



# Predictors of the Frequency of Ethanol Injections for Renal Cyst Ablation: A Preliminary Study

신장 낭종 경화술에서 에탄올 주입의 횟수에 영향을 미치는 효과적인 예측인자에 대한 고찰: 초기 보고

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**Purpose:** To assess the factors facilitating the prediction of the frequency of ethanol injections in successful renal cyst ablation.

**Materials and Methods:** We retrospectively reviewed the computed tomography and ultrasonography scans of 37 renal cysts. Two radiologists evaluated the characteristics of the presenting renal cysts, including size, calcification, septation, and lobulated configuration. Patients were divided into an "above-four" group and "below-three" group, according to the number of ethanol injections.

**Results:** Among the 37 renal cysts, six belonged to the "above-four" group and 31 to the "below-three" group. The mean volume of "above-four" group was 409.48 cc and that of the other group was 301.64 cc. Seven renal cysts included three belonging to the "above-four" group, which showed calcification. Twelve renal cysts presented a multilocular appearance with thin septa, and included a cyst classified under the "above-four" group. Three renal cysts had lobulated configuration, with one of them belonging to the "above-four" group.

**Conclusion:** No significant correlation was found among the different factors in the prediction of the frequency of renal cyst ablation. However, calcification was the most useful parameter for prediction of the number of renal cyst ablations needed.

## Index terms

Kidney Diseases

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## INTRODUCTION

Recently, percutaneous ablation has become a commonly used method in the treatment of renal cysts, and our preferred method for this procedure is multiple session sclerotherapy using ethanol. In this case, in order to decide upon a treatment plan, it is very important for both the patient and the physician to know whether the average length of stay in hospital or the number of ethanol injections needed can be predicted, but there has not yet been any research on criteria for making these predictions prior to treatment. Thus, the present study aimed to

examine findings from pre-treatment imaging that could predict the number of ethanol injections.

## MATERIALS AND METHODS

### Patient Population

This retrospective study was approved by our Institutional Review Board, and the need for written informed consent was waived (CBNUH 2016-05-006). The study protocol conforms to the ethical guidelines of the 1975 declaration of Helsinki as reflected in a prior approval by the Institutional Human Re-

search Committee.

This study initially included a total of 39 patients (16 males and 23 females) with 40 renal cysts, who underwent percutaneous renal cyst ablation at our hospital between December 2007 and May 2016. The mean age of the patients was 62 years (range: 29–81 years).

The included patients were diagnosed with renal cysts either at our hospital or another hospital using abdominal computed tomography (CT) or abdominal ultrasonography (USG). Three patients without pre-procedure CT or USG images were ultimately excluded from the study, and the remaining 36 patients (37 renal cysts) were included in the analysis. The mean time between imaging and treatment was 24 days (range: 1–130 days).

Twenty-two cysts were asymptomatic, or were discovered incidentally during examinations for other diseases, while the presence of fifteen cysts were accompanied by symptoms of flank pain, flank discomfort, abdominal pain, or hematuria.

For patients with CT images, we only included those patients with benign cysts corresponding to Bosniak classification I or II. For the two patients without CT images, prior to including them in the study, we confirmed that there was no solid portion or thick wall of 1 mm or greater in size on USG examination. Renal cyst cytology was performed on the fluid obtained during renal cyst ablation, and malignant cells were not observed in any of the patients. The majority of patients underwent treatment due to symptoms such as abdominal or flank pain. Asymptomatic patients were treated when the cyst measured at

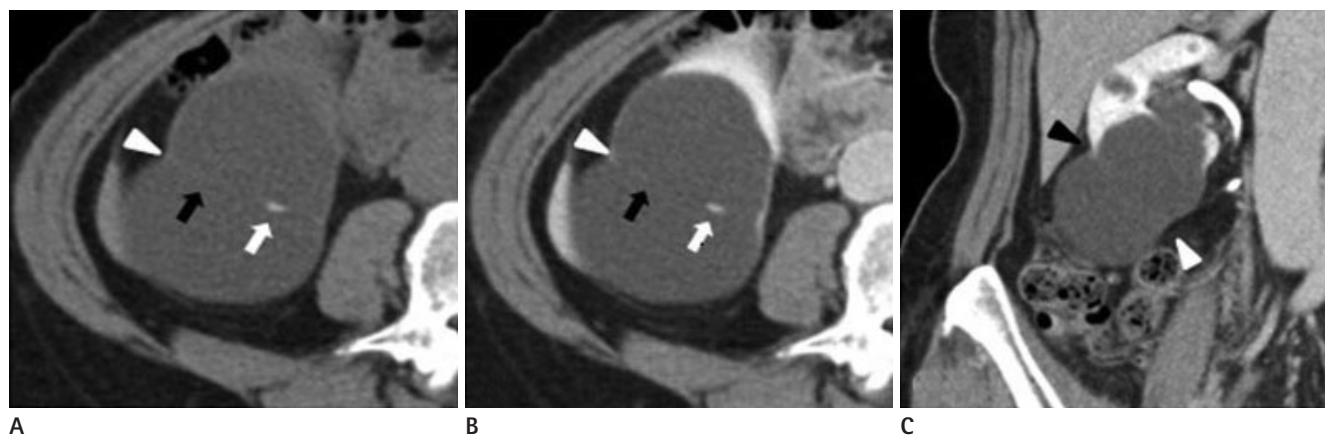
least 5 cm in diameter, and/or when the patients themselves wanted treatment.

### Imaging Analysis

Two genitourinary radiologists confirmed the radiological findings retrospectively, with a conclusion reached by consensus when there were conflicting opinions. CT findings were considered when CT images were available, while USG findings were used in the analysis of the two patients who did not have CT images. A 64-channel multiple detector CT system (Brilliance 64; Philips Medical Systems, Best, Netherlands) was used for CT imaging with the following parameters: detector configuration,  $64 \times 0.625$  mm; section thickness, 3.0 mm; reconstruction interval, 2 mm; table speed, 46.8 mm per rotation; effective amperage setting, 150 mA; rotation time, 0.75 s; tube voltage, 120 kVp; and matrix,  $512 \times 512$ .

A workstation (Marosis M-view; Infinitt, Seoul, Korea) and picture archiving communication system were used to examine the radiological findings.

Radiological findings were analyzed and the presence or absence of internal septa, calcification, and lobulated contours was noted (Figs. 1–3). The volume of each renal cyst was calculated using the ellipsoid formula ( $\text{width} \times \text{height} \times \text{length} \times 0.523$ ) following measurement of the length in three axes based on the available images.

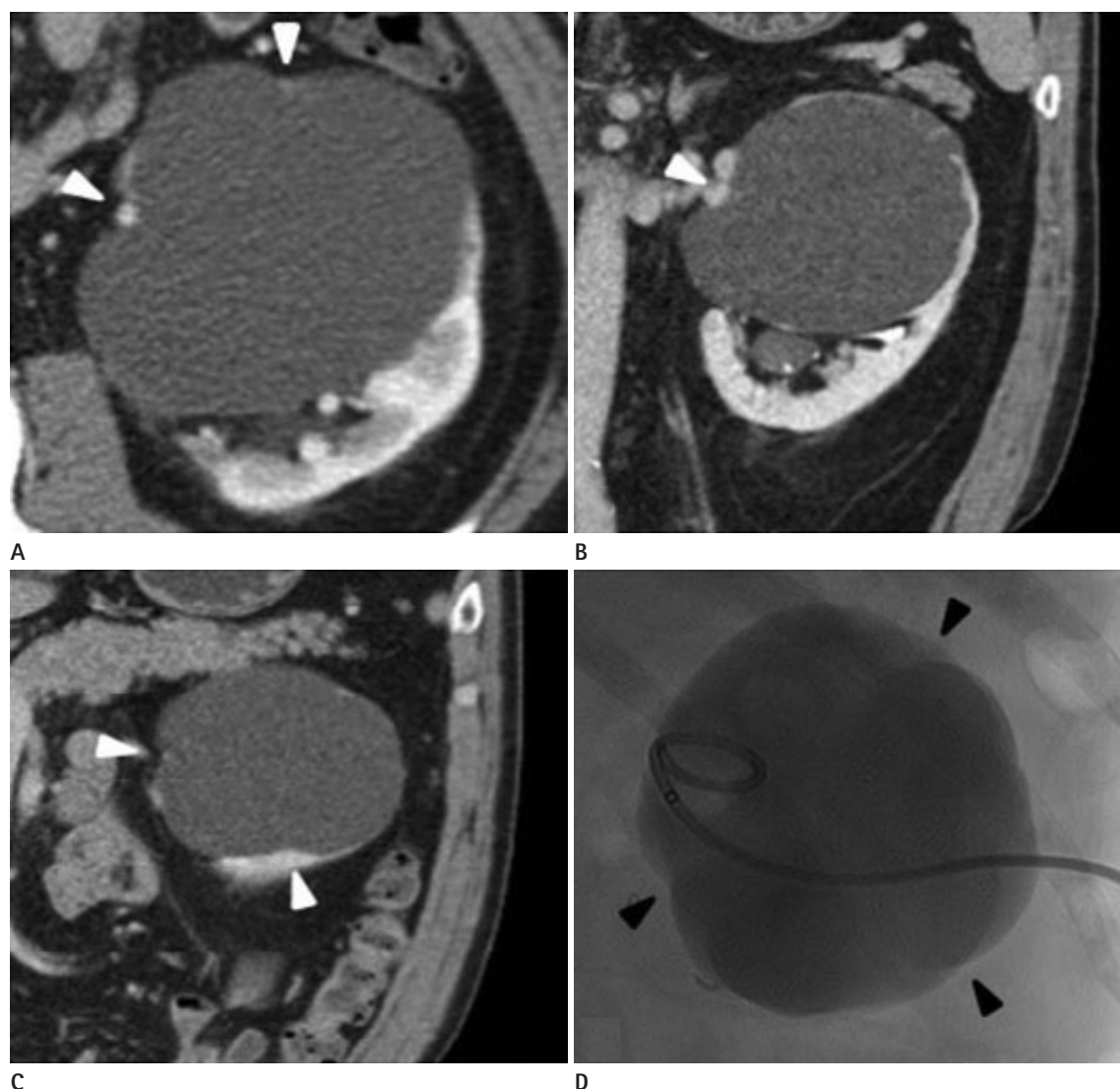


**Fig. 1.** A 55-year-old woman with a Bosniak classification II lesion in the right kidney and she was performed four times ethanol injections. **A, B.** The renal cyst in the right kidney shows calcification (white arrows) and septa (black arrows) in non-contrast-enhanced (**A**) and contrast-enhanced (**B**) axial computed tomography scans. In addition, it has a lobulated margin (white arrowheads) with at least one lobule. **C.** Like the axial axis view, the coronal axis view shows a lobulated margin (arrowheads) with at least one lobule; since the lobulated margin is visible in two planes, this cyst was classified as a lobulated renal cyst with calcification and thin septa.

## Procedure

All patients were hospitalized for the procedure. After marking the position of the cyst with the patient in the prone position under USG guidance, 2% lidocaine was used to induce local anesthesia at the puncture site. A 21-gauge puncture needle was used to puncture the cyst, and then a pigtail catheter (8.5Fr; Cook Medical, Bloomington, IN, USA) was placed inside the cyst. In all patients, a contrast agent was injected to check that there was no communication with the pelvicalyceal collecting system, extravasation, or leakage of the contrast agent into the retroperitoneum. At this point, the fluid in the cyst was aspirat-

ed as much as possible and, after noting the volume of the aspirated fluid, it was subjected to cytological and biochemical examinations. Following aspiration, sclerotherapy was performed using 99% ethanol; the amount of ethanol injected was one-third the total volume of the aspirated fluid, but no more than 100 cc. Following the injection of the ethanol into the renal cyst, to achieve an even application, the patient was placed in the supine, prone, and both decubitus positions for five minutes each, and then the ethanol was removed. The drainage volume after 24 hours was inspected via the catheter, and after using USG to check for any remaining fluid in the cyst, aspiration was

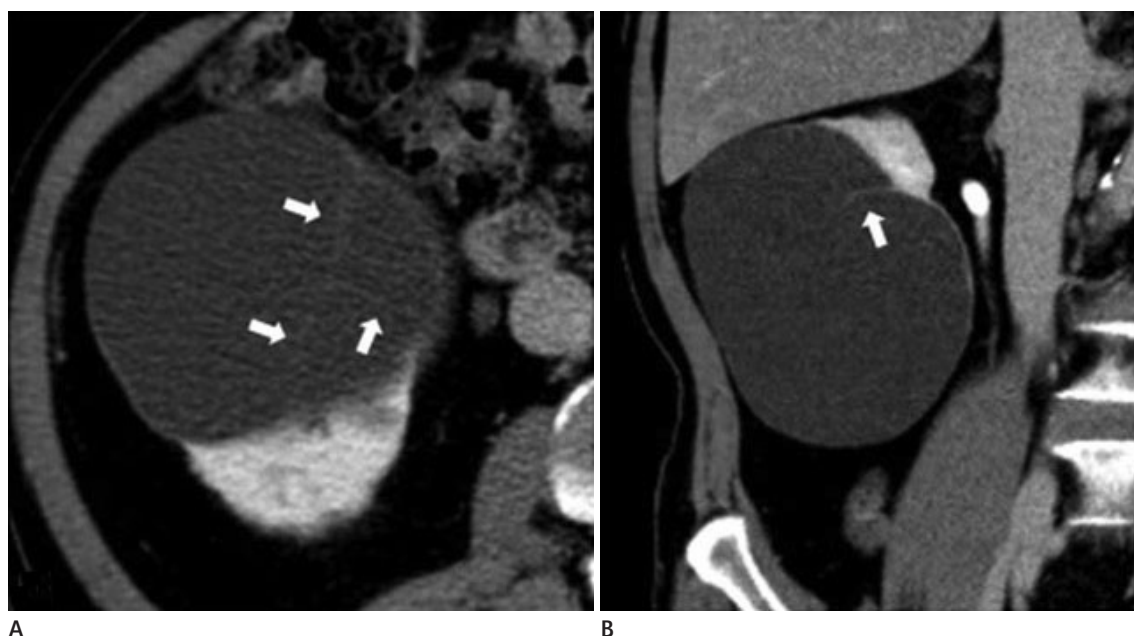


**Fig. 2.** A 57-year-old man with a Bosniak classification I lesion in the left kidney and he was performed two times ethanol injections.

**A.** The contrast-enhanced computed tomography axial scan shows a lobulated margin (arrowheads).

**B, C.** The coronal scan also shows a renal cyst with a lobulated margin (arrowheads) renal cyst; however, this is not accompanied by internal septa or calcification. Hence, this case was classified as a lobulated renal cyst in the left kidney without internal septa or calcification.

**D.** Similarly, a sonogram performed during sclerotherapy also demonstrated a lobulated contour (arrowheads).



**Fig. 3.** A 71-year-old man with a Bosniak classification II lesion in the right kidney and he was performed two times ethanol injections. **A, B.** The axial and coronal contrast-enhanced CT scans show a renal cyst with internal linear density (white arrows). This was classified as a smooth margined renal cyst with thin septa and no calcification.

**Table 1.** Image Features of Renal Cysts and the Comparison between the Two Groups

Group	Mean Volume (cc)	Calcification		Septa		Lobulated	
		Positive	Negative	Positive	Negative	Positive	Negative
Above-four	409.48	3	3	1	5	1	5
Below-three	301.64	4	27	11	20	2	29
Total	319.12	7	30	12	25	3	34
<i>p</i> -value	0.408	0.068		0.350		0.421	

Numbers are mean volume and number of patients. *p*-values are for the difference between results for the "above-four" group and the "below-three" group. The subjects were divided according to the number of rounds of renal cyst ablation, with the "above-four" group including those who underwent at least four ethanol injections, and the "below-three" group including those who underwent three or fewer ethanol injections.

performed with a 10 cc syringe. When the total drainage volume after 24 hours was over 5 cc, ethanol was injected to a volume of one-third the total drainage volume, but no more than 100 cc, and further follow-up examinations were performed after another 24 hours. When the total drainage volume was 5 cc or less, the procedure was considered a complete success and the pigtail catheter was removed (1).

### Statistical Analysis

We examined the correlation between the number of ethanol injections, and the following four criteria: volume, septa (or not), calcification (or not), and margin (lobulated or smooth). The mean total number of ethanol injections was obtained, and the subjects were divided into an "above" group and a "below" group based on the rounded mean; the volume, septa (or not),

calcification (or not), and margin (lobulated or smooth) were then compared between the two groups.

An independent sample *t*-test was used to compare the volume between the two groups. Due to the small sizes of the two groups, Fisher's exact test was used to compare the values of each variable between the groups.

SPSS ver. 18.0 (SPSS Inc., Chicago, IL, USA) was used for all statistics. *p*-values < 0.05 were considered to be statistically significant.

## RESULTS

A total of 37 renal cysts were included in the study, and renal cyst ablation was performed 2.5 times on average (range: 1–7 times). And all patients were no significant problem except mi-

nor pain at procedure site. The mean number of procedures was rounded to three, and the subjects were divided into two groups based on this criterion. There were six cases in the “above-four” group and 31 cases in the “below-three” group.

The mean volume of the renal cysts was 319.12 cc, with a mean volume of 409.48 cc in the “above-four” group and 301.64 cc in the “below-three” group. The difference between the two groups was not statistically significant ( $p = 0.408$ ) (Table 1).

A total of seven cases showed calcification, with three such cases in the “above-four” group and four cases in the “below-three” group. This was not a statistically significant difference ( $p = 0.068$ ) (Table 1).

A total of 12 cases showed septa, of which only one case was in the “above-four” group and 11 cases were in the “below-three” group. With a  $p$ -value of only 0.350, this was also not a statistically significant difference (Table 1).

Finally, there were three cases in total with lobulated margins, of which only one case was in the “above-four” group and the other two cases were in the “below-three” group. With a  $p$ -value of 0.421, this was not a statistically significant difference (Table 1).

## DISCUSSION

Renal cysts are the most common disease in the kidneys, and are known to occur in approximately 50% of the population aged 50 years and older. Treatment is indicated in patients with symptoms such as pain, hematuria, hypertension, or pelvicalyceal dilatation due to pressure from the cyst, as well as in some patients in who the diameter of the cyst is at least 5 cm (2-6). Renal cyst sclerotherapy is a minimally invasive method for the treatment of renal cysts. It is being used increasingly often due to its high performance relative to cost and good success rate (3).

Drugs used for renal cyst sclerotherapy include ethanol, minocycline hydrochloride, povidone iodine, acetic acid, ethanolamine oleate and holmium-166 chitosan complex. Of these, ethanol is the most widely used because it is considered to be safer and more effective than the other drugs (7-18). The present study used 99% ethanol.

When a sclerosing agent such as ethanol is injected into a renal cyst, one of the best-known mechanisms of cyst ablation is necrosis of the fluid-secreting epithelium via coagulation (19, 20). In addition, the space for the cyst to grow into is believed to be

reduced by adhesion due to secondary inflammation; although the effectiveness of this mechanism is not clear, it seems possible given the effects of pleurodesis in the lungs (21, 22).

The methods of percutaneous renal cyst sclerotherapy include single-session sclerotherapy and multiple session sclerotherapy. Chung et al. (5) reported that multiple sessions of percutaneous sclerotherapy had a superior effect as compared to the effect of a single session, and the present authors also implement multiple session sclerotherapy with positive outcomes. In interviews conducted between the patient and physician prior to treatment, we are often asked about the expected length of stay in the hospital. However, there has not yet been enough research conducted to predict the average number of ethanol injections and the average number of rounds of renal cyst sclerotherapy that could be required.

In the present study, 2.5 ethanol injections on average were completed until the total drainage volume reached a level of less than 5 cc. And average length of hospital stay was 6.8 days. Using the rounded average of three injections as the criterion value, the authors divided the patients into two groups, and compared a series of variables between these groups. Specifically, the comparative analysis showed  $p$ -values of 0.408, 0.068, 0.350, and 0.421 for renal cyst size, calcification, septa, and lobulated margin, respectively, meaning that there were no statistically significant results for any of these variables. However, although the  $p$ -value of 0.068 for calcification was higher than the significance level of 0.05, it was lower than 0.1. Given that this was a preliminary study involving only small groups of patients, this is considered a relatively meaningful result that will require additional research.

The reason that calcification showed a more significant result than the other factors is not clear. Calcification is more likely to develop in older cysts than acute cysts, and can be caused by a particular patient history, such as the onset of previous inflammation in the cyst. Taking this into account, research will be required with respect to the association between calcification and time since onset or history of inflammation (23, 24).

Moreover, although it is not clear, when considering the mechanism of pleurodesis discussed above, calcification could have caused an increase in the duration of treatment by interfering with cyst adhesion.

This was a single-center preliminary study, in advance of a



multicenter study, to identify predictive factors for the number of ethanol injections administered in percutaneous renal cyst sclerotherapy. Hence, the study's greatest limitation was the small number of cases included. Another limitation of this study is that the cyst features were examined by USG for two cases, which could have resulted in differences between these cases and the cases examined by CT.

The average number of ethanol injections for successful renal cyst sclerotherapy was 2.5 (average length of hospital stay was 6.8 days), and this number was not greatly affected by features including renal cyst volume, intracystic septa, or a lobulated margin. However, wall and septal calcification showed a relatively significant *p*-value of 0.068, suggesting the need for future research in a multicenter study with a larger patient population.

In conclusion, there were no significantly correlated factors for predicting the number of renal cyst ablations. However, in our study, calcification was determined to be the most useful factor for predicting the number of renal cyst ablations that may be performed. Additional research is needed to clarify this correlation.

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## 신장 낭종 경화술에서 에탄올 주입의 횟수에 영향을 미치는 효과적인 예측인자에 대한 고찰: 초기 보고

김용훈<sup>1</sup> · 조범상<sup>1,2\*</sup>

**목적:** 신장 낭종 경화술에서 어떤 인자가 횟수를 예측할 수 있는 효과적인 인자인지를 고찰하고자 하였다.

**대상과 방법:** 전산화단층촬영 혹은 초음파를 시행한 37개의 신장 낭종을 후향적으로 검토하였다. 두 명의 영상의학과 의사가 신장 낭종의 크기, 석회화, 중격 그리고 소엽모양의 외형을 평가하였다. 환자는 에탄올을 주입한 횟수에 따라서 '4번 이상' 그리고 '3번 이하'의 군으로 나누었다.

**결과:** 37개의 신장 낭종 중 6개가 '4번 이상' 군에 속하였으며, 31개가 '3번 이하' 군에 속하였다. '4번 이상' 군은 평균 크기가 409.48 cc였으며, 다른 군은 301.64 cc였다. 7개의 신장 낭종에서 석회화가 있었으며, 이 중 3개의 신장 낭종이 '4번 이상' 군에 속하였다. 중격이 있는 신장 낭종은 12개가 있었으며, 이 중 1개만이 '4번 이상' 군에 속하였다. 소엽모양을 보이는 신장 낭종은 3개가 있었으며, 이 중 1개만이 '4번 이상' 군에 속하였다.

**결론:** 신장 낭종 경화술의 횟수에 영향을 주는 중요한 인자는 확인되지 않았다. 그러나, 석회화는 신장 낭종 경화술의 시술 횟수를 예측할 수 있는 인자가 될 수 있을 것으로 생각된다.

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