Original Article

Relationship between Cyst of Visceral Organ and Autosomal Dominant Polycystic Kidney Disease

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Objective: To retrospectively assess whether the size of renal cyst in autosomal dominant polycystic kidney disease (ADPKD) patient correlated with the cystic lesion in visceral organs and enlargement of visceral organ.

Materials and Methods: The Institutional Review Board approval was obtained for the present study. The authors measured the size of renal cysts from 85 abdominal ultrasound images, and CT studies randomly sampled from Thai population. The dataset had been verified by two certified radiologists within the last ten years. Additionally, the authors also collected the size of the largest liver cyst, the amount of liver cyst, splenomegaly, the amount of pancreas and splenic cyst, adrenal lesion, hepatomegaly, splenomegaly, the size of liver, paraaortic lymphadenopathy, and fatty change of liver. The present study used ANOVA, and t-test to analyze the results with p-value of less than 0.05 to infer a statistically significant difference.

Results: There was correlation between the size of renal cysts and the size of liver cysts, as well as the amount of liver cysts within the authors' dataset of 85 samples. Correlation coefficient (r) of 0.3 was chosen as weak positive correlation. Moreover, the size of renal cysts also correlated with hepatomegaly. Nonetheless, gender, age group, pancreatic cyst, adrenal lesion, splenic cyst, splenomegaly, fatty liver, and paraaortic lymphadenopathy showed no significant correlation.

Conclusion: There is a strong correlation between the size of the largest liver cyst, amount of liver cysts, and hepatomegaly compared with the size of the largest renal cyst. Other factors showed no significant correlation. Nonetheless, when the size of liver cysts and the amount of liver cysts increase, the size of liver span always increase.

Keywords: Liver cyst, ADPKD, Renal cyst, Retrospective studies

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Adult polycystic kidney disease is a common disease (1/1,000) responsible for about 10% of chronic renal failure[1]. Patients with autosomal-dominant polycystic kidney disease present most commonly in the third or fourth decades. They often suffer from flank pain caused by a variety of etiologies. Although their kidneys still maintain the basic reniform shape, they are markedly enlarged. Other abnormalities that could be associated with autosomal-dominant polycystic kidney disease are hepatic cysts, mitral valve prolapse, and colonic diverticulosis. Sonography and computed tomography (CT) have replaced nephrotomography as standard methods for examining patients with autosomal dominant polycystic kidney disease (ADPKD). Imaging study is also useful in identifying hepatic cysts, which are presented in 54% to 74% of ADPKD cases[2].

In 1997, Ha et al reviewed 30 patients of autosomal-dominant polycystic kidney disease from Korean population and found pancreatic cysts in 16.7%, thyroid cysts in 6.7%, and splenic cysts in 6.7%[3]. Although several studies have reported the massive effect of hepatomegaly on ADPKD patients, none has studied the correlation between hepatomegaly and ADPKD. One of the complications of ADPKD is the infected renal cysts. No detectable abnormality was found in CT scans of many patients exhibiting clinical of infected renal cysts. In 2015, Paschali et al found a correlation between the fluorodeoxyglucose (FDG) uptake in paraaortic nodes, which were more

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sensitive than CT abnormality of renal cyst, and the infected renal cysts[4]. The paraaortic node abnormality in CT or ultrasound showed more sensitivity than in cystic anomaly to detect infection. There is a correlation between the increase in cholesterol level, and the decrease of glomerular infiltration rate in ADPKD, which could correlate with the level of fat deposited in the liver parenchyma[5].

Kim et al has discovered a significant correlation between ADPKD in pancreatic cyst and ADPKD[6]. Moreover, there is some correlation between liver cyst progression and patient's gender (especially in female) in ADPKD[7]. However, there is no evidence of correlation between patient's age, and ADPKD progression, occurring from chromosome ADPKD-1 abnormality[8].

Materials and Methods

With an approval from the Bhumibol Institutional Review Board, the authors searched through historical records of patients that underwent CT abdomen or ultrasound between August 2008 and August 2018 in a computer tomography and ultrasound imaging database for the patients diagnosed with ADPKD. One hundred three patients were found but due to the lack of data in PACS database, 18 patients were excluded from the study. As a result, the present study randomized a control trial that comprised of 85 patients, 40 males and 45 females, in random age ranges.

CT and ultrasound measurement

All examinations were performed by either a CT abdomen with 1.25 mm slice thickness with contrast administration, or an ultrasonography of abdomen that measured in axial scan to find out which slice has the maximal diameter of the largest renal and liver cysts, pancreatic, splenic, adrenal, paraaortic node, and liver abnormality.

Age and gender were recorded to determine relationship between these factors and progression of size of parts of renal cyst.

Using Cohen's (1992) Interpreting for effect size value[9], the authors chose the medium effect size r=0.3 (weak positive correlation), then calculated sample size with type I acceptable error (α)=0.05 and type II acceptable error (β)=0.2.

H0: Rho = r_0 = 0 (correlation coefficient)

H1: Rho = r_1 = 0.3 (expected correlation coefficient – medium size)

n = sample size

$Z_{(r_0)} = 1/2 \ln[(1+r_0) / (1-r_0)]$

$Z_{(r_1)} = 1/2 \ln[(1+r_1) / (1-r_1)]$

$n = [(Z\alpha+Z\beta) / (Z_{(r_0)} - Z_{(r_1)})]^2 + 3$

After using the aforementioned value, the resulting sample size (n) was 85.

Statistical analysis

The mean, standard deviation and median were evaluated for the distribution of the quantitative value. Non-parametric one sample Kolmogorov-Smirnov test was used for normality testing with a significant level of 0.05, meaning that the authors reject the hypothesis of normality when the p-value is less than or equal to 0.05. Correlation coefficient was used to evaluate correlation between each parameter with the threshold of higher than 0.25 of being significant. ANOVA and t-test were used to evaluate relationship between factors and ultrasound or CT measurement value with 95% confidence interval. The analysis determined the statistically significant variables of p-value of less than 0.05 to model the probability of relation of increasing age, visceral organ cysts, visceral organ abnormality, and gender with increase of renal cyst size.

Results

The non-parametric one sample Kolmogorov-Smirnov test that showed asymmetrical distribution of the size of the largest renal cyst (2-tailed) was approximately 0.060 while the amount of liver cysts, age and largest size of liver cysts showed normality.

When focusing on the correlation of coefficient, the authors observed some correlations between the size of the largest renal cysts and the size of liver cyst or the amount of liver cyst as shown in Table 1. However, there was no significant correlation between age, and the mentioned factors on the study date. Spearman technique was used due to non-normality distribution of data.

The distribution of correlation between amount of liver cysts and the largest size of renal cysts showed minimal trend of correlation in Figure 1. Further analysis in Table 2 showed significant correlation between size of the largest renal cyst and amount of liver cyst with p=0.035 (<0.05).

Comparison between hepatomegaly and the size of the largest renal cysts, divided into two groups of diameter size of less than 8.5 centimeters and more than 8.51 cm, showed statistical significance via chi-square tests with significant value of less than 0.001 as showed in Table 3.

Dividing size of the largest liver cysts into two groups with 1 cm diameter threshold demonstrated a statistical correlation with the size of the largest renal

Table 1. Correlation coefficient between size of the largest renal cysts and others

Correlations			Size of the largest renal cyst	Amount of liver cysts	Size of the largest liver cyst	Age on study date
Spearman's rho	Size of the largest renal cyst (cm)	Correlation coefficient		0.229*	0.274*	0.039
		Sig. (2-tailed)		0.035	0.011	0.720
		n		85	85	85
	Amount of liver cysts	Correlation coefficient	0.229*		0.825**	0.136
		Sig. (2-tailed)	0.035		<0.001	0.215
		n	85		85	85
	Size of the largest liver cyst (cm)	Correlation coefficient	0.274*	0.825**		0.156
		Sig. (2-tailed)	0.011	<0.001		0.154
		n	85	85		85
	Age on study date	Correlation coefficient	0.039	0.136	0.156	
		Sig. (2-tailed)	0.720	0.215	0.154	
		n	85	85	85	

* Correlation is significant at the 0.05 level (2-tailed), ** Correlation is significant at the 0.01 level (2-tailed)

Table 2. Relationship between amount of liver cysts and size of the largest renal cysts

Correlations			Size of the largest renal cyst	Amount of liver cysts
Spearman's rho	Size of the largest renal cyst (cm)	Correlation coefficient		0.229*
		Sig. (2-tailed)		0.035
		n		85
	Amount of liver cysts	Correlation coefficient	0.229*	
		Sig. (2-tailed)	0.035	
		N	85	

* Correlation is significant at the 0.05 level (2-tailed)

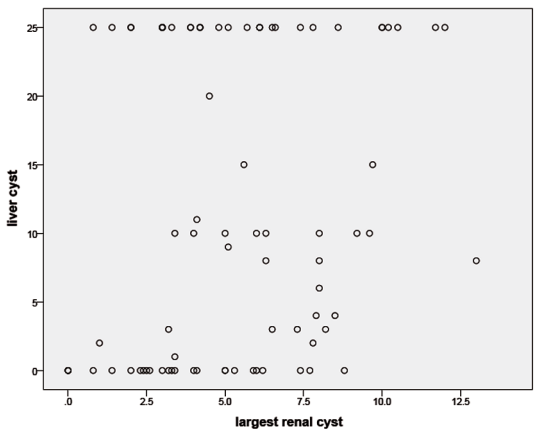

Figure 1. Relationship between amount of liver cysts and size of the largest renal cysts.

cyst (p=0.008 in each) as shown in Table 4.

Splenomegaly, gender, paraaortic nodes enlargement, splenic cyst, adrenal lesion, pancreatic cyst, and fatty liver did not showed significant correlation with the largest size of renal cysts.

Discussion

At first, the authors expected all visceral cysts to correlate with the progression of the size of renal cysts and age because autosomal dominant polycystic kidney disease has an adult onset. Although, the amount and the size of liver cysts have demonstrated significant correlation as expected, the result showed no relationship with age.

As previously known, liver cysts are more common in females rather than male[10], and together with the fact that the progression of liver and kidney

Table 3. Relationship between hepatomegaly and size of the largest renal cysts

Size of the largest renal cyst and liver enlargement	Non-hepatomegaly	Hepatomegaly	p-value
Group 1: size of the largest renal cyst (0 to 8.5 cm)	86.3%	13.7%	<0.001
Group 2: size of the largest renal cyst (>8.5 cm)	33.3%	66.7%	

Table 4. Correlation between size of the largest liver cysts and size of the largest renal cysts

	Group 1 Mean±SD	Group 2 Mean±SD	Mean difference	p-value (2-tailed)
Size of the largest renal cyst	4.16±2.88	5.92±2.88	–1.7517	0.008

Group 1: Liver cyst <1 cm in size, Group 2: Liver cyst ≥1 cm of the largest liver cyst

Table 5. Distribution of size of the largest renal cyst (cm)

Valid	Frequency	Percent	Valid percent	Cumulative percent	Valid	Frequency	Percent	Valid percent	Cumulative percent
0.0	4	4.7	4.7	4.7	6.0	2	2.4	2.4	61.2
0.8	2	2.4	2.4	7.1	6.1	3	3.5	3.5	64.7
1.0	1	1.2	1.2	8.2	6.2	1	1.2	1.2	65.9
1.4	2	2.4	2.4	10.6	6.3	2	2.4	2.4	68.2
2.0	3	3.5	3.5	14.1	6.5	2	2.4	2.4	70.6
2.3	1	1.2	1.2	15.3	6.6	1	1.2	1.2	71.8
2.4	1	1.2	1.2	16.5	7.3	1	1.2	1.2	72.9
2.5	1	1.2	1.2	17.6	7.4	2	2.4	2.4	75.3
2.6	1	1.2	1.2	18.8	7.7	1	1.2	1.2	76.5
3.0	7	8.2	8.2	27.1	7.8	2	2.4	2.4	78.8
3.2	2	2.4	2.4	29.4	7.9	1	1.2	1.2	80.0
3.3	2	2.4	2.4	31.8	8.0	3	3.5	3.5	83.5
3.4	3	3.5	3.5	35.3	8.2	1	1.2	1.2	84.7
3.9	2	2.4	2.4	37.6	8.5	1	1.2	1.2	85.9
4.0	2	2.4	2.4	40.4	8.6	1	1.2	1.2	87.1
4.1	2	2.4	2.4	42.4	8.8	1	1.2	1.2	88.2
4.2	3	3.5	3.5	45.9	9.2	1	1.2	1.2	89.4
4.5	1	1.2	1.2	47.1	9.6	1	1.2	1.2	90.6
4.8	1	1.2	1.2	48.2	9.7	1	1.2	1.2	91.8
5.0	3	3.5	3.5	51.8	10.0	2	2.4	2.4	94.1
5.1	2	2.4	2.4	54.1	10.2	1	1.2	1.2	95.3
5.3	1	1.2	1.2	55.3	10.5	1	1.2	1.2	96.5
5.6	1	1.2	1.2	56.5	11.7	1	1.2	1.2	97.6
5.7	1	1.2	1.2	57.6	12.0	1	1.2	1.2	98.8
5.9	1	1.2	1.2	58.8	13.0	1	1.2	1.2	100.0
					Total	85	100	100	

cysts is often similar in ADPKD, the authors' hypothesis was that kidneys cysts would demonstrate more progression in female than in male as progression of liver cysts. The authors separated female and male in equal number of sample size but the present study showed no significant increase size of kidney cysts

in females as compared to males as well as an equal amount of cases with the largest kidney cyst in each size as shown in Table 5.

The authors also expected lymphadenopathy to spread the infection, which is a common complication of multiple renal cysts. All of the paired organs including kidney, upper collecting systems, adrenal glands, and gonad are all first drain in the paraaortic region[11]. Recurrence of infection could affect the size of the paraaortic lymph nodes. Nonetheless, the present research showed no significant correlation between paraaortic lymphadenopathy and progression of polycystic kidneys disease. However, probability of incorrect result could be affected by the small number of cases with paraaortic lymphadenopathy.

In conclusion, the present study support the hypothesis about the progression of liver cyst along with progression of renal cysts in ADPKD patient, while cysts in other visceral organ showed no correlation. However, the small number of patients diagnosed with visceral organ cysts might cause an error.

Limitation

A limitation of the present study is the inappropriate separation of sample size in group of each parameter. The authors focused on gender and had many cases with hepatic cysts but few cases of other visceral cysts or paraaortic lymphadenopathy included in the present study, which might cause errors of the study.

What is already known on this topic?

There is strong correlation between liver cysts and ADPKD patient while pancreatic cysts and splenic cysts may demonstrate weak correlation with ADPKD patient.

What this study adds?

There is new correlation between progression of liver cysts and progression of renal cysts in ADPKD patient. Moreover, there is correlation between renal cysts progression and hepatomegaly.

Conflicts of interest

The authors declare no conflict of interest.

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