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Original Article

Evaluation of Epicardial Adipose Tissue in Pediatric Patients with Chronic Kidney Diseases

Kronik Böbrek Hastalıkları Olan Pediatrik Hastalarda Epikardiyal Yağ Dokusunun Değerlendirilmesi

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ABSTRACT

Objective: Since with chronic kidney disease (CKD) is an inflammatory process, and disorders of uremia, calcium, and phosphorus metabolism are associated with cardiovascular disease (CVD), patients CKD are at high risk for developing CVDs. This study aims to evaluate epicardial adipose tissue (EAT) parameters which play an active role in the development of CVD and atherosclerosis in patients with CKD.

Method: Twenty-seven CKD patients aged 0-18 and their age -matched 15 control patients were compared. Physical examination and laboratory findings of the patient group were recorded. Both groups evaluated EAT with M-mode echocardiographic measurements.

Results: There was no difference between the 2 groups in terms of age, gender, and body mass index. EAT1, and EAT2 values were higher in the patient group, and these two measurements increased correlatedly as the CKD stage increased. Additionally, the correlation of EAT with blood phosphorus level and parathyroid hormone was evaluated.

Conclusion: Cardiovascular morbidity and mortality are high in CKD. Therefore, early diagnosis is important. Evaluations of EAT and follow-ups at certain intervals can give us information in this sense as a non-invasive parameter.

Keywords: Cardiovascular disease, chronic kidney disease, and epicardial adipose tissue

ÖZ

Amaç: Kronik böbrek hastalığı (KBH) hastaları kardiyovasküler hastalıklar (KVH) açısından yüksek risk altındadır. KBH bir enflamatuvar süreç olduğundan üremi, kalsiyum ve fosfor metabolizması bozuklukları da KVH ile ilişkilidir. Bu çalışma, KBH'li hastalarda KVH ve ateroskleroz gelişiminde aktif rol oynayan epikardiyal yağ dokusunu (EYD) değerlendirmeyi amaçlamaktadır.

Yöntem: 0-18 yaş aralığındaki 27 hasta ve 15 kontrol hastası karşılaştırıldı. Hasta grubunun fizik muayene ve laboratuvar bulguları kaydedildi. Her iki grup da EYD'yi M-mod ekokardiyografik ölçümlerle değerlendirdi.

Bulgular: Yaş, cinsiyet ve vücut kitle indeksi açısından 2 grup arasında fark yoktu. Hasta grubunda EYD1 ve EYD2 değerlerinin daha yüksek olduğu ve bu iki ölçümün KBH evresi arttıkça korele olarak arttığı görüldü. Ayrıca EYD'nin kan fosfor seviyesi ve paratiroid hormonu ile korelasyonu değerlendirildi.

Sonuç: KBH'de kardiyovasküler morbidite ve mortalite yüksektir. Bu nedenle erken tanı önemlidir. EYD değerlendirmeleri ve belirli aralıklarla takipler bize bu anlamda invaziv olmayan bir parametre olarak bilgi verebilir.

Anahtar kelimeler: Kardiyovasküler hastalık, kronik böbrek hastalığı, epikardiyal yağ doku

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INTRODUCTION

The prevalence of chronic kidney disease (CKD) is increasing worldwide due to the use of both improved diagnostic methods and easier access to physicians. Fluid and electrolyte disorders, uremia, mineral and bone disorders, anemia, hypertension (HT), dyslipidemia, cardiovascular disease (CVD), infection, inflammation, endocrine abnormalities, growth retardation, and neurodevelopmental disorders are seen in these patients[1]. There are many problems associated with CKD, the most important of which are CVD and related pathologies. British physician Richard Bright was the first to report the relationship between CKD and CVD[2]. The primary pathology in these patients is increased oxidative stress and inflammation. In patients with CKD, CVD mnifests itself in the form of cardiomyopathy, atherosclerosis, peripheral arterial disease, coronary artery disease (CAD), heart failure, ventricular dysfunction, HT, arrhythmias, and sudden cardiac death (Figure 1)[1]. Echocardiography (ECHO) is an essential noninvasive and diagnostic cardiac imaging modality. In addition to being diagnostic, ECHO is the most frequently used method in the follow-up of patients[3]. Patients with CKD should have regular cardiac evaluations, mainly including assessment of left ventricular (LV) function[3]. Epicardial adipose tissue (EAT) is located on the epicardium (Figure 2). EAT secretes antiatherogenic, proatherogenic, and proinflammatory cytokines. Therefore, it is defined as an endocrine and inflammatory organ. Although EAT is cardioprotective, its increased thickness is considered a risk factor for atherosclerosis and CVD[4]. Life expectancy in pediatric patients is long. Therefore, as EAT is both an early and non-invasive indicator of atherosclerosis and CVD, EAT should be monitored at regular intervals to prevent both morbidity and mortality in patients with CKD.

Many studies have proven that increased thickness of EAT is a risk factor for atherosclerosis and CVD in CKD patients. The study was conducted to demonstrate the validity of increase in EAT thickness in pediatric patients, to show that EAT emerges as a more significant risk factor as the CKD stage increases, and to investigate the relationship between EAT and metabolic parameters.

MATERIALS and METHODS

This study was approved by University of Health Sciences Türkiye, İzmir Tepecik Training and Research Hospital, Ethics Committee (approval number: 2021/11-30, dated: 15.11.2021). Informed consent forms were obtained from all participants. Pediatric patients under the age of 18 who were followed up for CKD in our Pediatric Nephrology Clinic of Health Sciences University, İzmir Tepecik Training and Research Hospital, between January 2008 and March 2022, were included in this retrospectively planned study. Children who applied to the pediatric cardiology clinic for control purposes and had not any health problems were included in the study as the control group. Age, sex, body mass index (BMI), BMI percentiles, systolic and diastolic blood pressure (BP), and BP percentiles of patients with CKD and the control group were evaluated. CKD stage, blood parathormone, calcium, phosphorus, and vitamin D levels were recorded in the patient group. All cases were assessed with ECHO. Physical examination and ECHO findings were compared in 2 groups. The correlation of biochemical parameters with EAT was evaluated in the patient group.

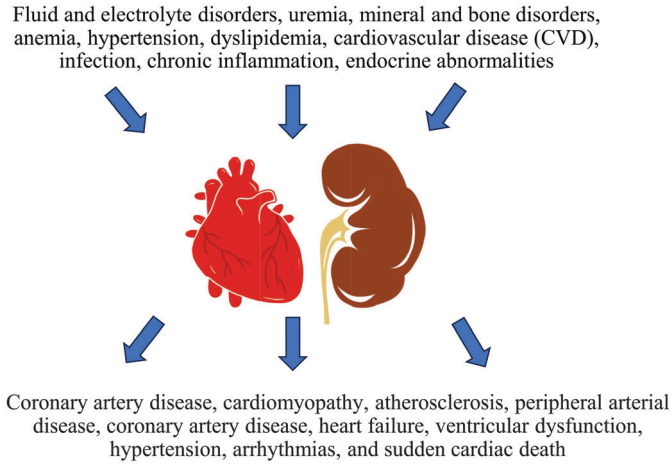

Figure 1. Effects related to chronic kidney disease

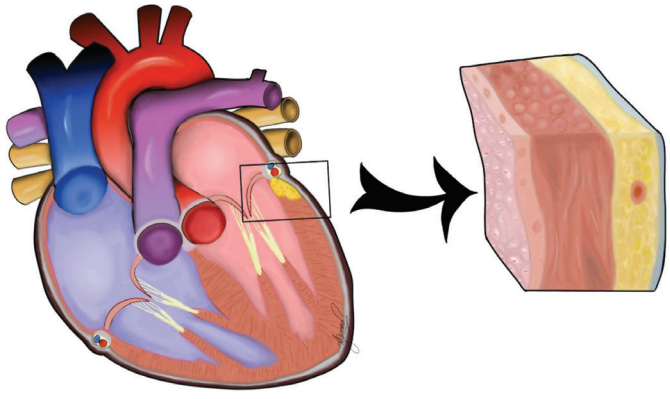

Figure 2. Location of epicardial adipose tissue in the heart

Echocardiographic Assessment and Evaluation of Epicardial Tissue

All patients underwent a complete ECHO examination, including EAT measurement. The same pediatric cardiologist performed the ECHO examinations using a Philips Affiniti 50 US device (Philips Healthcare, Andover, Netherlands) equipped with an S4-2 probe.

Conventional ECHO measurements including interventricular septal thickness (IVSd), LV dimensions, LV posterior wall thickness, and LV mass were made by M-mode ECHO. Ejection fraction (EF) and fractional shortening for etimation of EF were determined using standard methods[5]. In all patients. EAT was measured during ECHO. EAT of the right ventricular free wall at parasternal long- and short-axis was measured ECHO and EAT measurements were evaluated while the patient in the left decubitus position. EAT thickness was measured perpendicular to the free wall of the right ventricle at the end of diastole for three cardiac cycles. The EAT was visualized between the right ventricular free wall in the parasternal long (EAT 1) and short axis (EAT 2) views.

Statistical Analysis

The distribution characteristics of continuous numeric data were analysed by Kolmogrov-Smirnov test, presented as median values in hypertensive-healthy groups, and since critria of normal distribution were not met, they were compared using non-parametric Mann-Whitney U test. Pre- and post-treatment EAT1 and 2 and LVmass measurements were compared with the non-parametric Wilcoxon test. In imaging marker analysis, statistical significance of the receiver operating characteristic curve and area under the curve were evaluated. All statistical analyses were performed with SPSS 26.0 statistical software, $p<0.05$ was accepted as the limit of statistical significance.

RESULTS

The study population consisted of 27 children with CKD and a control group of 15 healthy children of the same age and gender. The average age of the patient and the control groups were 130.1±48.7 months and 142.4±43.2 months, respectively. The distribution of gender was equal in both groups. The average BMI was 19.2 kg/m^2 (13.75-24.4 kg/m^2) in the patient group and 20.8 kg/m^2 (15.94-28.3 kg/m^2) in the control group. IVSd, LVWd, LV mass, EAT1 and EAT2 measurements were statistically significantly increased in the patient group compared to the healthy group (p=0.019, 0.007, 0.000, 0.018, and 0.044, respectively) (Table 1).

The age at diagnosis of children with CKD was 24 (0-173) months, and the follow-up period was 73 (6-208) months. The patients were clasified in CKD stage I (n=10), II (n=1), III (n=8), and V (n=8). In the stage IV-V CKD group, one patient was on hemodialysis, five patients were on peritoneal dialysis, and two patients were preparing for renal replacement therapy. A statistically significant difference was found between CKD stages for LVmass, EAT1, and EAT2 (p=0.037, 0.028, and 0.021, respectively) (Table 2). Phosphorus, calcium, vitamin D, and parathyroid hormone levels according to the stages of CKD are given in Table 2 (p=0.043, 0.048, 0.021, and 0.004, respectively) (Table 2). PTH values of 27 pediatric patients were related to LVmass, EAT1, and EAT2 (r=0.986, 0.962, 0.876, respectively), and blood phosphorus values were associated with LVmass, EAT1, and EAT2 (r=0.989,

Table 1. Comparison of ECO parameters of the patient and control groups

ECHO findings	Patient group (n=27)	Control group (n=15)	p-value (p<0.05)
IVSd (mm), median (Q1-Q3)	0.60 (0.30-1.00)	0.50 (0.30-0.90)	**0.019**
LVIDd (mm), mean ± SD	4.05±0.71	3.91±0.51	0.245
LVIDs (mm), median (Q1-Q3)	2.20 (1.70-2.50)	2.10 (1.60-2.40)	0.437
LVWd (mm), median (Q1-Q3)	0.70 (0.40-1.30)	0.60 (0.4-0.80)	**0.007**
LVEF (%), mean ± SD	71.57±5.83	70.13±5.11	0.714
LVFS (%), mean ± SD	39.86±5.24	38.73±4.32	0.898
LVmass (g/m^2), median (Q1-Q3)	59.00 (40.00-121.00)	34.00 (20.20-45.30)	**0.000**
EAT 1 (mm), median (Q1-Q3)	2.00 (1.50-3.10)	1.90 (1.20-2.90)	**0.018**
EAT 2 (mm), median (Q1-Q3)	2.10 (1.40-3.50)	2.00 (1.00-3.10)	**0.044**

IVSd: Interventricular septum thickness in diastole (mm), LV: Left ventricular, LVIDs: Left ventricular internal dimension in systole, LVIDd: Left ventricular internal dimension in diastole, LVWd: Left ventricular posterior wall thickness in diastole (mm), ECO: Echocardiography, EAT: Epicardial adipose tissue

Table 2. Comparison of blood and cardiac parameters in groups			
	CKD stage 1-2	**CKD stage 3-4-5**	**p-value (p<0.05)**
LVmass (median) (min-max)	46 (40-72)	68 (56-121)	**0.037**
EAT1 (median) (min-max)	1.6 (1.2-1.9)	2.6 (1.6-3)	**0.028**
EAT2 (median) (min-max)	1.5 (1-1.8)	2.4 (2-3.5)	**0.021**
Phosphorus (median) (min-max) (mg/dL)	4.6 (3.8-5.7)	6.2 (5.2-8.6)	**0.043**
Calcium (median) (min-max) (mg/dL)	9.6 (9.1-10.4)	8.9 (8.6-9.5)	**0.048**
Parathyroid hormone (median) (min-max) (mg/dL)	79.4 (63.7-96.1)	362.1 (186-1924)	**0.004**
Vitamin D (median) (min-max) (ng/L)	30.4 (26.7-35.4)	22.6 (7.7-32.1)	**0.021**
LV: Left ventricular, CKD: Chronic kidney disease; EAT: Epicardial adipose tissue			

0.912, 0.876, respectively). LVmass, EAT1, and EAT2 measurements were negatively correlated with blood calcium levels and vitamin D levels (r=-0.752, -0.876, -0.865 for blood calcium; r=-0.732, -0.841, -0.897 for vitamin D, respectively). Cardiac involvement agravates, and symptoms became manifest in 16 (59%) patients with stage III and above. While 11 of 16 patients (69%) with stage III-IV-V had HT, 11 patients with stage I-II had not. The patient group was divided into stages I-II and advanced stages (stages III-IV-V). It was observed that LVmass, EAT1, EAT2, blood phosphorus, and PTH values significantly increased in the advanced stages of CKD. On the contrary, blood calcium and vitamin D levels significantly decreased in the advanced stages of CKD (Table 2).

DISCUSSION

Our retrospective study revealed significant increases in LVmass, EAT1, and EAT2 measurements in the CKD group. Our EAT measurements have not yet been validated in the literature. These parameters are affected by many factors, such as age, gender, BMI, and other concomitant diseases. Therefore, EAT is evaluated by comparing groups in studies. EAT is most frequently affected by HT, obesity, insulin resistance, dyslipidemia, oxidative stress, increased cytokine release, medication use, and non-adherence to treatment[6]. CKD is a state of increased inflammation, and patients have multiple risk factors. CAD is one of the most critical adverse outcomes of CKD. CVD in CKD has been associated with calcium, phosphorus metabolism, and uremia[7]. One of the first studies on this topic compared 80 CKD patients on dialysis with 27 controls. A significant association was found between EAT and coronary artery calcification (CAC)[8]. Another study evaluating 94 adults with stage III-V CKD found a correlation between EAT and CAC[9]. A study evaluating a total of 411 stage IV-V CKD patients, including those on hemodialysis (n=284) and peritoneal dialysis (n=70), determined that EAT was a risk factor for CAC and had effects on the myocardium related to perfusion damage[10]. Studies in the literature report that increased EAT in CKD is associated with left ventricular hypertrophy[11]. A meta-analysis of 17 studies of 1205 CKD patients and 756 healthy controls showed that EAT thickness was increased in the CKD group compared to healthy individuals[12]. In our research, LVmass, EAT1, and EAT2 measurements were significantly higher in the CKD group.

A study conducted on 277 adult patients with stage III-IV-V CKD who were not receiving dialysis treatment found that EAT increased as visceral adipose tissue increased. Increased EAT in CKD was associated with an increased risk of CVD independent of visceral adipose tissue and other factors[13]. A study comparing 59 chronic hemodialysis patients with healthy controls showed a significant increase in EAT and that this increase was associated with age, BMI, and CAC[14]. A study examining 109 hemodialysis patients showed a significant increase in EAT from the date of starting dialysis and that it was a predictor of mortality independent of all risk factors[15].

In a study examining 104 patients diagnosed with CKD, EAT thickness was shown to be negatively correlated with blood calcium levels and positively correlated with blood phosphorus levels[16]. Increased EAT is a hallmark of CAD, as is atherosclerosis[17]. EAT increases if blood phosphorus and parathyroid hormone levels are not well managed, as in CKD. EAT also increases when blood calcium levels are low[18]. In the examinations performed before and after parathyroidectomy in 34 CKD patients diagnosed with hyperparathyroidism, it was observed that EAT thickness decreased[19]. A significant negative correlation was found between vitamin D level and EAT thickness[19]. In our study, when CKD cases were grouped as stage I-II and stage III-IV-V, it was observed that EAT thickness showed a positive correlation with blood phosphorus and parathyroid hormone levels and a negative correlation with calcium and vitamin D levels in advanced CKD stages.

CONCLUSION

This study has again shown that EAT can be used as an imaging marker in the diagnosis and follow-up of patients because it is a non-invasive method. Because of this, it is crucial in childhood and CKD. Many studies are in the literature on both adults and dialysis patients. Our analysis is critical because it evaluates all stages related to childhood CKD. The number of patients is enough for childhood CKD. Future studies with larger samples will better confirm these results and explain the underlying mechanisms.

Ethics

Ethics Committee Approval: This study was approved by University of Health Sciences Türkiye, İzmir Tepecik Training and Research Hospital, Ethics Committee (approval number: 2021/11-30, dated: 15.11.2021).

Informed Consent: Retrospective study.

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Footnotes

Author Contributions

Surgical and Medical Practices: Ö.Ö.Ş., T.D., C.A., D.A., Concept: Ö.Ö.Ş., C.A., G.E., D.A., Design: Ö.Ö.Ş., T.D., C.A., S.A.Ç., D.A., Data Collection or Processing: T.D., B.E., G.E., C.A., S.A.Ç., F.M., B.K.D., Analysis or Interpretation: T.D., B.E., B.K.D., Literature Search: Ö.Ö.Ş., T.D., S.A.Ç., F.M., D.A., Writing: Ö.Ö.Ş., C.A.

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REFERENCES

1. Furth SL, Abraham AG, Jerry-Fluker J, Schwartz GJ, Benfield M, Kaskel F, et al. Metabolic abnormalities, cardiovascular disease risk factors, and GFR decline in children with chronic kidney disease. Clin J Am Soc Nephrol. 2011;6(9):2132-40. doi: 10.2215/CJN.07100810.
2. Jankowski J, Floege J, Fliser D, Böhm M, Marx N. Cardiovascular disease in chronic kidney disease: pathophysiological insights and therapeutic options. Circulation. 2021;143(11):1157-72. doi: 10.1161/CIRCULATIONAHA.120.050686.
3. Shenasa M, Shenasa H. Hypertension, left ventricular hypertrophy, and sudden cardiac death. Int J Cardiol. 2017;237:60-3. doi: 10.1016/j.ijcard.2017.03.002.
4. Ouwens DM, Sell H, Greulich S, Eckel J. The role of epicardial and perivascular adipose tissue in the pathophysiology of cardiovascular disease. J Cell Mol Med. 2010 Sep;14(9):2223-34. doi: 10.1111/j.1582-4934.2010.01141.x.
5. Lopez L, Colan SD, Frommelt PC, Ensing GJ, Kendall K, Younoszai AK, et al. Recommendations for quantification methods during the performance of a pediatric echocardiogram: a report from the Pediatric Measurements Writing Group of the American Society of Echocardiography Pediatric and Congenital Heart Disease Council. J Am Soc Echocardiogr. 2010;23(5):465-95; quiz 576-7. doi: 10.1016/j.echo.2010.03.019.
6. Zoccali C, Mallamaci F. The location of adipose tissue is important: epicardial fat in patients with chronic kidney disease. J Intern Med. 2015;278(1):88-91. doi: 10.1111/joim.12356.
7. D'Marco L, Cortez M, Salazar M, Lima-Martínez M, Bermúdez V. Epicardial adipose tissue: a cardiovascular risk marker to evaluate in chronic kidney disease. Clin Investig Arterioscler. 2020;32(3):129-34. English, Spanish. doi: 10.1016/j.arteri.2019.10.006.
8. Turkmen K, Kayikcioglu H, Ozbek O, Solak Y, Kayrak M, Samur C, et al. The relationship between epicardial adipose tissue and malnutrition, inflammation, atherosclerosis/calcification syndrome in ESRD patients. Clin J Am Soc Nephrol. 2011;6(8):1920-5. doi: 10.2215/CJN.00890111.
9. Kerr JD, Holden RM, Morton AR, Nolan RL, Hopman WM, Pruss CM, et al. Associations of epicardial fat with coronary calcification, insulin resistance, inflammation, and fibroblast growth factor-23 in stage 3-5 chronic kidney disease. BMC Nephrol. 2013;14:26. doi: 10.1186/1471-2369-14-26.
10. Karohl C, D'Marco L, Bellasi A, Raggi P. Hybrid myocardial imaging for risk stratification prior to kidney transplantation: added value of coronary calcium and epicardial adipose tissue. J Nucl Cardiol. 2013;20(6):1013-20. doi: 10.1007/s12350-013-9761-8.
11. Ayan H, Akilli R, Kaya B, Paydas S, Kara E, Cureoglu A. Relationship between SCUBE1 levels and echocardiography and electrocardiography findings and epicardial adipose tissue/carotid intima-media thickness in patients receiving renal replacement therapy. Exp Clin Transplant. 2019;17(Suppl 1):181-187. doi: 10.6002/ect.MESOT2018.P58.
12. Song G, Qiao W, Liu K, Yu X. Epicardial adipose tissue in patients with chronic kidney disease: a meta-analysis study and trial sequential analysis. Int Urol Nephrol. 2020;52(12):2345-55. doi: 10.1007/s11255-020-02575-y.
13. Cordeiro AC, Amparo FC, Oliveira MA, Amodeo C, Smanio P, Pinto IM, et al. Epicardial fat accumulation, cardiometabolic profile and cardiovascular events in patients with stages 3-5 chronic kidney disease. J Intern Med. 2015;278(1):77-87. doi: 10.1111/joim.12344.
14. Barros X, Dirrichs T, Koos R, Reinartz S, Kaesler N, Kramann R, et al. Epicardial adipose tissue in long-term hemodialysis patients: its association with vascular calcification and long-term development. J Nephrol. 2016;29(2):241-50. doi: 10.1007/s40620-015-0221-1.
15. D'Marco LG, Bellasi A, Kim S, Chen Z, Block GA, Raggi P. Epicardial adipose tissue predicts mortality in incident hemodialysis patients: a substudy of the Renagel in New Dialysis trial. Nephrol Dial Transplant. 2013 Oct;28(10):2586-95. doi: 10.1093/ndt/gft264.
16. Cano Megías M, Guisado Vasco P, Bouarich H, Aguilera IL, de Arriba-de la Fuente G, Rodríguez-Puyol D. Epicardial fat tissue, coronary arterial calcification and mortality in patients with advanced chronic kidney disease and hemodialysis. Nefrologia (Engl Ed). 2021;41(2):174-81. English, Spanish. doi: 10.1016/j.nefro.2020.09.005.

17. Djaberi R, Schuijf JD, van Werkhoven JM, Nucifora G, Jukema JW, Bax JJ. Relation of epicardial adipose tissue to coronary atherosclerosis. Am J Cardiol. 2008;102(12):1602-7. doi: 10.1016/j.amjcard.2008.08.010.

18. Park MJ, Jung JI, Oh YS, Youn HJ. Assessment of epicardial fat volume with threshold-based 3-dimensional segmentation in CT: comparison with the 2-dimensional short axis-based method. Korean Circ J. 2010;40(7):328-33. doi: 10.4070/kcj.2010.40.7.328.

19. Kızılgül M, Çalışkan M, Beysel S, Özbek M, Çakal E. Effect of parathyroidectomy on epicardial fat thickness as a cardiovascular risk factor in patients with primary hyperparathyroidism. Turk J Med Sci. 2019;49(4):1165-9. doi: 10.3906/sag-1902-40.