

**Comparing two different surgical approaches (Conservative and Radical) in
combination with Albendazole for the treatment of hydatid cyst. A 30-year
retrospective study from a large series of patients.**

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Abstract

Background: Hydatid disease management varies from medical treatment or percutaneous drainage to different surgical procedures. The aim of this study is to evaluate different surgical approaches with a specific administration of Albendazole.

Methods: One hundred fifty four patients underwent conservative surgery (Group A, unroofing with marsupialization, capitonnage, omentoplasty or external drainage) and seventy five patients radical surgery (Group B, pericystectomy or hepatectomy). Albendazole was given 5 days preoperatively in both groups and continued for 1 month postoperatively only in patients of Group A with viable protoscolices at the time of operation.

Results: No deaths occurred intraoperatively or during the first 30 postoperative days in both Groups. The mean hospital stay in Group A was 10.8 days (range 7-43) while in Group B was 11.7 days (range 7-46). Only one patient in Group A (0.6%) having viable protoscolices at the time of operation developed relapse of the disease after 52 months of follow-up. The complication rate in Group A was 23.3 % whereas in Group B was 30.6%. No statistical differences were observed in terms of hospitalization, complication and relapse rate ($p=0.43$, 0.83 and 0.48 respectively). The only independent variable that could affect the treatment is the diameter of the cysts ($B=0.442$, $P<0.001$).

Conclusions: Conservative and radical surgery have almost zero recurrence when they are combined with a specific administration of Albendazole. Furthermore we deemed that unroofing procedure with the administration of Albendazole five days prior and one month postoperatively only in the presence of viable protoscolices should be the first line procedure for most of Hydatid liver disease as the procedure is simpler, easier to perform and requires no advanced surgical skills or a certain degree of experience.

Keywords: liver hydatid cyst, surgical treatment, postoperative recurrence, complication rate, comparison of radical and conservative approaches.

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Section 1: Introduction

Cystic echinococcosis is a zoonotic ailment with a worldwide distribution. It was named in the first studies in the late 18th century, although it had been known to humans from time immemorial⁽¹⁾. Only three of the six known species of *Echinococcus* are of medical importance to humans. These are *Echinococcus granulosus* causing cystic echinococcosis, *Echinococcus multilocularis* causing alveolar echinococcosis and *Echinococcus vogeli* causing polycystic echinococcosis. The majority of cases in humans are caused by *Echinococcus granulosus* and rarely by the other two types⁽²⁾.

Echinococcus Granulosus is a small tapeworm displaying three forms during its life cycle: the adult form in the definite host, the egg stage in the environment, and the metacestode form in the intermediate host. The hosts include carnivores (dogs, cats, wolves, foxes, hyenas, jackals, coyotes, lynxes) constitute the definite hosts, whereas ungulates (sheep, pigs, goats, horses, cattle, camels) and humans act as the intermediate hosts. The adult form reaches 3-6 mm long, resides in the small intestine of the definite hosts, brings about intestinal parasitosis but not organ disease, and lives approximately for five months in the intestine of carnivores⁽³⁾. The adult form consists of a head (or scolex) and a body (or strobila) with 3 proglottids (immature, mature and gravid). Gravid proglottids split and release eggs which are passed in the faeces. The life cycle of the parasite begins when the eggs are

excreted with faeces in the environment. Eggs contain oncospheres (embryos) and are resilient to extremely poor weather conditions⁽⁴⁾. After ingestion by an intermediate host, eggs are digested in the gastrointestinal tract and oncospheres come out. Then, oncospheres adhere to the intestinal wall with their hooks, penetrate the mucosa and enter into the blood circulation through which they migrate to various organs. The liver is infected in about 60% of the cases, the lung in about 20% and remaining organs in about 20% (kidney, brain, bone, heart, central nervous system, muscles and others)⁽⁵⁾. When the oncospheres access as an organ, the stage of metacestode begins, which is a transitory stage between oncospheres and adult forms. Oncospheres lose their scolex when they settle in an organ and take on the cyst form. The hydatid cyst has 3 layers: the outer pericyst which is composed of modified host cells that form a dense and fibrous protective zone, the middle laminated membrane which is acellular and allows the passage of nutrients, and the inner germinal layer where the scolices (the larval stage of the parasite) and the daughter cysts (brood capsules) are produced. The cyst has sterile, clear fluid inside and grows slowly: 2-3 cm/year⁽⁶⁾. Once the live hydatid cysts are eaten by the definite host, the infection chain is completed and the life cycle is set in motion⁽⁷⁾.

Current estimates indicate a prevalence of 2-3 million global cases and incidence of around 200,000 new detected infections/year⁽⁸⁾. The endemic areas encompass the Mediterranean countries,

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the Middle East, the southern part of South America, Iceland, Australia, New Zealand, southern parts of Africa and the Central Asia, particularly China⁽⁹⁾. Though population screening in Greece is still not performed, the northwest of the country is deemed an endemic area. This is the main reason why early diagnosis of the parasitic disease is extremely rare⁽¹⁰⁾.

Hydatid cysts mostly remain asymptomatic and almost one-third of all cases are detected incidentally. Symptoms can be produced due to mass effect from the large size of the lesion or its complications. The most common symptoms are abdominal pain, vomiting and dyspepsia whereas the most frequent signs are hepatomegaly and a palpable mass⁽¹¹⁾. Bacterial infections of cysts can be either primary or secondary. A rupture occurs in the peritoneal cavity, into the biliary tree or into the bronchi. Routine blood tests are not specific. Eosinophilia is present in 25% and hypogammaglobinemia in 30%. The diagnosis of hydatid cyst is achieved by a combination of anti-Echinococcus IgG antibodies and ultrasound, CT or MRI of abdomen⁽¹²⁾.

There are three available therapeutic options for the management of hydatid cysts: medical treatment, PAIR technique, and surgery (conservative and radical). The medical treatment has a relapse rate 20-40% whereas the main risks in the PAIR technique are spillage, anaphylaxis, sclerosing cholangitis, and biliary fistulas. As for the conservative surgery, the incidence of recurrence and morbidity

are 3-30% and 21-80% respectively. Radical surgery which increases the operative risk it lowers the likelihood of relapse^(13, 14).

The aim of this study is to present the experience of our clinic in the surgical management of liver hydatid disease over the last 30 years. We describe different surgical procedures with a specific administration of anthelmintic therapy in order to achieve zero recurrence afterwards.

Section 2: Materials and methods*Section 2.1: Patients*

Between October 1988 and December 2017 a total of 262 patients undergoing surgery for hydatid cysts were being diagnosed retrospectively. Thirty-three patients were excluded from the study: while 23 patients were excluded because of extra hepatic Echinococcus cysts, and 10 patients did not turn up in the follow up period. The preoperative assessment of the patients included complete blood count, liver function tests, indirect hemagglutination antibody (IHA), abdominal ultrasound and abdominal computer tomography. The initial diagnosis was confirmed in all cases postoperatively by histological and anatomopathological examinations. All patients included in this study were treated surgically. Indications for surgery were in agreement with the World Health Organization (WHO) as follow: large liver cysts (>5 cm) with multiple daughter cysts, single liver cysts (>5 cm),

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superficially located cysts that may rupture (traumatically or spontaneously), infected cysts, cysts communicating with the biliary tree, cysts that bring about local pressure to adjacent organs and complicated cysts (such as bleeding into the cyst or rupture) ⁽¹²⁾.

Section 2.2: Methods

The 229 remaining patients were divided into two arms according to the surgical procedure carried out. One hundred and fifty four patients underwent conservative surgery (Group A) and seventy five patients underwent radical surgery (Group B). Among the patients of group B, nine patients (12%) showing recurrence of hydatid cyst were treated with partial hepatectomy. The surgical method performed depended on the location and the features of the cysts as well as the general condition of the patient. For cysts located peripherally, where possible, pericystectomy was performed. For bulky cysts, cysts occupying a major part of a liver lobe or recurrent cysts, hepatectomy was carried out. For deeper cysts with proximity to vascular or biliary organs, bilateral cysts or cysts with portal vein/inferior vena cava involvement, unroofing procedure was the treatment of choice.

The conservative surgery group (Group A) included patients who underwent unroofing. The basic steps of the unroofing technique are eradication of the parasite by mechanical removal, sterilization of the cyst cavity by injection of a scolicedal agent and protection of the surrounding tissues and cavities. The

operative area was protected against iatrogenic spillage by covering the entire area with abdominal towels soaked in hypertonic saline. The anterior wall of the cyst was incised and the cyst content was aspirated via strong suction. Afterwards the cyst cavity was filled with hypertonic saline and allowed to sit undisturbed for 10 minutes, after which it was emptied out. The inside of the cyst was inspected and any biliary communication was sutured individually. We employed several techniques to deal with the residual cavity: marsupialization, capitonnage, omentoplasty and external drainage. Marsupialization entailed stitching of the remaining wall circumference to avoid its reaccumulation. Capitonnage consisted of folding the residual cavity by means of a series of loose absorbable sutures between one end of the pericyst and the other, thus enabling the progressive reduction of the cavity, which was sometimes obliterated. Omentoplasty involved the filling of the cavity with a greater omentum flap. This flap was sufficiently voluminous and vascularized and it was fixed to the residual pericyst with loose absorbable sutures.

The radical surgery group (Group B) was made up of patients whose treatment involved pericystectomy or some kind of hepatectomy. In the pericystectomy technique, the cyst was removed en block with the pericyst, thus avoiding intraoperative spillage by accidental rupture. After completion of the pericystectomy, the cyst was totally separated from the liver and the smooth

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surface of the liver parenchyma was examined for bile leakage or bleeding. As for the hepatectomies, we performed right and left hepatectomies.

In both groups A and B, one or two drains were placed in the surgical area. Broad spectrum antibiotics were routinely administered intraoperatively and up to the second postoperative day. Albendazole (10 mg/kg body weight/day) was given to all patients 5 days preoperatively. The viability of the protoscolices was assessed at the time of operation in the conservative surgery group (Group A) by their flame cell activity, motility and ability to exclude 5% aqueous eosin ⁽¹⁵⁾. Seventy two patients in Group A had viable protoscolices and received Albendazole (10 mg/kg body weight/day) one extra month postoperatively whereas the remaining eighty two patients of Group A had dead protoscolices and did not receive Albendazole postoperatively. All patients were evaluated postoperatively every six months for the first two years and then annually. Abdominal ultrasonography or computer tomography, serodiagnosis and immunoglobulin (Ig) were tested at each evaluation.

The primary end points were to assess mortality, morbidity, recurrence and complication rates in two groups.

The data was analyzed by Statistical Package for the Social Sciences” (SPSS), version 21.0 (IBM). Statistical

significance was defined as p-values less than 0.05 throughout.

Section 3: Results

Section 3.1: General results

A total of 229 medical records of patients treated surgically for hydatid cysts between October 1988 and December 2017 were analyzed retrospectively. Key demographic and patients information with respect to cysts are summarized in Ref. Table 1. The median age was 44.3 years (range 13-86). The whole group comprised 131 males (57.2%) and 98 females (42.8%) whereas 171 patients were Greek citizens (from northwestern Greece, 74.7%) and 58 were Albanians (from southern Albania, 25.3%). The study population in Group A consisted of 95 males (61.7%) and 59 females (38.3%) with median age 44.6 (range 15-86) and in group B 36 males (48%) and 39 females (52%) with median age 43.8 (range 13-82). No statistically significant differences between the two groups were observed in terms of sex and age (p=0.05 and p=0.6 respectively).

Abdominal pain, dyspeptic complaints and hepatomegaly were the major symptoms that led patients to seek help. Cholestatic jaundice and itching were observed in 46 patients (20%). All symptoms and major clinical findings can be seen in Ref. Table 1. Interestingly, 21% of the cases of Echinococcus cysts were found incidentally. Eosinophilia was present in 57 patients (24.9%).

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Table 1. Demographic and clinical features of the patients				
Features	Whole group	Group A (conservative surgery)	Group B (radical surgery)	p-value
• Patients:				
Number	229	154 (67.2%)	75 (22.8%)	
Age (years):				0.6
• Median	44.3	44.6	43.8	
• Range	13-86	15-86	13-82	
Sex:				0.05
• Male	131 (57.2%)	95 (61.7%)	36 (48%)	
• Female	98 (42.8%)	59 (38.3%)	39 (52%)	
Country of birth				
• Greece	171(74.7%)	115 (74.7%)	56 (74.6%)	
• Albania	58 (25.3%)	39 (25.3%)	19 (25.4%)	
Presenting symptoms/signs				0.05
• Abdominal pain	156 (68%)	113 (73.3%)	43 (57.3%)	
• Dyspepsia	102 (44.5%)	74 (48%)	28 (37.3%)	
• Jaundice and itching	46 (20%)	29 (18.8%)	17 (22.7%)	
• Fever	20 (8.7%)	14 (9%)	6 (8%)	
• Weight loss	82 (35.8%)	53 (34.4%)	29 (38.7%)	
• Hepatomegaly	131 (57.2%)	92 (59.7%)	39 (52%)	
• Palpable mass	40 (17.4%)	26 (16.9%)	14 (18.7%)	
• Incidentally	48 (21%)	31 (20%)	17 (22.7%)	
• Cysts:				
Number				0.32
• Single	158 (69%)	103 (66.9%)	55 (73.3%)	
• Multiple	71 (31%)	51 (33.1%)	20 (26.7%)	
Mean diameter (cm)	7.61 (5-11.3)	7.17 (5-10.4)	8.05 (6.3-11.3)	0.006
Location				0.063
• Right lobe	136 (59%)	95 (61.7%)	41 (54.7%)	
• Left lobe	31 (14%)	19 (12.3%)	12 (16%)	
• Both lobes	62 (27%)	40 (26%)	22 (29.3%)	
Biliary communication	36 (15.7%)	23 (14.9%)	13 (17.3%)	0.64

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The majority of patients presented with one solitary cyst. A single cyst was detected in 158 patients (69%) whereas the remaining 71 patients (31%) presented with multiple cysts. The mean diameter of the cysts was 7.61 cm (range 5-11.3). The right lobe was affected in 136 patients (59%) whereas the left lobe and both the lobes were affected in 31 (14%) and 62 (27%) patients respectively. Communication with the biliary system was shown in 36 patients (15.7%). The cysts were bigger in radical surgery group ($p=0.001$), but no others differences as for the number, the location of the cysts and the communication with the biliary tree were noticed ($p=0.994$, $p=0.170$ and $p=0.448$ respectively).

Group A included 154 patients who were treated by unroofing procedure. Among the patients of Group A 121 patients underwent unroofing + marsupialization

(78.6%), 25 patients unroofing + capitonnage (16.2%), 3 patients unroofing + omentoplasty (2%) and 5 patients unroofing + external drainage (3.2%). A cholecystectomy was indicated in 106 cases (68.8%) on account of the localization of the cyst and to prevent gallstone formation. In 17 cases (11%) a common bile dust exploration was performed, followed by a T-tube insertion because of daughter cysts present in the common bile duct. The T-tube was removed from all patients on the 12th postoperative day after a cholangiography was performed through the tube without any resulting disturbances. Group B included 75 patients receiving a radical procedure. Among the patients of Group B 61 patients underwent pericystectomy (81.3 %), 10 patients right hepatectomy (13.3%), 4 patients left hepatectomy (5.4%). The main surgical procedures are shown in Ref. Table 2.

Table 2. Surgical procedures.			
Surgical procedures	Whole group	Group A (conservative surgery)	Group B (radical surgery)
A. Unroofing with	154 (67.2%)	154 (100%)	0
1. Marsupialization	121 (52.8%)	121 (78.6%)	0
2. Capitonnage	25 (10.9%)	25 (16.2%)	0
3. Omentoplasty	3 (1.3%)	3 (2%)	0
4. External drainage	5 (2.2%)	5 (3.2%)	0
B. Radical procedures	75 (32.8%)	0	75 (100%)
1. Pericystectomy	61 (26.7%)	0	61 (81.3%)
2. Hepatectomy:			
a) Right hepatectomy	10 (4.3%)	0	10 (13.3%)
b) Left hepatectomy	4 (1.8%)	0	4 (5.4%)

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Section 3.2: Follow-up, postoperative complications and recurrence

Two hundred twenty nine patients turned up for regular follow-up. The median follow up period was 52 months (range 23-78). Complications in both groups are shown in Ref. Table3. In Group A the mean hospital stay was 10.8 days (range 7-43). Only one patient (0.6%) having viable protoscolices at the time of operation developed relapse of the disease after 52 months of follow-up. He was treated by partial hepatectomy. No deaths occurred intraoperatively or during the first 30 postoperative days. There were thirty six complications (23.3%). Six patients suffered from wound infections that were treated appropriately. Two elderly patients developed atelectasia and

two others pneumonia all of whom were treated with respiratory physiotherapy and antibiotics. Four patients had pleural effusion but only one required a percutaneous drainage. Bile leak was identified within suction drains in seven patients, all of whom were managed conservatively with antibiotic administration. Percutaneous drainage under ultrasonographic guidance was carried out in two patients with hepatic abscess and in one patient with bilioma. Three patients came up with a cutaneous fistula that was treated conservatively and healed over time. Postoperative bleeding occurred in two patients but neither needed reoperation. Finally two patients developed pancreatitis while one patient had deep venous thrombosis and four patients had incisional hernia.

Table 3. Postoperative complications and recurrence.

A. Complications	Whole group	Group A (conservative surgery)	Group B (radical surgery)	p-value
Wound infection	11 (4.8%)	6 (3.9%)	5 (6.6%)	
Bile leak	11 (4.8%)	7 (4.5%)	4 (5.3%)	
Bilioma	1 (0.4%)	1 (0.6%)	0	
Hepatic abscess	3 (1.3%)	2 (1.3%)	1 (1.3%)	
Postoperative bleeding	4 (1.7%)	2 (1.3%)	2 (2.6%)	
Pancreatitis	3 (1.3%)	2 (1.3%)	1 (1.3%)	0
Atelectasia	4 (1.7%)	2 (1.3%)	2 (2.6%)	
Pneumonia	3 (1.3%)	2 (1.3%)	1 (1.3%)	
Pleural effusion	7 (3%)	4 (2.6%)	3 (4%)	
Incisional hernia	5 (2.2%)	4 (2.6%)	1 (1.3%)	
Cutaneous fistula	4 (1.7%)	3 (2%)	1 (1.3%)	
DVT	3 (1.3%)	1 (0.6%)	2 (2.6%)	
Total	59 (25.7%)	36 (23.3%)	23 (30.6%)	0.83
B. Recurrence	1 (0.4%)	1 (0.6%)	0	0.48

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In Group B the mean hospital stay was 11.7 days (range 7-46). No relapse was observed nor were there deaths intraoperatively, or during the first 30 postoperative days. Morbidity reached 30.6%. Overall, twenty three complications were documented. Wound infection was observed in four patients that predictably managed, while one patient who required surgical cleansing. Atelectasia, pneumonia and pleural effusion developed in two, one and three patients respectively, all of which were treated as expected. Four patients had bile leak that resolved spontaneously except in two cases that required endoscopic retrograde cholangiopancreatography (ERCP) for definite control. Percutaneous drainage under ultrasonographic guidance was performed in one patient with hepatic abscess. Two patients developed postoperative hemorrhage immediately after surgery, but only in one case surgical exploration was required with ligation of the bleeding vessel. One patient came up with cutaneous fistula that was treated conservatively. One patient developed pancreatitis, and finally, one patient developed incisional hernia and two of them deep venous thrombosis respectively.

Comparing the two different surgical approaches, one realizes that Group A does not have any statistically significant differences as for the hospitalization, the complications and the relapse rate with Group B ($p=0.43$, $p=0.83$ and $p=0.48$ respectively). Pearson correlation revealed a strong correlation between treatment and cysts diameter at the 0.01 level ($p=0.006$).

Then in order to identify the covariates independently associated with the treatment, binomial logistic regression with enter variable selection has been performed. Binomial logistic regression model demonstrated an accuracy of prediction of 90,3%. Moreover it has been shown that the only independent variable that could affect the treatment is the diameter of the cysts ($B=0.442$, $p<0.001$), which means that as the diameter of the cysts grows the radical treatment should be chosen. Since the variables hospitalization, complications and recurrence had not been shown any correlation, they had not be included in the binomial logistic regression model.

Section 4: Discussion

Hydatid disease is a widely endemic zoonotic disease caused by the tapeworm of the genus *Echinococcus*. The most common type is *Echinococcus granulosus* which affects mainly the liver and brings about Cystic echinococcosis. Overall, there are three therapeutic modalities to treat Cystic echinococcosis: medical management, PAIR technique and surgical management⁽¹⁶⁾.

Medical management is indicated in patients with inoperable primary liver or lung cysts, patients with cysts in two or more organs and peritoneal cysts⁽¹²⁾. However, it yielded a success rate of 10-30% while failure and recurrence rates at 20-40% and 3-30% respectively⁽¹⁷⁾. PAIR technique is the percutaneous drainage of echinococcal cysts located in the abdomen due to a fine needle or a catheter, followed by the killing of the protoscolices

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remaining in the cyst cavity by a protoscolicide agent. The main indications are inoperable patients, patients who refuse surgery or collapse after surgery or chemotherapy and multiple cysts in segments I, II and III of the liver. The main benefits of PAIR technique are the reduced cost, the lower risk and the shorter hospital stay compared to surgery. Nevertheless, the risk of spillage and anaphylaxis is considerable. Other risks are sclerosing cholangitis if cysts communicate with the biliary tree, sudden intracystic decompression leading to biliary fistulas, and systemic toxicity of alcohol or hypertonic saline in case of large cysts⁽¹²⁾.

Surgery is still the gold standard of treatment of the Hydatid disease. Conservative operations (unroofing) drain the content of the cyst without removal of the pericyst. Radical operations (pericystectomy and hepatectomy) remove the cyst completely with the pericyst. There are no randomized clinical trials to date that could compare different treatment modalities and consequently controversy exists over the most appropriate surgical approach. Therapeutic options depend on patient's age, comorbidities, the exact number and location of the cysts and the clinical experience⁽¹⁸⁾. In the present study, all patients were treated surgically and Albendazole was routinely administered five days prior to surgery. Only in patients undergoing conservative operation and having viable protoscolices received Albendazole for one month

postoperatively so as to minimize the risk of recurrence.

Several studies have demonstrated that conservative operations are associated with higher recurrence and complication rates compared to radical ones. A comparative retrospective study by Audin et al of 242 patients reported significantly higher morbidity and recurrence rates with conservative surgery (11% vs 3% and 24% vs 3%)⁽¹⁹⁾. Similar results were shown by Tagliacozzo et al, Yorganci et al and Magistrelli et al in their studies that included 454, 95 and 135 patients respectively^(20, 21, 22). The studies by Georgiou et al and Safioleas et al also displayed that radical procedures are superior to conservative methods^(23, 24). Yuksel et al have compared radical surgery versus conservative surgery. In this randomized study comprising 32 patients radical surgery scored over conservative surgery both in terms of recurrence ($p=0.04$) and complications ($p=0.01$)⁽²⁵⁾.

Nonetheless, other studies demonstrated different results. In a retrospective study of 59 patients, Akbulut et al found that recurrence was significantly increased in the conservative group ($p=0.045$) but no difference observed with respect to complications between the two groups⁽²⁶⁾. Comparable results were shown by Martel et al in the retrospective study of 40 patients. The 3-year recurrence –free survival was significantly lower in the conservative group (71% vs 100%, $p=0.002$) whereas there was no difference in complications between the groups⁽²⁷⁾.

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A recent retrospective study of 69 patients by Marom et al indicated that recurrence was significantly higher after the unroofing procedure ($p=0.05$) whereas the postoperative complications as assessed by Clavien-Dindo classification were significantly higher in the hepatectomy group⁽²⁸⁾. Finally, two retrospective studies consisting of 672 and 35 patients displayed that conservative and radical procedures have no differences as to recurrence and complication rates^(29, 30).

This study evaluated the incidence of complications and the relapse rate of different surgical approaches in patients with hydatid liver cysts over a period of thirty years (1988-2017). In general, our results showed a very low recurrence rate with no mortality and an acceptable postoperative morbidity. Specifically, there was no statistical difference in the relapse rate between the two groups whereas conservative procedures had significantly diminished complications compared with radical procedures. Theoretically, a radical surgery is the ideal surgical operation because the cyst and the pericyst are removed en block, leaving no chance for recurrence. Pericystectomy rather than hepatectomy, is the treatment of choice for Hydatid cyst since destruction of healthy liver parenchyma is minimal, but it is not always feasible. On the other hand, hepatectomy was necessary for bulky cysts. Cysts occupying a major part of a liver lobe or recurrent cysts, however, all efforts should be made to spare normal liver parenchyma on account of the benign nature of the disease. Whenever pericystectomy cannot

be achieved, unroofing procedure should be carried out. The main disadvantage of unroofing is that echinococcus cyst is capable of forming exogenous daughter cysts in the capsular membrane. These daughter cysts can persist in situ after endocystectomy leading to in the recurrence of the disease. Pericystectomy with excision of the cyst, including the surrounding fibrous lawyer, could minimize this risk⁽³¹⁾. In a previous study, Tsimoyiannis et al demonstrated that a five day preoperative Albendazole therapy in both conservative and radical procedures, combined or not with a monthly postoperative course according to the viability of the protoscolices at the time of the operation in unroofing approaches, may minimize the risk of recurrence in both after any surgery treatment for liver hydatid disease⁽³²⁾. In our study, the administration of Albendazole five days preoperatively in both groups and one month postoperatively in unroofing group according to the viability of protoscolices, resulted in a single recurrence in unroofing (0.6%) and 0 recurrences in radical surgery, which was not statistically significant. We conclude that both conservative and radical procedures with an appropriate administration of Anthelmintic therapy are safe and effective methods. Besides, this study demonstrates that conservative operations are efficacious and safe compared to radical procedures. We propose that unroofing with the administration of Albendazole five days prior and one month postoperatively only in the

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presence of viable protoscolices should be the first line procedure for most of Hydatid liver disease as the procedure is simpler, easier to be performed and requires no advanced surgical skills or a certain degree of experience. Finally, the only independent variable that could affect the treatment is the diameter of the cysts.

The present study has several limitations. To start with, it was a retrospective review of medical charts and surgeons' records. As with all retrospective series, controls are often recruited by convenience sampling and are thus not representative of the general population and prone to selection bias. Besides, the retrospective aspect may introduce selection bias and mis-classification or information bias. With retrospective studies, the temporal relationship is frequently difficult to assess. Furthermore, other risk factors that were not evaluated may be present. Finally, researchers cannot control exposure or outcome assessment, and must rely on others for accurate recordkeeping instead. When relying on individual recall of former exposure to risk variables, thus recall may be inaccurate and subject to biases. It can be very difficult to make accurate comparisons between the exposed and the non-exposed.

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- i. Tepelenis K: Concept and design of study, manuscript preparation.
- ii. Stefanou S: Acquisition and interpretation of data follow up.
- iii. Stefanou C: Acquisition and interpretation of data follow up.
- iv. Pappas-Gogos G: Statistical analysis.
- v. Zikos N: Literature research.
- vi. Spyrou S: Revising the article critically for important intellectual content, manuscript editing.
- vii. Koulas S: Final approval of the version to be published.

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