# A comparison of PAIR and catheterization methods in the percutaneous treatment of liver hydatid disease

Karaciğer kist hidatik hastalığının perkütan tedavisinde kullanılan PAIR ve kateterizasyon yöntemlerinin karşılaştırılması

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Background and Aims: The aim of this study was to compare the puncture-aspiration-injection and re-aspiration and catheterization methods in the percutaneous treatment of hydatid cyst disease of the liver. Materials and Methods: Thirty-three hydatid cysts of 25 patients who applied to this clinic with a diagnosis of hydatid cyst disease of the liver underwent percutaneous treatment using puncture-aspirationinjection and re-aspiration or catheterization method, accompanied by ultrasonography. Following aspiration, absolute alcohol and saline solutions were injected into the cyst as sclerosant agent. Subsequent observations were carried out using ultrasonography and computed tomography, and cyst morphologies were examined in varying intervals. Results: The rate of complications and hospitalization period of patients in the puncture-aspiration-injection and re-aspiration treatment group were lower while the rate of relapse was found higher when compared to the patients in the catheterization treatment group. No statistically significant correlation in pre-intervention and post-intervention cyst size was determined in the puncture-aspiration-injection and re-aspiration and catheterization groups. Conclusions: We believe the catheterization method is preferable over the puncture-aspiration-injection and re-aspiration method to ensure optimal drainage and scolicidal effect in large, infected and complicated hydatid cysts.

**Keywords:** Hydatid cyst, echinococcosis, percutaneous treatment, PAIR, catheterization method

**INTRODUCTION** 

Echinococcosis is a significant health problem in regions in which the disease is endemic, such as South America, Eastern Europe, Mediterranean countries, North Africa, and Australia (1,2). While hydatid cysts usually manifest in the liver (45-75%) and lungs (10-50%), they can also be seen in almost every part of the body, including the kidneys, heart, spleen, brain, and musculoskeletal system (3-5). Giriş ve Amaç: Bu çalışmanın amacı, karaciğer kist hidatik hastalığının perkütan tedavisinde kullanılan perkütan aspirasyon, enjeksiyon, reaspirasyon ve kateterizasyon yöntemlerinin karşılaştırılmasıdır. Gereç ve Yöntem: Kliniğimize karaciğer kist hidatik hastalığı tanısı ile başvuran, 25 hastada, 33 adet hidatik kiste, ultrasonografi eşliğinde, perkütan aspirasyon, enjeksiyon, reaspirasyon ve kateterizasyon yöntemleri ile perkütan tedavi uygulandı. Aspirasyon sonrası sklerozan ajan olarak, kist içerisine saf alkol ve hipertonik salin solüsyonları enjekte edildi. Takip incelemeler ultrasonografi ve bilgisayarlı tomografi yardımı ile yapılmış olup, perivodik aralıklarla, kist morfolojileri incelendi, **Bulgular:** Perkütan aspirasyon, enjeksiyon, reaspirasyon yöntemi uygulanan hastalarda işlem sırasında komplikasyon gelişme oranı ve hastanede yatış süreleri, kateterizasyon yöntemi uygulanan hastalara oranla daha az bulunmuş olup, takip süresince nüks gelişme oranı perkütan aspirasyon, enjeksiyon, reaspirasyon yöntemi uygulanan hasta grubunda daha yüksek bulunmuştur. Takipte perkütan aspirasyon, enjeksiyon, reaspirasyon ve kateterizasyon yöntemi uygulanan her iki grup hastada, işlem öncesi ve işlem sonrası kist boyutları arasında istatistiksel olarak anlamlı korelasyon saptanmamıştır. Sonuç: Büyük boyutlu, enfekte ve komplike hidatik kistlerde, optimal drenaj ve skolisidal etkinin sağlanabilmesi için, kateterizasyon yönteminin, perkütan aspirasyon, enjeksiyon, reaspirasyon yöntemine tercih edilmesi gerektiğini düşünmekteyiz.

**Anahtar kelimeler:** Kist hidatik, ekinokokkozis, perkütan tedavi, PAIR, kateterizasyon yöntemi

Although cyst hydatid is usually a benign disease, the symptomatic and active cysts present a high risk of fatal complications, making treatment mandatory (6,7). While the fundamental method of treatment for the disease is surgical, the high rate of complications, mortality rate and long hospitalization periods in surgical treatment have led to the consideration of non-surgical methods as alternatives (7,8).

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Non-surgical methods (percutaneous, endoscopic and medical therapies, or their combinations) have been used in the last three decades to treat the disease. Patient tolerance to benzimidazole compounds used in medical treatment is generally low and the post-treatment relapse rate is high and usually not curative (9,10). The indication for endoscopic treatment is limited to biliary hydatid disease (11). Since its first application in 1985 by Mueller et al., the percutaneous treatment methods have seen increasing acceptance due to the benefits achieved in the treatment of disease, the low incidence of side effects and low mortality rates (12,13). The main concern in percutaneous treatment methods is the risk of spreading echinococci into the peritoneum and anaphylaxis development. However, numerous studies report that the risk of complications is very low (14,15).

This study assesses the results of two percutaneous treatment methods applied to 25 patients who were admitted to the clinic with diagnosis of hydatid cyst of the liver.

## **MATERIALS and METHODS**

Between June 2011 and April 2013, a total of 25 patients (5 males, 20 females, age range: 25-61 years, average age: 44,1) and 33 cysts in total were treated with a percutaneous intervention method. The patients were checked after the intervention using USG either the next day or within one week at most. The radiological follow-up of patients was rendered using ultrasonography (USG) and computed tomography (CT), with total follow-up periods varying from 6-18 months. The examination criteria in the follow-up were related to the cyst size, structure of the cyst wall and sonographic echo pattern of the cyst. The patients involved in the study were basically determined according to the sonographic type of the cyst, and the classification described by Gharbi et al. (16).

Type 1 (pure cystic lesion), Type 2 (cyst formation consisting of septated membranes) and Type 3 (cyst containing multiple septa and daughter vesicles) cysts with drainable matrices were included in the study. Type 3 cysts with degenerate matrices, which cannot be discharged due to solid components, Type 4 cysts (high internal echo, lesion resembling hyperechoic heterogeneous solid mass) and Type 5 cysts (cyst with thick calcific wall) were not included in the study.

Fifteen (60%) patients had 1 cyst, 7 (28%) had 2 cysts, 2 (8%) had 3 cysts, and 1 (4%) had 4 cysts. The number of treated cysts was 33. Four (16%) patients had undergone a previous operation for hydatid cystic disease before the intervention, and percutaneous treatment was planned due to relapse.

Twenty-two (88%) of the patients were admitted with complaints of right upper quadrant pain, abdominal discomfort and swelling. The other 3 (12%) patients were asymptomatic during diagnosis. All patients were diagnosed with the help of USG or CT. A signed consent form was obtained from all patients prior to the intervention.

All patients received prophylactic albendazole (Andazol; Biofarma, Istanbul, Turkey) 15-20 mg/kg, twice a day by mouth, starting 1 week before the intervention, which they used for 4 weeks in total.

An anesthetics team was kept ready during the intervention to treat any developing hypersensitivity reactions. All patients were treated after opening the peripheral intravenous (IV) vascular access under local anesthesia.

The Puncture-Aspiration-Injection-Reaspiration (PAIR) method defined and developed by Ben Amor et al. was applied in 16 (64%) patients (3 males, 13 females; age range: 26-56 years, average age: 43.9) (17). The catheterization method described by Akhan et al. was applied in 9 (36%) patients (2 males, 7 females; age range: 25-61 years, average age: 44.3) (18).

The PAIR method can be summarized as follows: the cyst is punctured with an 18 gauge needle under USG guidance, approximately half of the cyst volume is aspirated, and then absolute alcohol or 20% hypertonic saline solution of approximately one-third of the initial cyst volume is injected into the cyst and re-aspirated after 15-20 minutes.

The catheterization method involves the following: hypertonic saline solution is injected into the cyst and 6-9 French (F) pigtail catheters are placed that will ensure drainage for 24 hours. If no connection between the biliary tracts and cyst cavity is found in the cystography that follows, absolute alcohol in the amount of approximately half the initial volume of the cyst is injected into the cyst. It is re-aspirated after 20 minutes. If the cystography reveals a connection between the cyst and the biliary tracts, alcohol is not injected as it would trigger secondary sclerosant cholangitis.

There is a risk of cyst liquid spreading over the area of intervention, contaminating the surrounding tissue, during the first penetration of the cyst due to the high pressure inside the cyst. To avoid such complications, sheathed 18 gauge needles adapted with a unilateral valve system were used.

Before and after the hypertonic saline injection, the aspirated cyst liquid was sent for cytological and microbiological examination.

## RESULTS

Of the 25 patients undergoing percutaneous treatment, PAIR was planned for 16 (64%) and catheterization treatment for 9 (36%). Of the patients receiving PAIR treatment, 3 (23%) were male and 13 (77%) were female, with an age range of 26-54 years (average age: 43,2±11,8). Of the patients undergoing catheterization method, 2 (22%) were male and 7 (78%) were female, with an age range of 25-61 years (average age: 44,3±11,6). No statistical variation was found between the two groups in terms of age range (p>0,05). In 1 (6%) of the patients in the PAIR group and 1 (11%) of the patients in the catheterization group, the procedures could not be completed due to complications developing during the intervention.

With respect to the type of percutaneous treatment, PAIR method was applied to 23 (69%) cysts and catheterization method to 10 (31%) cysts.

According to Gharbi classification, among the cysts treated with PAIR, 18 (78%) were Type 1 and 5 (22%) were Type 2 hydatid cysts, while among those treated with catheterization, 4 (40%) were Type 1, 3 (30%) were Type 2 and 3 (30%) were Type 3 hydatid cysts (Table 1). The rate of Type 1 cysts was found higher in the PAIR-applied group (p<0,05).

None of the patients in the PAIR group had a history of surgery prior to the intervention. Four (44%) of the patients in the catheterization group had a history of surgery due to hydatid cyst prior to the intervention, and had applied for percutaneous treatment due to relapse. The rate of surgical history was statistically higher in the catheterization patient group (p<0,05).

The largest cysts in the PAIR-applied group were 34-200 mm prior to intervention (average:  $89,6\pm39,5$  mm). The largest cysts in the catheterization-applied group were 47-190 mm prior to intervention (average:  $94,5\pm39,7$  mm). In the follow-up, no statistically significant relation

was found between the cyst size before and after the intervention in the two groups (p>0,05).

One (6%) of the patients in the PAIR method group developed cardiac arrest associated with severe anaphylactic reaction during alcohol injection and underwent immediate cardiopulmonary resuscitation (CPR). The patient responded to CPR and was kept under observation in the intensive care unit. Upon improvement in their general condition, the patient was discharged after 5 days, surgery was planned for a future date, and the patient underwent elective surgery 3 months later.

Urticaria developed during the alcohol injection in 1 (6%) patient in the PAIR group, and respiratory issues associated with allergic reactions developed in 2 (12%) patients, and antiallergic treatment was applied. All 3 patients responded to the antiallergic treatment and the PAIR intervention was resumed and procedures were completed.

It was observed that 1 (4%) of the cysts in the PAIR group ruptured during alcohol injection. The cyst was completely aspirated and the intervention was concluded. The USG follow-up examinations carried out the next day and the observations over 6 months revealed no further complications or relapses.

In 1 (4%) of the cysts in the PAIR group, liquid with hemorrhagic qualities, which implied hemorrhage inside the cyst, and the cyst was aspirated during re-aspiration after alcohol injection. The patient was kept under observation in the intensive care unit. The USG examinations carried out the next day revealed millimetric echogenicities belonging to hemorrhage inside the cyst and minimal free liquid in the pelvis. The patient's general condition improved and no further complications occurred, and the patient was discharged after 5 days. The pursuant observations over approximately 15 months revealed no additional complications or any indication of relapse.

In 1 (4%) cyst in the PAIR group, the bilirubin level was found to be high in the aspirated cyst fluid. The intervention was halted and the patient underwent endoscopic

Table 1. Distribution of cysts according to Gharbi classification prior to intervention							
Gharbi Classification	Lesion Features	Number of Cysts Treated With PAIR	Number of Cysts Treated With Catheterization	Total			
Type 1	Pure cystic lesion	18	4	22			
Type 2	Cystic formation containing segregated membranes	5	3	8			
Type 3	Cyst containing multiple septa/daughter vesicles	-	3	3			
Type 4	Semisolid heterogeneous lesion	-	-	-			
Type 5	Walled calcific hyperechogenic lesion	-	-	-			
Infected	Abscess-like lesion	-	-	-			
Total		23	10	33			

retrograde cholangiopancreatography (ERCP) on the suspicion of biliary fistula. ERCP demonstrated a spill from the biliary tracts into the cyst cavity, and a 7 F nasobiliary drainage (NBD) catheter was placed in the biliary tract. No spillage was found in the follow-up ERCP carried out 1 week later and the NBD was removed.

In 1 (11%) of the patients in the catheterization group, high positive levels of bilirubin were found in the aspirated cyst fluid, and cystographic examination showed biliary spillage. External percutaneous drainage catheter was placed in the cyst cavity. An increase in the cyst size was detected during the observation and the percutaneous treatment was cancelled. The patient was discharged and elective surgery was planned for a later date.

In 1 (11%) patient with a history of surgery before the intervention, the aspirated cyst fluid was found to have purulent qualities during the catheterization procedure. The patient was hospitalized for 16 days for drainage and antibiotic treatment. The patient was discharged upon improvement in their general condition. The examination performed 6 months after the intervention revealed a relapse of abscess in the cyst cavity, and the patient underwent elective surgery.

In 3 (33%) of the patients in the catheterization group, biliary fistula developed during the intervention and a stent was placed in the biliary tract with ERCP guidance. One of the patients was found to have biliary spillage in their examination 1 week later, and the stent was removed with ERCP guidance. In the follow-up, the examination in the 6th month revealed the operated cyst was calcific obliterated. The other 2 patients were kept under observation for approximately 8 months, and the initial cyst sizes were found to have reduced by less than 50%, with no indication of activity found inside the cyst cavity. The stents placed in the biliary tracts in both patients were not removed as a precaution.

In 1 (11%) patient in the catheterization group, the follow-up imagings taken after alcohol injection into the

<b>Table 2.</b> Complications encountered during   intervention						
Complications	PAIR Method	<b>Catheterization Method</b>				
Anaphylaxis	3 Patients (18%)	-				
Biliary fistula	1 cyst (3%)	3 cysts (30%)				
Urticaria	1 Patient (6%)	-				
Cyst rupture	1 cyst (3%)	-				
Hemorrhage	1 cyst (3%)	-				
Infection	-	1 cyst (10%)				
Extravasation	-	1 cyst (10%)				

cyst showed minimal extravasation outside the cyst. An external percutaneous drainage catheter was placed inside the cyst cavity and the intervention was concluded. The drainage catheter was removed 3 days later.

In the PAIR group, 1 (6%) of the patients showed severe anaphylactic reaction, 2 (12%) showed allergic reaction and respiratory issues, and 1 (6%) showed urticaria, and all cases were treated immediately. The patients responded to the treatments and no death occurred. No allergic reaction during the intervention was observed in the patients in the catheterization group (Table 2).

Of the cysts treated with the PAIR method, 1 (4%) developed rupture, 1 (4%) developed hemorrhage inside the cyst and 1 (4%) developed biliary fistula, all of which were treated. In the catheterization group, 3 (30%) of the cysts developed biliary fistula, 1 (10%) developed infection and 1 (10%) developed extravasation outside the cyst, all of which were treated (Table 2).

Ten (62%) of the patients in the PAIR group and 15 (65%) of the treated cysts did not develop any complications during the intervention. Three (33%) of the patients in the catheterization group and 5 (50%) of the treated cysts did not develop any complications during the intervention.

The follow-up period for the patients treated with the PAIR method varied from 6-18 months (average:  $11\pm5,1$  months). The follow-up period for the patients in the catheterization group varied from 6-18 months (average:  $12,3\pm5,3$  months).



In the follow-up observations, it was found that 5 (22%) of the cysts treated with the PAIR method showed a shrinkage of more than 50% compared to initial size, while 17 (74%) showed a shrinkage less than 50% of the initial size (Figure 1). One (4%) did not show any shrinkage in the initial size of the cyst in the follow-up, and examinations in the 6th month revealed daughter vesicles inside the cyst cavity, which imply relapse. Of the 17 cysts that showed shrinkage of the initial cyst size of less than 50% in the follow-up, 2 revealed findings implying relapse, and these cases underwent elective surgery. Consequently, the follow-up observations revealed relapse in 3 (13%) of the 23 cysts that were treated with the PAIR method. The observations found that the possibility of living without relapse for more than 6 months is 0,87 for the patient group treated with PAIR (Tables 3, 4).

One (10%) of the cysts treated with catheterization method was seen to be completely obliterated in the examination in the 6th month. The follow-up observations revealed shrinkage in the initial cyst size of more than 50% in 1 cyst (10%). The follow-up observations revealed shrinkage in the initial cyst size of less than 50% in 7 (70%) cysts (Figure 2). One (10%) cyst showed no shrinkage during the observation and the examinations carried out one year later showed abscess formation inside the cyst, and the patient underwent elective surgery. In the catheterization method group, there was no relapse of the treated cysts during the follow-up (Table 4).

The hospitalization period of patients treated with the PAIR procedure was 2-10 days (average: 4,1±2,4 days). The hospitalization period of patients treated with the catheterization method was 3-60 days (average: 12,9±18,1 days). The hospitalization period of the patient group treated with catheterization was longer than in the patient group treated with the PAIR method (p<0,05). Hospitalization of patients for pre-medication one day before the intervention as well as hospitalization

<b>Table 4.</b> Distribution of treatment results in the follow- up observation							
Appearance After Intervention	Cysts Treated With PAIR Method	Cysts Treated With Catheterization Method	Total				
Obliterated	-	1 (10%)	1 (3%)				
More than 50% volume loss	5 (22%)	7 (70%)	12 (36%)				
Less than 50% volume loss	17 (74%)	1 (10%)	18 (55%)				
No significant change in size	1 (4%)	1 (10%)	2 (6%)				
Relapse	3 (13%)	-	3 (9%)				

required for the treatment of complications developing during the intervention were included in the hospitalization periods in both treatment groups.

USG monitoring of all patients in the PAIR and catheterization groups was carried out the week after the intervention. At the first check-up, 22 (96%) of the 23 cysts treated with the PAIR method and all (100%) of the 10 cysts treated with catheterization method revealed a collapse of the cyst wall and membranes, endocyst-ectocyst segregation and no daughter vesicles inside the cyst cavity. The first USG examination of 1 cyst treated with the PAIR method showed segregation in the germinative membrane with no collapse of the cyst wall and no significant daughter vesicles inside the cyst cavity.

None of the patients that received percutaneous treatment with PAIR or catheterization method showed significant variations in liver function tests or in hematocrit and electrolyte levels during the intervention and hospitalization.

### DISCUSSION

Hydatid disease must be treated due to the significant risks including secondary infection, rupture in biliary tracts or peritoneum cavity and spread to other organs (19,20). Surgery remains the gold standard in the treatment of hydatid disease (21).

Percutaneous intervention is a treatment alternative to surgery to ensure the elimination of the parasite and prevent disease relapse. The increasing data in the literature regarding the percutaneous treatment method and its results indicate that percutaneous treatments are easy to implement, cheap and effective in treating the disease (22). Therefore, it is accepted as an alternative treatment method to surgery in the regions in which the disease is endemic.

Despite numerous successful attempts published in the literature, however, there are still doubts regarding the long-term effects of the percutaneous treatment in hydatid disease. The follow-up radiological imaging after percutaneous treatment displays an appearance that is assumed as the inactive cyst, appearing as 'calcific obliterate', 'partial calcific' or 'solidified lesion'. However, some of the daughter lesions can be very small in size and can be missed in the USG examination (23). Furthermore, the publications in the literature show that it is not always possible to attain exact evidence of inactivity, even in the cases examined using advanced serological methods (24-26).

The publications in the literature demonstrate that per-

cutaneous intervention on Type 1 and Type 2 cysts according to Gharbi classification achieved more successful results, with Type 1 having a higher rate of success. The rate of failure of interventions to Type 3 cysts was found higher (27). In this study, the PAIR method was applied to Type 1 and Type 2 cysts, and the follow-up observation found relapse in 3 of the Type 1 cysts. The complications that developed in the Type 2 and Type 3 cysts, which were treated with the catheterization method, included biliary fistula, infection and extravasation, but did not include relapse. No complications developed in the Type 1 cysts that were treated with the catheterization method and no case of relapse was identified in the follow-up observations.

Generally, the success criteria indicating the inactivation of the cyst following percutaneous treatment are: collapse of the cyst wall and membranes, endocyst-ectocyst segregation, shrinkage in cyst size during follow-up, and absence of daughter vesicles in the cyst cavity during subsequent observations. However, a number of studies in the literature reported shrinkage of the cyst size in patients that could not be treated after percutaneous intervention (28,29). In our cases, in 3 (13%) cysts that were treated with the PAIR method, the follow-up observations found indication of relapse, despite shrinkage in the cyst size.

Nearly all cases in both patient groups showed endocystectocyst segregation and collapse of the cyst wall and membranes in the early periods following intervention.

The average observation periods of the two patient groups were virtually equal, while the rate of shrinkage of the cyst size was found to be higher in the cysts treated with PAIR compared to those treated with catheterization. Furthermore, the rate of complications during the intervention and hospitalization periods was found lower in patients treated with PAIR method compared to the catheterization treatment group (p<0,05). The effective factors can be considered as easier implementa-



**Figure 1.** Female patient aged 26 years treated with the PAIR method: **(A)**. The contrasted computed tomography image taken prior to the intervention shows 3 Type 1 cysts in the liver.**(B)**. The contrast computed tomography image taken in the 3<sup>rd</sup> month of the follow-up observation shows collapse of the cyst wall and shrinkage in cyst size. **(C)** and **(D)**. The sonographic image taken in the 8<sup>th</sup> month of the follow-up observation indicates increasingly solid components are settling.



**Figure 2.** The contrast computed tomography images of a 48-yearold female patient, treated with the catheterization method, show a large Type 1 cyst in the liver **(A)**. The tip of the catheter is visible on the anterior wall of the cyst during intervention **(B)**, and the follow-up examination 6 months after the intervention indicates endocyst-ectocyst segregation and shrinkage in size **(C)**.

tion of the PAIR procedure, higher rate of Type 1 cysts according to Gharbi classification prior to intervention in the PAIR application group, and the absence of a history of surgery and relapse prior to the intervention. In contrast, the cysts treated with the catheterization method comprised Type 1, Type 2 and Type 3 cysts according to Gharbi classification, and 50% of the cases had a history of surgery and relapse prior to the intervention.

Although the number of cases in this study is not high, relapse was not observed among the patients with cysts treated with the catheterization method, while the rate of relapse was 13% among cysts treated with the PAIR method. Although the rate of complications in the cysts treated with the PAIR method was lower, the higher rate of relapse in the observation is associated with the larger sizes of the cysts treated with the PAIR method. The publications in the literature indicate that it is more difficult for the scolicidal agent injected into a large cyst to reach the parasite inside the cyst and eliminate all of scoleces.

While the biliary fistula and allergic reactions encountered occasionally during percutaneous treatment are serious complications, they do not dictate that the physician avoid implementing the method when it is indicated. In our study, biliary fistula was encountered at a rate of 4% with the PAIR method and 30% with the catheterization method; the intervention was cancelled in one case. while in the other cases, a stent was placed in the biliary tract and the intervention was continued. Significant allergic reaction was found in 18% of the PAIR cases, all of whom responded to antiallergic treatment. No allergic reactions were observed in the cases treated with the catheterization method. No exitus cases were encountered. It should be remembered that the rate of recurrence in surgery varies from 10-30%, with a hospitalization period of two weeks, and shows serious complications and cases of exitus (30,31). In our study, the rate of relapse following percutaneous treatment was 13% in an average observation period of 11±5,1 months in PAIR-treated cases and 0% in an average observation period of 12,3±5,3 months in catheterization-treated cases.

The factors of limitation in this study include the small number of cases, comparably shorter period of follow-up observations, and lack of comparison with surgical methods. However, this study was intended to compare only percutaneous interventions.

Some of the previous studies in the literature indicate that the catheterization method should be used in infected and complicated cysts, while in other cases, the PAIR method should be used without considering the cyst size (32).

In our study, it was observed that the rate of complications was lower, hospitalization period shorter and implementation easier with the PAIR method in comparison to the catheterization method. However, the rate of relapse was found higher in the cysts treated with the PAIR method, which implies that the cyst size prior to intervention is the contributing factor. Therefore, we believe the use of the catheterization method is necessary in large cysts as well as in infected and Gharbi Type 3 cysts to ensure maximum drainage and scolicidal effect.

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