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The Relationship Between Hemorrhagic Renal Cysts and Renal Function in Polycystic Kidney Disease

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Abstract

Objective: Autosomal dominant polycystic kidney disease (ADPKD) is characterized by progressive enlargement of kidneys, development of multiple cysts, and decrease in glomerular filtration rate (GFR). Total kidney volume can predict progressive kidney damage. This study investigated the relationship between hemorrhagic cysts and GFR in patients with ADPKD.

Methods: Patients with ADPKD whose serum creatinine was studied in less than 1 month of computed tomography (CT) scan between 2015 and 2021 in our clinic were included. Radiologically, ADPKD was defined as the presence of 10 or more cysts larger than 5 mm in enlarged kidneys. Race, age, gender, and creatinine data of all patients were obtained from the hospital database. Estimated GFR was calculated according to the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) formula. The kidney volumes and the presence of hemorrhagic cysts were recorded.

Results: Overall, 114 patients [60 (52.6%) male, age 59 (44-69) years] with ADPKD were included. The creatinine, GFR, and total kidney volume were 1.25 (0.82-2.86) mg/dL, 56.5 (17.5-90.75) mL/min/1.73 m^2, 916 (499-1543) mL, respectively. Hemorrhagic cyst was observed in 76 (66.7%) patients. A moderate inverse correlation was observed between total renal volume and GFR (Spearman's rho = −0.34, $P < .001$). Total renal volume ($P = .02$) was higher and GFR ($P = .009$) was lower in the group with hemorrhagic cysts. When corrected for age and total renal volume, the presence of hemorrhagic cysts was independently associated with GFR.

Conclusion: Hemorrhagic cyst detected by CT in patients with ADPKD is associated with reduced GFR regardless of age and kidney volume.

Keywords: Adult polycystic kidney disease, chronic kidney disease, multislice computed tomography

Polikistik Böbrek Hastaliğinda Görüntülemede Hemorajik Renal Kist Varliğinin Böbrek Fonksiyonu ile Ilişkisi

Öz

Amaç: Polikistik böbrek hastalığı (PKBH) her iki böbrekte ilerleyici boyut artışı, çoklu kist gelişimi ve glomeruler filtrasyon hızı (GFH) azalması ile seyreder. Görüntüleme ile saptanan total böbrek hacminin ilerleyici böbrek hasarını öngördürebileceği gösterilmiştir. Bu araştırmada PKBH'li hastalarda birlikte bilgisayarlı tomografi (BT) ile saptanan hemorajik renal kistlerin GFH ile ilişkisi incelendi.

Yöntemler: Kliniğimizde 2015 ve 2021 yılları arasında BT çekiminden1 aydan kısa zaman içerisinde serum kreatinini çalışılmış olan PKBH'li hastalar dahil edilmiştir. Radyolojik olarak PKBH, her böbrekte 5 mm'den büyük boyutlarda olmak kaydıyla 10 veya daha fazla kist varlığı ve buna eşlik eden böbrek boyutlarının artışı şeklinde tanımlandı. Hastane veri tabanından tüm hastalara ait ırk, yaş, cinsiyet, kreatinin verileri alındı. CKD-EPI formülüne göre tahmini GFH hesaplandı. BT'de her iki böbreğin volümleri ve hemorajik kist varlığı kaydedildi.

Bulgular: Araştırmaya PKBH'li 114 hasta [60 (%52,6) erkek, yaş 59 (44-69) yıl] alındı. Kreatinin, GFH ve total böbrek volümü sırasıyla, 1,25 (0,82-2,86) mg/dL, 56.5 (17,5-90,75) mL/dk/1,73 m^2 ve 916 (499-1543) ml idi. Hemorajik kist 76 (%66,7) hastada izlendi Total böbrek volumü ile GFH arasında istatistiksel olarak anlamlı ve orta düzeyde ters korelasyon gözlendi (Spearman's rho = −0,34, $P < ,001$). Hemorajik kistli (n = 76) ve hemorajik kist olmayan (n = 38) gruplar arasında yaş ($P = ,54$) benzerdi. Hemorajik kistli grupta total böbrek volümü ($P = ,02$) daha yüksek, GFH ($P = ,009$) daha düşüktü. Çok değişkenli lineer regresyon analizinde yaş ve total böbrek volümüne göre düzeltildiğinde hemorajik kist varlığı GFH ile bağımsız ilişkili idi.

Sonuç: PKBH'lilerde BT ile saptanan hemorajik kist, böbrek volümü ve yaştan bağımsız olarak azalmış GFH ile ilişkilidir.

Anahtar Kelimeler: Erişkin polikistik böbrek hastalığı, kroni böbrek hastalığı, çok kesitli bilgisayarlı tomografi

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Autosomal dominant polycystic kidney disease (ADPKD) is the most common hereditary renal disorder.[1] Autosomal dominant polycystic kidney disease characteristically begins in adulthood and progresses with the development of multiple cysts in both the kidneys and an increase in kidney size. Loss of kidney function is often inevitable in ADPKD and is followed up clinically by creatinine and estimated glomerular filtration rate (eGFR).[2] It has been shown that the total renal volume detected by imaging can predict progressive kidney damage.[3] Intrarenal complications such as kidney stones, hemorrhagic cysts, and infected cysts can be observed in patients with ADPKD.[4,5] However, the relationship between hemorrhagic cysts on imaging and eGFR is not extensively studied. In this study, the relationship between the presence of hemorrhagic renal cysts detected by computed tomography (CT) and eGFR in patients with ADPKD was investigated.

Methods

Patients with ADPKD whose serum creatinine was studied within 1 month of CT scan date in our Institute between 2015 and 2021 were included. Radiologically, ADPKD diagnosis criteria were defined as the presence of 10 or more cysts in each kidney, with a size larger than 5 mm, and the accompanying increase in kidney size.[6] The research was conducted in accordance with the Declaration of Helsinki. Istanbul Medeniyet University Göztepe Training and Researching Hospital Ethics Committee approval was obtained (Decision number: 2021/0197). Race, age, gender, and creatinine data of all patients were obtained from the hospital database. The estimated glomerular filtration rate was calculated according to the CKD-EPI formula recommended by the latest Kidney Disease: Improving Global Outcomes (KDIGO) guideline by using the creatinine value in the calculation. The CT scans were made with a 128-channel (GE Healthcare Optima CT660, USA) device without using contrast material. Reformatted images were obtained in the axial, oblique, and coronal planes. The slice thickness was set to be 2.5-3 mm and the reconstruction interval was 1.5-2 mm. Volumes of both kidneys and the presence of hemorrhagic cysts were recorded on CT. The volumes of both kidneys were calculated separately and then were summed up to obtain the total kidney volume. The largest anteroposterior- and transverse diameters from the axial plane and the longitudinal length from the coronal view were used for kidney volume measurements (Figure 1). Both kidney volumes were automatically calculated using the online calculator at the https://jscalc.io/calc/EbgTWdRdVXaqRoEk website. The hemorrhagic cyst was defined as a homogeneous, well-defined subcapsular cyst with a size less than 3 cm and attenuation more than 50 HU on non-contrast-enhanced CT (Figure 2).[7]

Statistical analysis

Statistical analysis of the data was performed using SPSS 19 (IBM SPSS Inc., Chicago, Ill, USA) software. The distribution of normality of continuous variables was examined using the Shapiro–Wilk test. Since the data were not distributed normally, the descriptive statistics of continuous variables were given as medians and quartiles. The frequencies of categorical variables were given as percentages. Intergroup frequency comparisons of categorical variables were made using the Pearson chi-square test if the assumptions were met, otherwise Fisher's exact test was used. Comparisons of continuous variables between groups were made using the Mann–Whitney U-test. Since the data were not normally distributed, the Spearman test was used for correlation analysis. Multivariate linear regression analysis was used to determine the CT parameters that would independently predict the estimated eGFR. The significance level was accepted as $P < .05$ for all tests.

Results

Overall, 114 patients [54 (47.4%) female, 60 (52.6%) male] with ADPKD were included in the study. The patients' characteristics are demonstrated in Table 1. The median age was 59 (44-69). The median values of urea was 45 (30-76) mg/dL, creatinine was 1.25 (0.82-2.86) mg/dL, eGFR was 56.5 (17.5-90.75) mL/min/1.73 m^2, right kidney volume was 448 (243.5-779) mL, left kidney volume was 448.5 (226.5-847.25) mL,

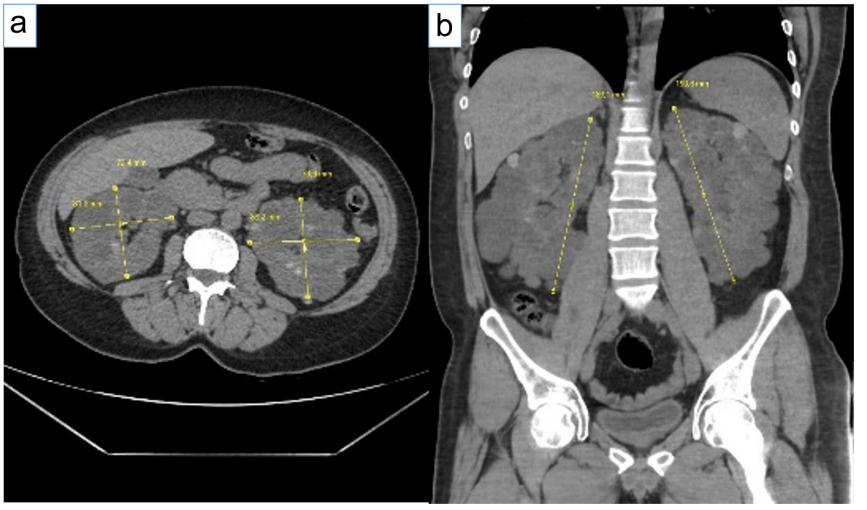

Figure 1. a, b. (a) Demonstration of measurement of transverse- and anteroposterior diameters of polycystic kidney in axial section. (b) Demonstration of measurement of the longitudinal length of polycystic kidney in coronal.

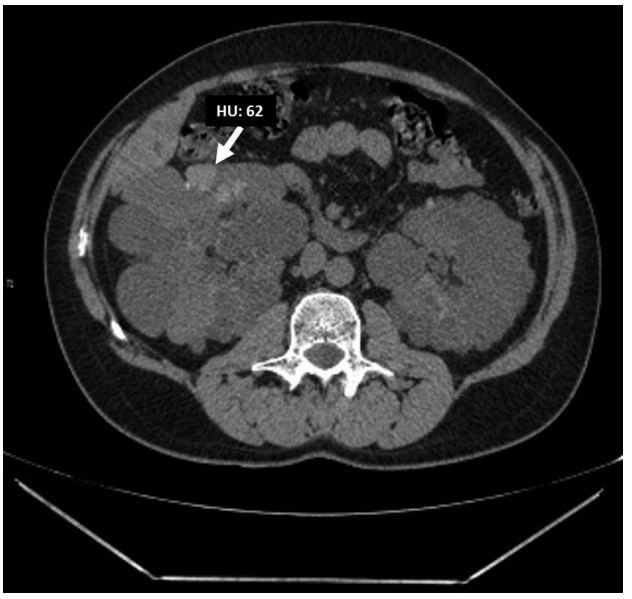

Figure 2. High-density, well-circumscribed hemorrhagic cyst (arrow) is seen on non-contrast computed tomography in an adult patient with polycystic kidney. HU, Hounsfield unit.

and total kidney volume was 916 (499-1543) mL. The intrarenal hemorrhagic cyst was observed in 76 (66.7%) patients. A statistically significant and moderate inverse correlation was observed between total renal volume and eGFR (Spearman's rho = −0.336, $P < .001$). The eGFR did not differ between patients with [53.5 (16-90)] or without [61 (35-92)] hypertension ($P = .303$). The eGFR was similar between males [57.5 (29.5-83.5)] and females [57 (21-97)], $P = .773$. Patients were divided into 2 groups as per the presence of hemorrhagic cyst. Group 1 included (n = 76) cases with hemorrhagic cyst and Group 2 included those without (n = 38). Age [58.5 (46-67) vs 60 (40-78), respectively, $P = .542$] and urea [46 (32-77) vs 36 (28-64), respectively, $P = .218$] were similar between the groups. Right [494 (281-881) vs 329 (221-594), respectively, $P = .046$] and left kidney [561.5 (298-894) vs 317 (213-518), respectively, $P = .008$] volumes and total renal volume [1125 (573-1789) vs 710 (432-1082), respectively, $P = .021$] were significantly higher in Group 1 compared to Group 2. The eGFR [43.5 (16-83) vs 68 (47-103), respectively, $P = .009$] was significantly lower in Group 1. The presence of hemorrhagic cysts was independently associated with eGFR even after adjustment for age, sex, hypertension, and total renal volume in multivariate linear regression analysis (Table 2).

Discussion

This study revealed that the presence of hemorrhagic cyst is associated with decreased eGFR regardless of the total kidney volume and age. Hemorrhagic cysts occur commonly in ADPKD.[8] Hemorrhagic cysts are commonly recognized in asymptomatic patients with ADPKD during imaging.[9] They are most commonly considered as innocent bystanders by clinicians or radiologists in clinical practice, hence their clinical significance is not extensively studied. The proposed underlying mechanism for the formation of hemorrhagic cysts is either the spontaneous bleeding within cysts due to the natural history of ADPKD or minor trauma.[10] A very recent study showed that the number of hemorrhagic cysts is more significant than total kidney volume in predicting future eGFR reduction.[11] This observation is in line with the results of the current study. One may argue that hemorrhagic cysts are observed in larger kidneys, and a poor renal outcome cannot be simply attributed to its presence in patients with ADPKD. However, our results are in favor of independent association of hemorrhagic cysts with decreased renal function, despite controlling for age and kidney volume. We suggest that hemorrhagic cysts are a complication of progressive kidney injury, and may be used as a complementary, rather than an alternative, imaging finding in addition to total kidney volume for predicting future adverse renal outcomes.

The major limitation of our study is its retrospective nature. Moreover, we recognize that hyperattenuated hemorrhagic cysts and malignancy can be differentiated by contrast

Table 1. Patient Characteristics

Clinical Characteristic*	All Patients with ADPKD (N = 114)	Hemorrhagic Cyst Group (N = 76)	No-Hemorrhagic Cyst Group (N = 38)	*P*
Age (years)	59 (44-69)	58 (45.5-67)	60 (40-78)	.542
Males (n, %)	60 (52.6)	37 (48.7)	23 (60.5)	.352
Urea (mg/dL)	45 (30-76)	47 (33-79)	36 (28-64)	.218
Creatinine (mg/dL)	1.25 (0.82-2.86)	1.57 (0.93-3.2)	1 (0.74-1.4)	**.004**
eGFR (mL/min/1.73 m^2)	56.5 (17.5-90.75)	43.5 (16-83)	68 (45-103.5)	**.009**
Glucose (mg/dL)	90 (78-119)	91 (80-122)	89 (78-116)	.353
Total cholesterol (mg/dL)	185 (151-209)	181 (145-206)	187 (149-211)	.652
Hypertension (n, %)	52 (45.6)	37 (48.7)	15 (39.5)	.352

*The values are medians with quartiles.
eGFR, estimated glomerular filtration rate; ADPKD, polycystic kidney disease.

Table 2. Linear Regression Model of Parameters Associated with Estimated Glomerular Filtration Rate

Model (Dependent Variable: eGFR)	Unstandardized Coefficients		Standardized Coefficients		
	B	Standard Error	Beta	*t*	*P*
(Constant)	139.954	12.908		10.842	.000
Sex	8.231	5.682	.109	1.449	.150
Age	−1.215	.172	−.535	−7.074	.000
Hemorrhagic cyst	−16.300	5.974	−.205	−2.728	.007
Total renal volume	−.006	.002	−.198	−2.611	.010
Hypertension	−15.036	5.665	−.199	−2.654	.009

eGFR, estimated glomerular filtration rate.

enhancement properties. However, since our study group was comprised of patients already having kidney disease that render them prone to the risk of contrast-induced kidney injury, we used only non-enhanced CT imaging.

In our study, the presence of hemorrhagic cysts was found to be associated with decreased eGFR, regardless of kidney volume and age, with CT in patients with ADPKD. Hemorrhagic renal cysts in CT can be used as a predictor of kidney damage in patients with ADPKD, in addition to increasing age and kidney volume. This data should be supported by prospective studies.

Ethics Committee Approval: Ethics committee approval was received for this study from the ethics committee of İstanbul Medeniyet University, Göztepe Training and Research Hospital (Date: January 23, 2018, Decision Number: 2021/0197).

Informed Consent: Informed consent could not be taken due to the retrospective design of the study.

Peer Review: Externally peer-reviewed.

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Hasta Onamı: Araştırma tasarımı retrospektif olduğundan hasta onamı alınamadı.

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