



## PAIR vs Örmeci technique for the treatment of hydatid cyst

### LIVER

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#### ABSTRACT

Hydatid disease is caused by the larval stages of *Echinococcus Granulosus*. Most patients with hydatid disease have no symptoms, unless there is compression of vital organs such as the hepatic veins, portal vein, hepatic artery in the liver, bronchia in the lungs or the brain, resulting in life threatening complications like anaphylactic shock and sudden death. There are four treatment strategies for cystic echinococcosis (CE)- surgery, percutaneous methods, medical treatments and watch and wait strategies.

Medical treatment with albendazol, mebendazole or prazyquantel may cure only 2/3 of patients with CE. More than 30% of patients will reoccur after stopping the treatment. Watch and wait strategy is followed for asymptomatic and small cysts or CE type IV and Type V cysts. Surgical treatments were the gold standard for treatment of CE until the last 30 years. Consequently, surgical methods decreased while percutaneous methods of treatment increased. Due to higher mortality, morbidity, recurrence rates, longer hospital stays and higher costs in comparison to percutaneous methods like PAIR and ÖRMECİ technique, surgical treatment must be limited for the complicated hydatid cyst. Both the PAIR and Örmeci techniques are safe and effective. However, the Örmeci technique offers a simpler, inexpensive method of treatment, with no mortality, lower morbidity, low recurrence rate, while being out patient based. It can be used as the first choice of treatment modality in patients with cysts type CE type one, CE type two, CE Type 3A and CE Type 3B.

In this review, treatment modalities for CE, but mainly percutaneous treatment, will be discussed.

**Keywords:** Hydatid cyst, PAIR, Örmeci technique, albendazole

#### INTRODUCTION

Hydatid disease is caused by the larval stages of *Echinococcus Granulosus* (2-7 mm in length) and is found in the bowel of definitive hosts such as dogs and other canines. This serious public health concern is endemic especially in economically depressed areas in the Middle East, Eastern Europe, South America, Australia and New Zealand.

The definitive hosts are infected by eating offal containing hydatid cysts. Adult forms of the parasite live in the small bowel of dogs and other canines, shedding their eggs in feces. Intermediate hosts and humans are accidentally infected by oral ingestion of the eggs.

Oncosphere larva released from eggs, penetrates the small bowel wall, enters a portal vein and/or lymphatic vessel, and is transported to the liver. Unable to pass through the sinusoids of the liver, it is here where the larva resides in 70% of patients. However, if the larva does pass through the sinusoids of the liver or lymphatic channels, they are transported into the systemic circulation and/or are localized in the lungs (20%), spleen, kidneys, peritoneum and elsewhere in the host. Oncosphere larvae grow 1-50 mm per year, when it becomes a methacestode or a mature hydatid cyst (1).

Most patients with hydatid disease have no symptoms, unless there is compression by the cyst on vital organs,

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**Table 1.** Treatment modalities for Echinococcus Granulosus

| Surgical procedures                          |                               | Medical therapies | Sclerosing therapies                   | Watch and wait |
|--|-------------------------------|-------------------|--|----------------|
| Open or close-type (Laparoscopic procedures) |                               |                   |  |                |
| Curative approaches                          | Palliative approaches         | Mabendazole       | PAIR Method                            |                |
| Pericystectomy                               | Marsupialization              | Albendazole       | Örmeci Method                          |                |
| Hepatectomy                                  | Capitonnage                   | Oxfendazole       | PEVAC                                  |                |
|  | Omentoplasty                  | Praziquantel      | MoCAT                                  |                |
|  | Closure without drainage      |                   | Dilatable multi-function trocar (DMFT) |                |
|  | Drainage to peritoneal cavity |                   |  |                |
|  | Cystojejunostomy              |                   |  |                |

PEVAC: percutaneous evacuation; MoCaT: modified catheterization technique; DMFT: dilatable multi-function trocar

hepatic veins, portal veins, hepatic arteries in the liver, bronchial tubes in the lungs or in the brain. The main symptoms are pain in right upper quadrant, nausea, urticarial, icterus, fever, coughing, hemoptisia and headache. Physical examinations are generally normal. Palpable mass is seldom found on the abdomen.

Diagnosis of cystic echinococcosis (CE) is often accidentally made by imaging modalities such as ultrasound, CT or MRI (2-5). Serological tests like hemagglutination or western blotting have a 5-98 % of diagnostic rate (6). In this review treatment modalities, but mainly percutaneous treatment, will be discussed.

## TREATMENT OF CE

Although some authors are against therapy because of the slow progression of the infection, actually the disease must be eliminated owing to probable and serious complications (7,8) as follows:

- CE may rupture into the peritoneum (1.6%) resulting in the occurrence of anaphylaxis and sudden deaths (9-11)
- Cholestasis and cholangitis may take place due to rupture into the biliary tree (12%).
- Pleural hydatidosis and bronchial fistula are uncommon, but a possible complication, due to rupture into the thorax (2%).
- Abscess may result owing to secondary infection of the cyst.
- Cystic mass may result as in Budd Chiari Syndrome, with portal hypertension and cholestasis due to pressure on adjacent organs (0.8%).
- CE may rupture into the digestive tract or skin (0.2%)

Although CE has been a disease that has been identified since the time of Hippocrates, treatment is still far from satisfactory, with only 4 methods of treatment modalities in practice today (Table 1). The rationale of treatment is to destroy the germinal membrane of the hydatid cyst which provides glucose, produces brood vesicles, protoscolices, and generates companion cysts and cystic fluids.

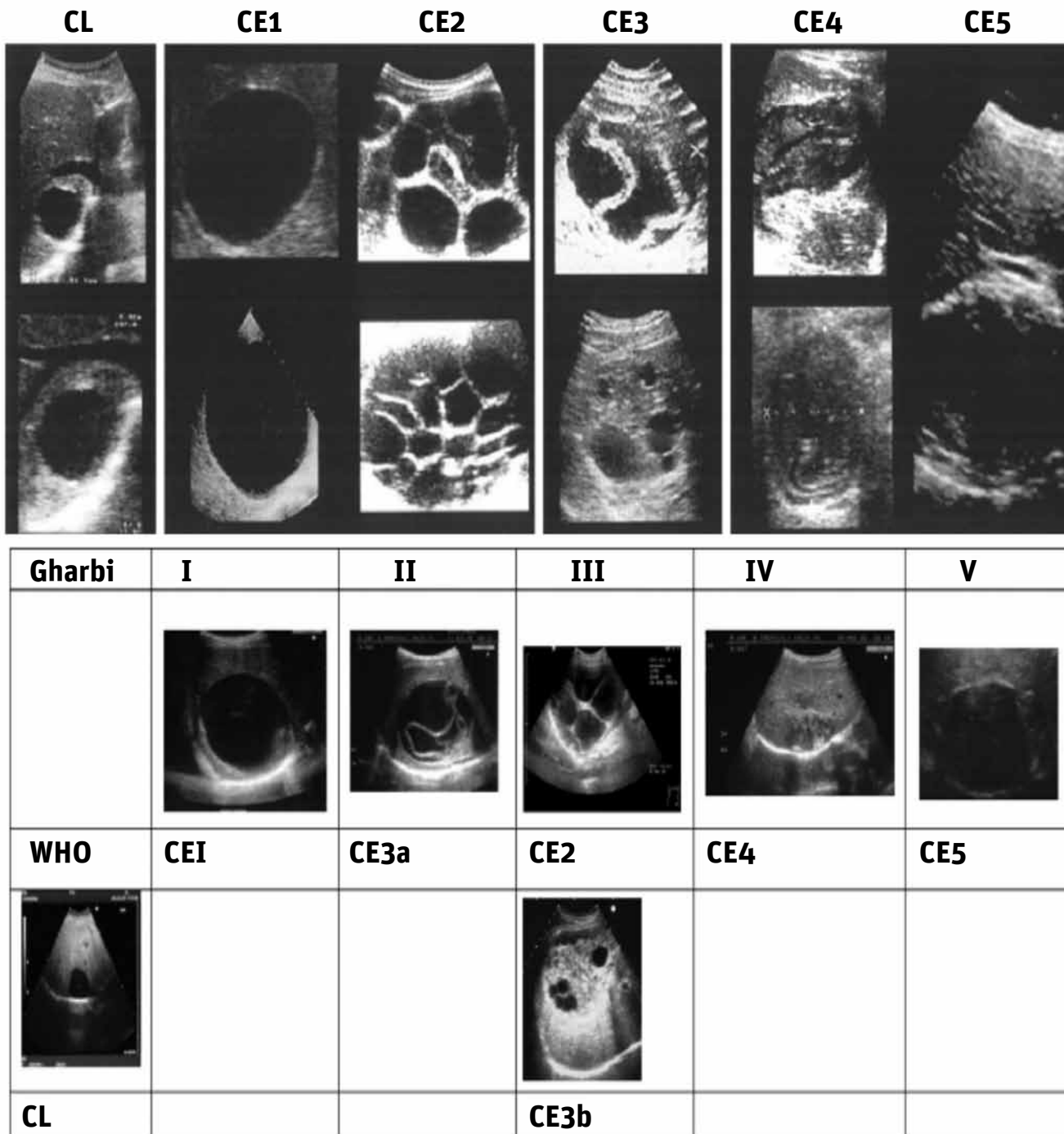
Surgical techniques remove the cyst, contents and germinal membrane; including laminated membrane, scolices and

daughter cysts. PAIR and Örmeci techniques destroy the germinal membrane with the use of different sclerosing agents. Pure ethanol (95% concentrate), 20% hypertonic saline, Betadine, silver nitrate, 50% dextrose, 20 % mannitol, 10% albendazole solution are all used for this purpose (12,13). Documented use of 1% polydocanol was first used in this treatment method (14). The significant advantage of 1% polydocanol is the closing of the connection between hydatid cysts and blood vessels or biliary tracts, if there are any. Benzimidazole derivatives inhibit the intake of glucose, resulting in the death of the metacystode. Prior to treatment, every cystic lesion should be evaluated in terms of the advantages and disadvantages of various treatment modalities.

## 1. Surgical methods

For the past two decades, invasive surgery was the recommended standard of practice for the treatment of CE. Today, only complicated cysts, such as biliary fistulae, ruptures in the peritoneum, invasion of the pleural cavity or bleeding into the cyst are surgically treated. Surgery can be performed radically, conservatively or by laparoscopic methods. In the radical technique, pericystic membrane and whole cyst material is removed with or without hepatectomy. However, in the conservative technique, only the cyst material is removed and the cavity of the cyst is treated by different methods such as capitonnage, omentoplasty or external drainage. The pericystic membrane is left insitu. Radical (cystectomy or lobectomy) and conservative surgical techniques (marsupialization, capitonnage, omentoplasty and external drainage) have a higher mortality (2-4%) and morbidity (11-23%) rate, with greater recurrence (2-10.4%) of re-infection and a longer rate of hospitalization than in PAIR and Örmeci treatments (15,16).

Post operative biliary fistulae, abscess of the cyst cavity and recurrence rates are higher in the conservative group than with radical surgery (16,17). Recently, laparoscopic surgery has been safely and effectively used. It has been reported that laparoscopic pericystectomy results in lower morbidity, shorter hospital stays and lower recurrence rates. Overall morbidity is 21.7 % (18). The treatment with albendazole before and after surgi-



**Figure 1.** The comparison of WGO and Gharbi ultrasound classification for CE (2,3,6). In both Gharbi and WGO Classifications, Type I or CE1 are the same. In Gharbi Classification Type II, became Type 3A in the WGO Classification. In Gharbi Classification Type III became CE2 in the WGO Classification. Gharbi does not include cystic lesion probable CE1 and CE3B. Gharbi and the WGO Type IV and V are the same.

cal treatment of patients with CE also reduces recurrence rates (19).

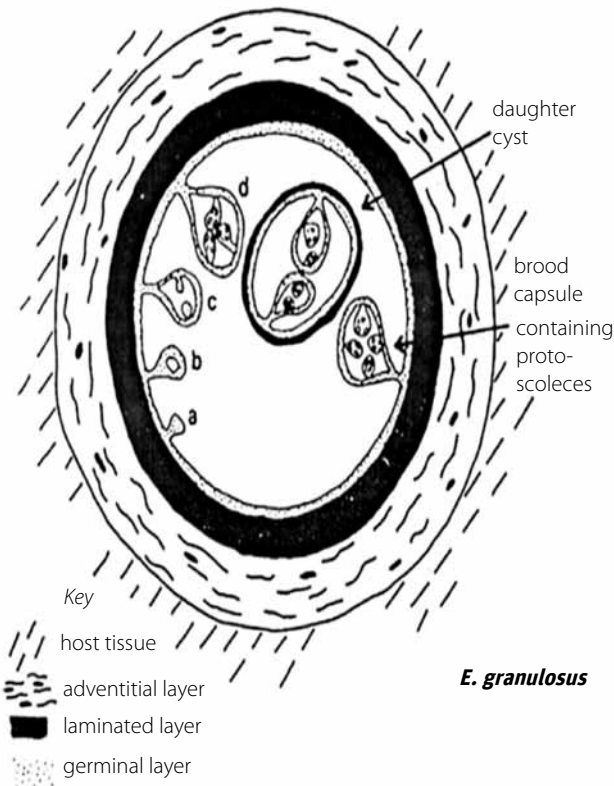
Surgical treatment is indicated in patients with (6,20);

- A. Cyst superficially located, at risk of rupture and where percutaneous methods are not an option.
- B. Complicated and ruptured biliary tract or pleural or peritoneal cavities.

- C. Cysts located in bone and brain.
- D. Bleeding into the cyst.

Surgical treatment is restricted in the patients with;

- A. Simple cysts, small cysts, multiple and located multi organ cysts.
- B. Cysts Type IV and V, according to WHO, and Gharbi classification.
- C. Cysts are difficult to reach with surgical treatment.



**Figure 2.** The schematic diagram showing the structures of the hydatid cyst (6).

**2. Medical treatments**

**A. Benzimidazole derivatives**

Mebendazole or albendazole is used for the treatment of CE. Albendazole has been found to be more effective than mebendazole. Albendazole is given in doses of 10-15 mg/Kg, continually or for three consecutive weeks with 1 week respite, or over a period of 3-6 months. Benzimidazole compounds inhibit glucose uptake and in addition, these molecules destroy the homeostasis of the cyst by decreasing the production of adenosine triphosphate, resulting in the depletion of glycogen stocks, resulting in the death of the metacestode (21,22). Smego et al. (23), reported that 448 patients with 882 hidatid cysts were treated with mebendazole or albendazole. Treatment with albendazole was more effective in 82 % in comparison to 56% of patients treated with mebendazole, respectively. A randomized clinical trial showed that albendazole treatment for CE is more effective than placebo and mebendazole (24,25). In another study, 929 patients were treated with either mebendazole or albendazole. The cysts were degenerated in 56.1% the mebendazole group and 82.2% of those in the albendazole group, respectively. Although 25% of cases relapsed, there was no significant difference between albendazole and mebendazole (26). In general, benzimidazole derivatives provided 20-50% cure for patients with CE, however almost 1/3 of the cysts recurred after treatment ended (27).

**B. Praziquantel**

Praziquantel increases the calcium absorption of the protoscolex cell membrane, resulting in paralysis and death. It is used in a dose of 50 mg /Kg for one week. Since its half life is short, the drug can be divided into 8-10 dosages. It is effective for small cysts with thin lamina, less than 4 cm in diameter. It must be given a few hours before the treatment and continued long after the surgery. It is ineffective for larger cysts (27,28). A combination of albendazole and praziquantel is more effective than albendazole alone when treating CE or for inhibition of recurrence after surgery or PAIR treatment.

**C. Oxfendazole**

When administered daily in 30 mg/kg doses in sheep, oxfendazole has been shown to decrease the viability of the protoscolexes, with a mortality rate 25% (29).

Albendazole alone or together with praziquantel, is indicated in patients with (19,23,27);

- A. Asymptomatic patients with small cysts, multiple cysts in one organ or multiple cysts in multiple organs.
- B. Pre and post operative period of CE treatment
- C. Pre and post treatment period of PAIR.
- D. Patients refusing surgical treatment or surgical treatment is restricted.

Benzimidazoles and praziquantel treatment is restricted in patients who are pregnant, have ruptured cysts, parenchymal liver disorders, bone marrow and renal disorders. The use of benzimidazole derivatives can cause adverse events such as nausea, abdominal pain, headache, vertigo, fever, tachycardia, urticaria, icterus, reversible alopecia, allergic shock and bone marrow toxicity (26,30).

**3. Wait and see strategy**

Patients with asymptomatic, small cysts, or type IV and V cysts according to Gharbi and/or WGO, can be followed up without any treatment. If the cysts are rapidly growing or became symptomatic, than optimal treatment can be administered.

**4. Percutaneous treatments**

**A. PAIR method (Puncture, aspiration, injection, re-aspiration)**

For many years, puncture of CE was encouraged to avoid severe complications, such as anaphylactic shock, the spread of hydatid scolexis and daughter cysts into the peritoneum. 1985 ushered in the era of sclerosing therapies, to which Mueller RP found that the administration of silver nitrate and hypertonic serum into the cyst cavity after aspirating a relapsed CE, was a safe method (31).

In the PAIR technique, CE is punctured with an 18 gauge needle under the guidance of sonogram or CT, where all of the fluid in the cyst is aspirated. Scholical agents, generally pure alcohol

**Table 2.** Main therapeutic differences between the PAIR and Örmeci techniques

|                           | PAIR                                     | Örmeci                        |
|---------------------------|--|-------------------------------|
| Needle type               | 18-20 gauge                              | 22 Gauge                      |
| Amount of fluid aspirated | 1/3-1/2 of cyst volume                   | 12-40 cc                      |
| Sclerozants               | Pure alcohol or hypertonic saline        | Pure alcohol plus Polydocanol |
| Drainage catheter         | 8-12 Fr catheter                         | No catheter                   |
| Time period               | Until the drainage is stop spontaneously | 5 minutes                     |
| Length of hospital stay   | Long                                     | Out-patient basis             |
| Chemotherapy              | Albendazole and or Praziquantel          | No chemotherapy               |
| Reoccurring treatment     | Rare                                     | As needed                     |

(95% concentrate), or a minimum of 20% saline, injected into the cyst cavity, replacing 1/3 of the original volume removed from the cyst. After 15-30 minutes, the scholoidal agents are re-aspirated. When the cyst is larger than 5 cm in diameter, a teflon catheter is placed into the cyst cavity in order to facilitate the procedure.

Technical success of PAIR varies between 88% and 100%, according to several published sources. The recurrence rate is between 1.6% and 10.9%, anaphylaxia 0.03%, while the mortality rate is so low it can be negated. Morbidity rates varies between 25.2-32% including cyst infection (22% in catheter group) and biliary fistulae (8.9%). Length of hospitalization depends on whether a drainage catheter is used or not, and then the length of stay varies from 2.1 to 8 days according to documented sources (13,32-44). Nearly 10,000 cases with CE have been treated by the PAIR technique and it can be concluded that PAIR is a safe and effective method for the treatment of non-complicated hydatid cysts as a first choice therapeutic modality.

There may be short period where complications such as infection of the cysts, bleeding into the cysts, perforation of the cysts, anaphylaxis, skin rashes, long term of complications like sclerosing cholangitis, seeding of the scolexis and recurrences after PAIR treatment (45).

In the D-PAI technique, the cyst is punctured, all of the fluid is aspirated and scholoidal agents are injected into the cyst without re-aspiration. One week later, the procedure is repeated again (46). One hundred seventy four cysts in 129 patients were treated using the D-PAI method. 45.8% of the cysts had a solid pattern. The mean hospital stay was 2.9 days. Intra cystic relapse occurred in 5 % of patients. Mortality rate was 1.3% and morbidity rate was 9 %. The overall median follow up was 48 months. Over a long period of time the D-PAI method is effective and safe (33).

The cysts which have a solid component, multivesiculated and daughter cysts like type CE3B, tend to relapse after the PAIR. Those cysts are treated by percutaneous evacuation (PEVAC) or modified catheterization technique (MoCaT) or dilatable multi-function trocar (DMFT). These techniques are

based on evacuating whole cystic materials, both germinative and laminated membranes (47-50). Even though these techniques are effective and safe in the treatment of cysts with a solid component and multivesiculated and multiple daughter cysts; catheter time (13.7 days- 72.3 days), hospitalization time (mean 38 days) and morbidity (21%) are higher than the PAIR technique, but comparable to surgery. Another drawback of these techniques is limited documentation from randomized clinical trials in order to conclude the effectiveness of treatment.

It was shown that a combination of albendazole therapy one week before and one month after PAIR treatment, decreases the recurrence rate (40). PAIR can be used as an effective and safe treatment modality in pregnant women (51).

Cysts found in the biliary tract should not be treated by the PAIR technique due to sclerosing cholangitis. CE2 and CE3B type of cysts have a tendency to recur after PAIR treatment. Those cysts with or without biliary fistulae, may be treated surgically or by modified catheterization or Örmeci techniques.

### Örmeci technique

Since 1992, the Örmeci Technique has been used in the Ankara University Medical School Hospital, resulting in great experience and to date, a wealth of unpublished data.

In this technique, the cyst is punctured by 22-gauge Chiba needle under USG or CT guidance. For each centimeter of the length of the cyst, three times the amount of fluid in the cyst is aspirated. This amount is equal to less than 2 % of the total cyst volume. The same amount of fluid is replaced by 2/3 volume of pure alcohol (95 %) and 1/3 volume aetoxysclerol (1% polydocanol) injected into the cyst. Five minutes after injection, the needle is withdrawn. The patient is then observed for two hours, and released to go to home. The primary differences between the Örmeci and PAIR techniques are summarized in Table 2.

There are several advantages of the Örmeci technique in comparison to PAIR or other modified techniques. They are as follows:



1. Only small amount (less than 2% of total volume) of fluid is aspirated from the cyst. This protects the biliary fistulae. In the PAIR technique, 1/3 or 1/2 the volume of the cyst is aspirated. This causes a decrease of the intracystic pressure under the biliary ducts, which is 16 mm Hg. The bile fills easily into the cyst cavity under low pressure. This is the reason that PAIR technique has 8.9% and 11% (in catheter group) biliary fistulae.
2. The scolicalid agents are not removed after injection, but are left in the cavity, with the rationale being that the longer the contact of pure alcohol and polydocanol with the germinal membrane and protoscolexes and/or daughter cyst, the probability of killing the CE is greater.
3. ERCP is performed with 99m Tc- labeled albumin macroaggregates injected into the hydatid cyst in order to discover the communication between the cyst and systemic venules, lymphatic channels and biliary ducts in 72 patients with CE (52). It was discovered that there was 15.4% of correlation between the systemic vessels and biliary ducts. This communication cannot be seen by USG or CT. Before the treatment, it was discovered that there was at least 15.4 % communication between the cyst and vessels or biliary duct.

As gastroenterologists, we have great experience in stopping varicose bleeding due to liver cirrhosis with 1% polydocanol. Polydocanol quickly obstructs leakage of the varicose veins to stop bleeding. Since 1992, in documented literature, we have been using polydocanol to disconnect the small venules, lymphatics or biliary ducts from the cyst cavity. For this reason Örmeci technique can be also used in patients with biliary leakage.

4. Catheters are not used, even in cysts as large as 10 cm in diameter. Introducing a catheter into the cyst cavity poses risk of infection and increasing hospital stay.
5. The use of benzimidazole derivatives before and/after the procedure are never used. It has been reported that use of albendazole together with PAIR may increase morbidity by 24% (40).
6. A thin 22 gauge needle is used to prevent leakage of cyst fluid and protoscolex. Secondary CE has never been experienced when using this method. However, thick needles (18 gauge) or large-bore catheters are used in the PAIR technique, which poses risk of recurrence and infection of the cyst cavity.
7. The Örmeci technique is as simple and effective as the PAIR technique, with no mortality, less morbidity, can be repeated as needed, inexpensive and performed by anyone having USG experience.

Örmeci technique can be used not only liver, spleen and kidney but also all of the soft tissues (53-55).

## CONCLUSION

Both the PAIR and Örmeci techniques are safe and effective. However, the Örmeci technique offers a simpler, inexpensive method of treatment, with no mortality, lower morbidity, low recurrence rate, while being out patient based. It can be used as the first choice of treatment modality in patients with cysts type CE type one, CE type two, CE Type 3A and CE Type 3B.

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