.06 ± 6.49, p = 0.025) and interventricular septum (53.53 ± 6.86 vs. 47.41 ± 7.63, p = 0.020), IVRT (isovolumic relaxation time) measured from tricuspid lateral annulus (58.41 ± 8.91 vs. 51.88 ± 8.40, p = 0.035) and interventricular septum (55.47 ± 6.77 vs. 47.41 ± 8.64, p = 0.005) were found to be statistically increased in children with urolithiasis. Additionally, mitral valve lateral annulus contraction time (CT) (184.94 ± 43.09 vs. 259.53 ± 16.46, p < 0.001), tricuspid valve lateral annulus CT (199.53 ± 37.22 vs. 254.82 ± 11.63, p < 0.001) and interventricular septum CT (187.29 ± 54.56 vs. 259.88 ± 16.77, p < 0.001) were significantly lower in the urolithiasis group. Also, e'/a' ratios measured from mitral valve lateral annulus and interventricular septum were statistically lower in patients with urolithiasis (p = 0.018 and 0.005, respectively). E/e' ratios measured from LV was found to be increased in the study group (p < 0.001). Furthermore, Tei indexes of LV, RV and septum were significantly higher in urolithiasis patients than in controls (Table 4).

The cIMT (0.041 ± 0.012 vs. 0.025 ± 0.002), EFT (0.432 ± 0.083 vs. 0.325 ± 0.032) and PFT thickness (0.138 ± 0.029 vs. 0.113 ± 0.008) of the study group were statistically higher than the control group (p < 0.001, p < 0.001 and p = 0.002, respectively) (Table 5).

Discussion

Besides urinary tract obstruction and related renal damage, urolithiasis may also cause the release of inflammatory cytokines due to crystal storage and this has been found to be associated with cardiovascular complications [22; 23]. Clinical and experimental studies have shown that there is a strong relationship between crystal adhesion and crystal formation in renal tubular cells and inflammation and oxidative stress [11; 24]. Taguchi et al. demonstrated genes related to oxidative stress and stated that proinflammatory conditions were highly expressed in calcium oxalate stone formers than normal renal papillary tissue [25]. Same group also demonstrated that M1 macrophages (inflammatory) stimulated renal calcium oxalate crystal deposition and M2 macrophages (anti-inflammatory) limited such crystal formation in a murine model of hyperoxaluria [23].

The persistent elevated levels of inflammatory cytokines result in a chronic condition, defined as subclinical or low-grade inflammation, which have a fundamental role in the development of cardiovascular disease. It can be assumed that systemic inflammation cause both the onset and progression of cardiovascular disease [8]. Cytokines like IL-6 and IL-8 play an important role in the development of atherosclerosis by promoting inflammatory response, progression, angiogenesis and plaque formation. IL-6 levels are a predictor for the development of cardiovascular disease in healthy individuals and thus, it may be a potential biomarker of early-stage atherosclerosis [26; 27].

Clinically, cIMT is used as a reliable marker in the evaluation of atherosclerotic change in the early period. In some studies that evaluate the progression of atherosclerosis, a strong relationship been reported between cIMT and IL-6 [26]. cIMT was reported to show subclinical atherosclerosis in different chronic diseases of childhood [14]. The only study in the literature in which cIMT was evaluated in children with urolithiasis, Kusumi et al. found cIMT was significantly higher in children aged 12–17 years and reported that urine osteopontin and fibronectin-1could predict elevated cIMT [10]. Similarly, in our study, cIMT was significantly higher in children with urolithiasis than in the control group, and this shows the presence of subclinical atherosclerosis in patients with pediatric urolithiasis. On the other hand, mean age of our study group was younger than those included in their study. Thus, it can be suggested that subclinical atherosclerosis begins at an even earlier age in children with urolithiasis.

Body fat distribution is an important cardiovascular risk factor, and fat depositions are associated with all-cause deaths. One component of the abnormal body fat depot, called ectopic fat, is the accumulation of adipose tissue around organs and vessels. Ectopic adipose tissue, unlike subcutaneous adipose tissue, is not an ordinary place for lipid storage [28]. Epicardial and periaortic adipose tissue, like other adipose tissues, has endocrine functions that can produce inflammatory cytokines and hormone secretions. Moreover, they have been recently identified as strong risk factors for cardiovascular disease due to their role in the inflammatory process in atherosclerosis [20; 28]. It was reported that EFT is a reliable parameter for cardiovascular risk in adult chronic kidney disease and EFT thickness can predict coronary artery disease [29]. In obese children, an increase in EFT thickness was found to be associated with coronary artery disease, magnified cIMT and arterial stiffness [30]. Studies also showed that in non-obese children with neurological disabilities, EFT thickness was significantly higher and correlated with clinical and metabolic risk factors [31]. Akyürek et al. evaluated the relationship between PFT thickness and cardiovascular risk in 135 children with type-1 DM and they showed a positive correlation between PFT thickness and cIMT and metabolic risk factors [15]. In our study, EFT and PFT thickness were significantly higher in children with urolithiasis.

It is known that E/e’ ratio shows the strongest correlation with LV/RV diastolic filling pressure and LV/RV compliance [32], whereas E/A and e’/a’ ratio correlates with relaxation type dysfunction [33]. Limited data from the children with chronic kidney diseases revealed that left ventricular E/A and e’/a’ ratios decreases and E/e’ ratio increases along with the worsening of renal functions from mild–moderate to severe renal failure [34]. On the other hand, Çelik et al. reported decreased E/A and increased e’/a’ ratios in non-obese-treated hypertensive patients [35]. These studies showed dysfunction of LV relaxation and diastolic filling

pressures, however, right ventricular functions were not studied and possibly RV dysfunction was underestimated. In this context, our study revealed that E/A ratio measured from RV and e'/a' ratios measured from LV were significantly lower in children with urolithiasis when compared with healthy controls ($p = 0.026$ and $p = 0.018$, respectively). Additionally, E/e' ratio measured from LV was detected to be increased in the patient group. This finding suggests that LV function and diastolic filling pressures are worsened in children with urolithiasis.

On the other hand, MPI or Tei index is a good predictor of ventricular systolic functions in children and adults [19]. MPI measured by PWD, M-mode and TDI methods is a valuable parameter indicating systolic and diastolic functions and also early deterioration in these parameters. The results from the study by Çelik et al. showed that left ventricular MPI was higher in non-obese-treated hypertensive children, but no significance was achieved [35]. However, in our study MPI values of LV was significantly higher in patients ($p = 0.013$) while no statistical significance was shown in right ventricular MPI. Besides, both Tei index values of LV, RV and septum were found to be significantly increased in the study group than in the controls (in all $p < 0.001$). By this way, we demonstrated a significant reduction of systolic and diastolic functions of LV and RV in children with urolithiasis compared to healthy children.

Limitations

Main limitation of our study is the limited number of patients. Also, inflammatory cytokines have not been studied in patients which is unfortunately, beyond the scope of our facility. However, extensive echocardiographic investigation for both the study and the control group were performed in this prospective study.

Conclusions

LV and RV early systolic and diastolic dysfunction, together with subclinical atherosclerosis, were detected in children with urolithiasis in early ages. Cardiovascular complications should be considered in the follow-up and treatment of these patients, and the pediatric urolithiasis patients deserve further studies in terms of cardiovascular risks. Longitudinal studies with long-term follow-up will enlighten the adulthood consequences of these findings.

Abbreviations

ER: Emergency Room

USA: United States of America

cIMT: Carotid Intima Media Thickness

EFT: Epicardial Fat Tissue

PFT: Periaortic Fat Tissue

TDI: Tissue Doppler Imaging

Mm: milimeters

HDL-C: High Density Lipoprotein Cholesterol

LDL-C: Low Density Lipoprotein Cholesterol

GFR: Glomerular Filtration Rate

BMI: Body Mass Index

MHz: Megahertz

VHS: Vertebral Heart Sign

LV: Left Ventricle

IVSs: Interventricular Septum Systolic

LVM: Left Ventricular Mass

LVMI: Left Ventricular Mass Index

E: Early

A: late

RV: Right Ventricle

MPI: Myocardial Performance Index

e': Peak Early Diastolic Myocardial

a': Peak Atrial Systolic

PWD: Pulse-wave Doppler

Declarations

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Conflict of Interest: The authors declare that they have no conflict of interest.

Ethical approval: All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. Approval for this study was obtained from KTO Karatay University Institutional Board (Number: 419011325-050.99).

Consent to Participate: Informed consent was obtained from parents of all participants included in the study.

Consent for Publication: N/A

Availability of Data and Material: Data and material of the study is stored in a database and can be shared upon request.

Code availability: N/A

Author Contribution:Contributor's statement:

Dr. Elmacı conceptualized and designed the study, carried out the initial analyses, drafted the initial manuscript, and reviewed and revised the manuscript.

Dr. Alp designed the data collection instruments, collected data, and reviewed and revised the manuscript.

Dr. Dönmez conceptualized and designed the study, coordinated and supervised data collection, and critically reviewed the manuscript for important intellectual content.

All authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

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Tables

Table 1. Demographic and laboratory data of study population.

	Patients (n=17)	Controls (n=17)	p
Age (years)	8.57±2.62	9.53±1.72	0.214
Gender (Male/Female)	10/7	12/5	0.473
BMI (kg/m^2)	16.09±2.83	16.50±2.01	0.592
BMI z score	0,09±1,43	-0,28±0,81	0.391
SBP (mmHg)	98.82±8.58	98.24±8.09	0.865
DBP (mmHg)	63.37±6.17	64.71±6.29	0.423
Glucose (mg/dL)	93.94±12.94	95.41±7.99	0.693
eGFR (ml/min/1.73 m^2)	91.03±10.82	92.94±9.06	0.586
Uric acid (mg/dL)	3.98±0.78	3.89±0.62	0.702
Total Cholesterol (mg/dL)	160.55±44.82	152.71±24.98	0.539
Triglyceride (mg/dL)	102.17±74.95	81.35±24.47	0.287
LDL-C (mg/dL)	93.03±37.56	83.75±26.96	0.596
HDL-C (mg/dL)	52.61±13.61	47.53±9.72	0.249
Hemoglobin (g/dL)	13.04±0.74	13.19±0.78	0.562
CRP (mg/dL)	2.46±1.31	2.31±1.53	0.436

Data are expressed mean±SD. **BMI:** body mass index, **SBP:** systolic blood pressure, **DBP:** diastolic blood pressure, **eGFR:** estimated glomerular filtration rate, **LDL-C:** low-density lipoprotein cholesterol, **HDL-C:** high-density lipoprotein cholesterol, **CRP:** C-reactive protein.

Table 2. M-mode echocardiographic measurements in patients with urolithiasis and control groups.

	Patients (n=17)	Controls (n=17)	p
	Mean±SD	**Mean±SD**	
IVSd (cm)	0.69±0.18	0.67±0.14	0.838
IVSs (cm)	1.09±0.22	1.10±0.20	0.876
LVPWd (cm)	0.71±0.10	0.64±0.18	0.180
LVPWs (cm)	1.12±0.21	1.17±0.21	0.342
LVEdD (cm)	3.79±0.39	3.82±0.36	0.121
LVEsD (cm)	2.21±0.26	2.28±0.27	0.350
EF (%)	72.98±3.44	72.86±10.54	0.23
FS (%)	41.26±3.19	39.45±3.59	0.130
LVM (gr)	66.18±29.26	70.57±24.44	0.322
LVMI ($g/m^{2.7}$)	32.59±12.14	29.85±4.95	0.433

IVSd: interventricular septum diastolic thickness; **IVSs:** interventricular septum systolic thickness, **LVPWd:** left ventricular posterior wall diastolic thickness, **LVPWs:** left ventricular posterior wall systolic thickness, **LVEdD:** left ventricular end-diastolic dimension, **LVEsD:** left ventricular end-systolic dimension, **EF:** ejection fraction, **FS:** fractional shortening, **LVM:** left ventricular mass, **LVMI:** left ventricular mass index.

Table 3. Pulsed Doppler echocardiographic measurements in patients with urolithiasis and control groups.

	Patients (n=17)	Controls (n=17)	p
	Mean±SD	**Mean±SD**	
Mitral valve blood flow			
Peak E (cm/s)	89.56±16.12	84.84±12.86	0.352
Peak A (cm/s)	60.51±15.95	59.52±10.94	0.834
E/A ratio	1.56± 0.49	1.45± 0.23	0.838
Tricuspid valve blood flow			
Peak E (cm/s)	61.21±10.41	62.29±7.45	0.322
Peak A (cm/s)	55.62±12.22	48.56±6.82	0.140
E/A ratio	1.13±0.24	1.29±0.19	***0.026***
LV ejection time (ms)	261.71±21.09	279.59±28.51	***0.046***
RV ejection time (ms)	263.76±24.89	271.29±19.66	0.341
LV MPI	0.283±0.27	0.166±0.07	***0.013***
RV MPI	0.231±0.24	0.166±0.08	0.658

Early **(E)** and late **(A)** mitral/tricuspid diastolic velocities, **LV:** left ventricle, **RV:** right ventricle, **MPI:** myocardial performance index.

Table 4. Tissue Doppler echocardiographic measurements in patients with urolithiasis and control groups.

	Patients (n=17)	Controls (n=17)	p
	Mean±SD	Mean±SD	
Mitral valve lateral annulus			
e' (cm/s)	11.34±2.08	16.23±3.16	***<0.001***
a' (cm/s)	7.07±1.11	8.49±2.14	***0.021***
s' (cm/s)	11.04±3.48	9.55±3.07	0.205
IVCT (ms)	55.64±8.87	50.35±11.94	0.152
IVRT (ms)	57.00±12.91	50.18±7.80	0.071
CT (ms)	184.94 ±43.09	259.53±16.46	***<0.001***
e'/a' ratio	1.62±0.29	1.99±0.54	***0.018***
E/e' ratio	8.22±2.47	5.38±1.14	***<0.001***
Tricuspid valve lateral annulus			
e' (cm/s)	11.67±1.66	13.56±1.94	***0.005***
a' (cm/s)	9.18±2.19	9.43±1.37	0.690
s' (cm/s)	11.56±2.79	13.09±1.95	0.074
IVCT (ms)	53.12±8.43	47.06±6.49	***0.025***
IVRT (ms)	58.41±8.91	51.88±8.40	***0.035***
CT (ms)	199.53±37.22	254.82±11.63	***<0.001***
e'/a' ratio	1.32±0.26	1.46±0.26	0.136
E/e' ratio	5.14±1.59	4.68±0.91	0.314
Interventricular septum			
e' (cm/s)	9.26±1.69	13.46±2.34	***<0.001***
a' (cm/s)	5.39±0.89	6.43±1.17	***0.007***
s' (cm/s)	8.19±2.44	8.29±1.22	0.866
IVCT (ms)	53.53±6.86	47.41±7.63	***0.020***
IVRT (ms)	55.47±6.77	47.41±8.64	***0.005***
CT (ms)	187.29±54.56	259.88±16.77	***<0.001***
e'/a' ratio	1.74±0.36	2.13±0.39	***0.005***
LV Tei index	0.642±0.195	0.362±0.102	***<0.001***
RV Tei index	0.581±0.144	0.393±0.047	***<0.001***
Septum Tei index	0.639±0.229	0.366±0.049	***<0.001***

e': peak early diastolic myocardial velocities, **a':** peak atrial systolic myocardial velocities, **s':** peak systolic myocardial velocities, **IVCT:** isovolumetric contraction time, **IVRT:** isovolumetric relaxation time, **CT:** contraction time, **LV:** left ventricle, **RV:** right ventricle.

Table 5. cIMT, EFT and PFT thickness measurements in patients with urolithiasis and control groups.

	Patients (n=17)	Controls (n=17)	p
	Mean±SD	Mean±SD	
cIMT (cm)	0.041±0.012	0.025± 0.002	***<0.001***
EFT thickness (cm)	0.432±0.083	0.325± 0.032	***<0.001***
PFT thickness (cm)	0.138±0.029	0.113± 0.008	***0.002***

cIMT: carotid intima-media thickness, **EFT:** epicardial fat tissue, **PFT:** periaortic fat tissue.