








Treatment Options and the Management of Complications in Hydatid Cysts of the Liver in Endemic Regions

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Yildiray Daduk¹, Ahmet Seker¹, Alper Sozutek¹, Tolga Olmez¹, Kuntay Kaplan¹, Huseyin Dur¹, Gorkem Ozdemir¹

¹Gastroenterological Surgery, Health Sciences University Adana City Training and Research Hospital, 01240 Adana, Turkey

Background: Hydatid cyst of the liver induced by *Echinococcus granulosus* is a pervasive zoonotic disease in our region. Its incidence varies across age groups, contingent on community lifespans and hygiene standards. Therapeutic modalities include Puncture, Aspiration, Injection, Re-aspiration (PAIR), and surgery. Due the limited feasibility of PAIR, we suggest that surgery represents the optimal treatment in all stages, especially in endemic regions, depending on patient-specific variables.

Method: Patients with hydatid cyst of the liver treated with PAIR and surgery in our center between January 2016 and January 2022 were analyzed retrospectively. PAIR or cystectomy were applied in treatment. These were then compared in terms of efficacy, feasibility, and complications.

Results: A single hydatid cyst of the liver was detected in 184 of the 225 cases, two cysts in 33, and three or more cysts in eight. The largest cyst diameter was 233 × 124 mm in the surgery group and 100 × 90 mm in the PAIR group. One hundred thirty-three of the 225 patients underwent open surgery, and no recurrence was encountered in these. However, recurrence was observed 19 patients treated with PAIR. Allergic reaction developed in one case during surgery, postoperative abscess in two cases, biliary fistula in five, and pneumonia in one.

Conclusion: Surgical treatment should represent the standard procedure since it is safe and effective, ensures complete elimination of the parasite, involves no intraoperative shedding, preserves healthy tissues, and minimizes the risk of long-term recurrence and cavity-related complications.

Keywords: hydatid cyst of the liver; surgery; PAIR

Introduction

Hydatid cyst is a disease caused by *Echinococcus granulosus* [1]. The disease is a parasitic zoonosis endemic in Turkey. In order to complete its life cycle, the parasite requires carnivorous animals as the primary host [2] and herbivorous animals as the secondary host [1]. Humans represent an incidental host. Transmission to humans generally occurs through water or foodstuffs contaminated with parasite eggs shed in canine feces [3]. It is asymptomatic during the incubation stage. Hydatid cyst is most frequently seen in the liver (60–70%) and lungs (20–30%) [4,5]. Complications such as rupture in the peritoneal cavity (10–16%), secondary infection, anaphylaxis, and secondary hydatidosis may be present [6]. Ultrasonography (USG) and computed tomography are the principal diagnostic tools and can identify related complications. Traditionally, surgical treatment has for long represented the gold standard for the majority of patients with hydatid cysts of the liver (HCL) [7].

Puncture, Aspiration, Injection, Re-aspiration (PAIR) and chemotherapy are non-invasive therapeutic options. However, the clinical efficacy of PAIR is controversial, and it is only suitable for small and unilocular cysts [8].

The purpose of this review study was to compare the effectiveness, feasibility, and complications of surgery and PAIR in the treatment and management of HCL in endemic regions.

Material and Methods

Ninety-two of the 225 patients presenting to our hospital with HCL between January 2016 and January 2022 were treated using PAIR and 133 by means of surgery. Cyst localization, stage, length of hospital stay, postoperative complications, and the reasons for the choice of treatment in the patients enrolled in the study were evaluated retrospectively. All cysts were staged using the Gharbi classification. Computed tomography and USG were used in diagnosis and follow-up. Cyst diameters were determined using USG.

Cystectomy with a right subcostal incision was performed on all our surgical cases. The remaining cavity was then evaluated in terms of biliary fistula and sutured if applicable.

Correspondence to: Yildiray Daduk, Gastroenterological Surgery, Health Sciences University Adana City Training and Research Hospital, 01240 Adana, Turkey (e-mail: ydadk@yahoo.com).

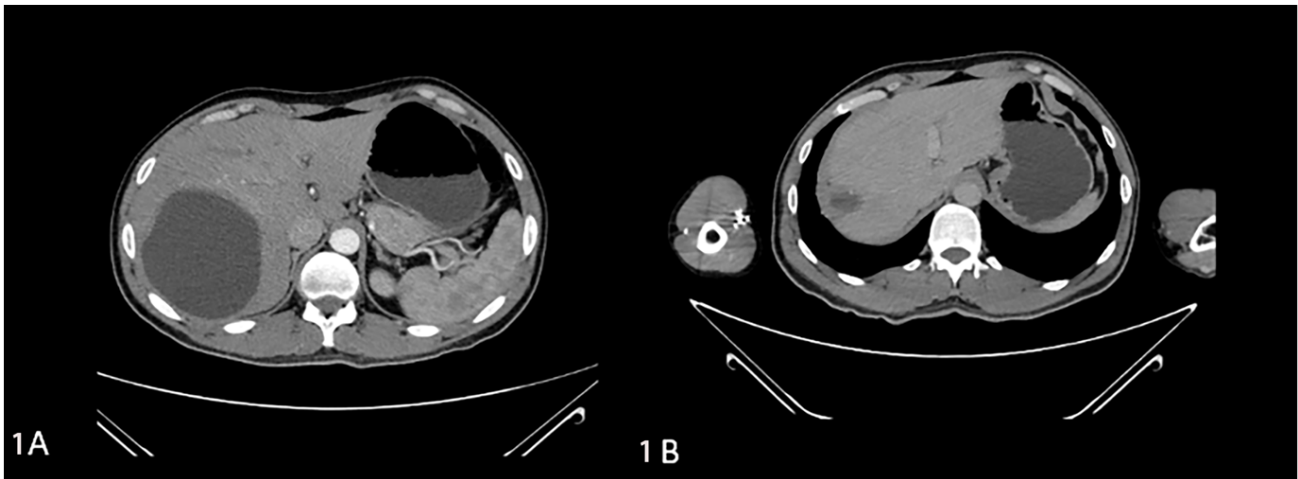


Fig. 1. Outcome of PAIR procedure in a patient. (A) A cyst as large as 100 mm in diameter (type 1 hydatid cyst) in liver segment 7–8 (pre-PAIR). (B) A heterogeneous area of 45 × 30 mm in diameter at the level of segment 7 in the right lobe of the liver, with contrast enhancement from the environment (Two years after PAIR). PAIR, Puncture, Aspiration, Injection, Re-aspiration.

Patients treated using PAIR were first investigated for biliary involvement using cholangiography. If this was not observed, on the first day, 20% NaCl solution was injected into the cyst at the same volume as the aspirated fluid, after which drainage was performed under USG guidance. On the second day, double aspiration, injection, and re-aspiration were performed using 96% absolute alcohol. On the third day, the drains were removed under USG guidance. A 5 F 40 cm cholangiography needle was used to drain the univesicular cyst and detect biliary involvement throughout the procedure.

Chemotherapy is initiated two weeks before the procedure for patients undergoing PAIR in our clinic and for eight weeks subsequently, while patients undergoing surgery due to cyst rupture receive 10 mg/kg albendazole for eight weeks after surgery.

The mean follow-up period after discharge was 25.6 ± 11.5 months. Our patients underwent USG examinations after six months and again after one year in the absence of suspicion of recurrence. Computed tomography was performed after two years. USG was also planned in the third year if no symptoms were observed. Patients with suspected recurrence were evaluated using computed tomography.

The immediate and long-term outcomes of the two methods were subjected to analysis.

Frequency and percentages from descriptive criteria and means from location criteria, the Mann-Whitney U test and the Independent-samples *T* test were used during data analysis.

Results

Two hundred twenty-five patients were treated for HCL in our center between January 2016 and January 2022. The mean age of the patients undergoing open surgery was 33.7 (3–83) years, and 39.2 (9–88) years in those treated using

Table 1. Demographic data.

	Surgery (N: 133)	PAIR (N: 92)
Age, years	33.7 (3–83)	39.2 (9–88)
Gender (f/m), N	71/62	50/42
Location (right/left/bilobar)	103/25/5	71/21/0
Size of cyst, mm	40–233	14–100
Single cyst, n	92	92
Multiple cysts (>2), n	41	0
Type (Gharbi), n (E1-2/E3-5)	78/55	85/7
Time of follow-up, months	25.6 ± 11.5	25.6 ± 11.5
Recurrence	0	19
Type 1	0	6
Type 2	0	9
Type 3	0	4
Type 4–5	0	0
Postoperative abscess	2	0
Postoperative biliary fistula	5	0
Postoperative pneumonia	1	0
Perioperative anaphylaxis	1	0

f, female; m, male.

PAIR.

A single cyst was present in 184 of the 225 cases, two cysts in 33, and three or more in eight cases. Cyst locations in the patients undergoing open surgery were on the right in 103, on the left in 25, and bilateral in five cases. Among the patients undergoing PAIR, 71 cysts were on the right and 21 on the left. The smallest cyst among the open surgery patients was 52 × 40 mm in size and the largest 233 × 124 mm, while the smallest cyst among the PAIR patients was 14 × 20 mm and the largest 100 × 90 mm (Table 1). Pre- and post-PAIR computed tomography images are shown in Fig. 1.

No recurrence was observed in 133 patients undergoing cystectomy with open surgery. However, recurrence was

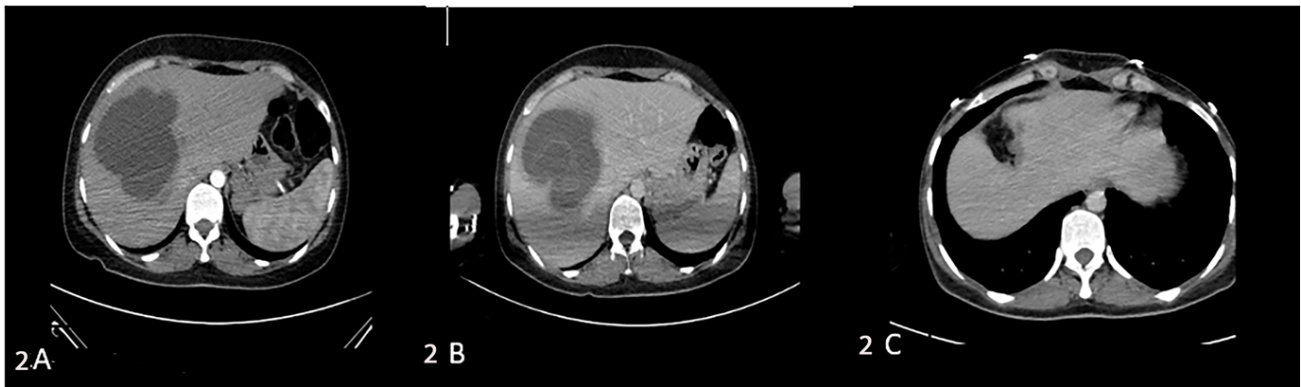


Fig. 2. Recurrence following PAIR procedure and subsequent surgical management. (A) Before PAIR. (B) Three months after PAIR. (C) Three months after surgery.

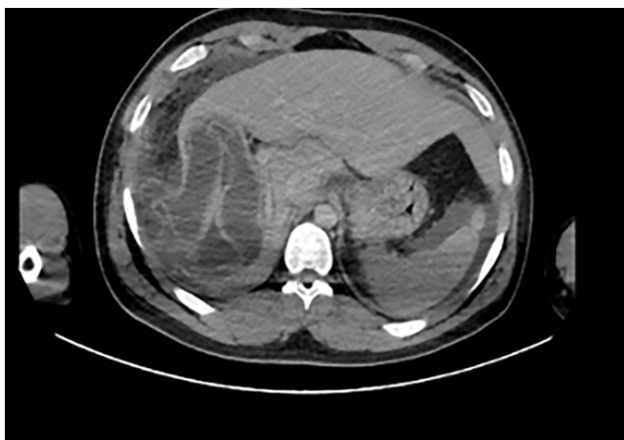


Fig. 3. Cystic lesion in the liver 100 mm in diameter extending to the perihepatic area and with loss of blood pressure at this level. Free fluid in the perihepatic and perisplenic spaces and bilateral paracolic gutters.

determined in 19 of the 92 patients undergoing PAIR (Fig. 2). These differences were statistically significant ($p < 0.05$). Success rates are generally low (39%) in Gharbi type 3 cysts due to the cyst content [5,9]. Seven of our patients were Gharbi type 3, and recurrence developed in these at the high rate of 57.1% (N: 4). These differences were statistically significant (MWU(Z) = -4.520, $p < 0.05$). One hundred thirty-five of the 225 cases were sent for PAIR, but 43 patients were not regarded as suitable for the procedure for various reasons, and these were instead treated surgically (Table 2). The five patients in whom biliary fistula was determined prior to the PAIR procedure were referred to the surgery department for treatment. No biliary fistula was encountered during surgery in any of the cases in which PAIR could not be performed, although postoperative biliary fistula developed in two patients 0.015% ($p > 0.05$). The cyst was found to be fistulized to the choledocum during tests in one patient who developed jaundice and fever prior to surgery. Intraperitoneal cyst rupture was determined in three patients presenting to the surgery de-

Table 2. Reasons why PAIR could not be performed.

Reason	N
Size smaller than 100 mm	13
Multiple septations	9
Postoperative biliary fistula	5
Type 4 (Gharbi), N	5
Multiple cysts, N	4
Cyst localization	2 (contiguity to the vena cava) 1 (superficial cyst)
Choledocal fistula	1
Allergic reaction	1
Hypertension	1
Previous history of surgery	1

partment with abdominal pain (Fig. 3). Biliary fistula was detected intraoperatively and sutured in 21 patients. Postoperative biliary fistula developed in three of the patients undergoing perioperative suturing.

Mean length of hospital stay in the open surgery cases was 7.3 (1–23) days. All patients undergoing PAIR were hospitalized for three days, but one of these who developed pneumothorax during surgery was hospitalized for 10 days with tube thoracostomy.

Allergic reaction developed perioperatively in one case, but the operation was completed uneventfully with intervention. Postoperative abscess developed in two cases, and these were treated with percutaneous drainage. Pneumonia developed in one case. Postoperative complications are shown in Table 1.

Discussion

Potential complications can be prevented with early diagnosis and treatment, even in asymptomatic cases [10]. Hydatid cyst is a condition requiring treatment irrespective of the diameter or stage. The incidental diagnosis of the majority of the patients operated on in our clinic with no symptoms and prompt treatment reduces the risk of the cyst opening to the bile ducts and rupture.

The basic aim in the treatment of hydatid cyst is to relieve symptoms such as infection, obstructive jaundice, and anaphylactic shock that may result from cyst rupture and to prevent complications [9]. This is done by inactivating and removing all viable scolices and germinal membranes and by managing the residual cavity with minimal morbidity and mortality [4,5,11]. The best means of achieving this and minimizing recurrence and complications is through surgery. In addition, total elimination of the parasite in the treatment of hydatid cyst also relies on the absence of intraoperative shedding and the preservation of healthy tissues [12]. In contrast to surgery, intraoperative shedding develops in an uncontrolled manner during PAIR, and chemotherapy is required in order to cope with potential complications. In our clinic, before surgical treatment is performed, contact between the contents of the cyst and the abdominal wall and internal organs is prevented by wrapping the cyst with compresses moistened with scolicidal agent.

The methods employed in the treatment of HCL include chemotherapy, percutaneous procedures, and surgery [10]. Indications for surgery depend on the nature of the cyst and the patient's general condition [11,12]. Surgery remains the standard treatment due to the largely inadequate effects of medical therapies and the complications of percutaneous techniques [6,8,12]. Surgical treatment is also our first choice, since we regard it as more effective, due to the fact that we are in an endemic region, and in the light of the morphology of the cyst. The surgical approach is usually preferred in large cysts with multiple offspring cysts, complicated cysts (such as rupture, biliary fistulas, compression of contiguous vital structures, bacterial infection, and bleeding), and superficial cysts [6,13]. Surgical procedures were performed due to cyst diameters exceeding 100 mm in 57 of our patients who underwent open surgery, multilocular cysts in 45, multiple cysts in 36, and biliary tract involvement in five, superficial cyst in one, and contiguity to the vena cava in one.

PAIR has been found to be particularly effective and safe in the treatment of Gharbi type 1 and 2 cysts [5]. However, it cannot be performed on all cysts at this stage. Its applicability is affected by the location and the morphology of the cyst. The PAIR procedure may be regarded as suitable for cysts >50 mm in size and Gharbi type 1 and 2 cysts [6]. However, PAIR is only a good option for univesicular cysts with a significant fluid component with an intact endocyst and absence of biliary communication [14]. Cholangiography was performed pre-procedurally in all our cases, and PAIR was not applied if biliary fistula was suspected. In our cases, PAIR was mostly applied to Gharbi types 1 and 2, and to a smaller number of type 3 cysts, between 20 mm and 100 mm in diameter, which were univesicular, not superficial, and with no wall calcification or biliary involvement.

PAIR can be performed on patients who refuse surgery or with a high anesthesia risk. However, we recommend re-

treatment with surgery in cases of postsurgical recurrence. Additionally, we do not recommend PAIR unless success has been achieved with chemotherapy, because chemotherapy is used to prevent hydatidosis and recurrence caused by leakage during PAIR. Complications may increase after PAIR if chemotherapy has been ineffective.

Recurrence was determined in four of our 17 patients with cyst diameters >50 mm. Small diameter does not constitute an obstacle in more experienced clinics. The important factors are the stage of the cyst, location site biliary involvement, and that the diameter should not exceed 100 mm. Although PAIR was not performed in large, multi-cystic, multi-local cases associated with biliary involvement before the procedure, our recurrence rate was significantly higher than in open surgery. This may have been due to deficient preoperative evaluation, inadequate evacuation of the cyst content, adequate scolicidal concentration not being achieved, a short duration of exposure to injected hypertonic fluid, or lack of contact with part of the offspring cysts. The experience of the radiologist performing the procedure and the imaging device employed may also affect the quality.

Occurrence developed in 17.6% of the 85 patients (N = 15) with Gharbi type 1–2 cysts who underwent the PAIR procedure in this study. Our failure rate among patients at this stage was low. The most important disadvantage of the PAIR technique was that the hypertonic saline infusion and injected alcohol cannot be aspirated during to separation of the membranes [9]. Aspiration can increase recurrence rates in case of multilocular and numerous offspring cysts. Success rates are low (39%) in Gharbi type 3 cysts due to the cyst content [5,9]. Seven of our patients were Gharbi type 3, and recurrence developed at the high rate of 57.1% (N: 4) in these cases. These differences were statistically significant (MWU(Z) = -4.520, $p < 0.05$). We do not therefore recommend PAIR in Gharbi type 3 cysts. In contrast to the previous literature, the PAIR recurrence rate in the present study was 20.6% (N: 19), while no recurrence was observed in open surgery. These differences were statistically significant ($p < 0.05$). Surgery may represent a definite solution in the treatment of recurrences.

Chemotherapy is not employed is not routinely employed in our clinic, except in case of spread of the cyst content into the abdomen during PAIR, rupture, and surgery. Albendazole together percutaneous drainage is thought to represent a safe and effective method for treating hydatid cyst. Our recurrence rate may have been high due to an insufficient duration of chemotherapy following PAIR. Albendazole taken at 800 mg twice daily day for at least six to 12 months after surgery may play a useful role in preventing recurrence [15].

However, we recommend chemotherapy in the event of the cyst fluid spreading to the abdomen in open surgery. Chemotherapy was applied for eight weeks postoperatively to three of our patients presenting due to perforation. We

attribute the absence of recurrence during the follow-up of patients operated due to perforation to careful exploration, removal of all cyst tissues from the body, and the effect of drainage and chemotherapy. The noteworthy point here is the considerable difference in terms of recurrence compared with PAIR, even though a large part of the abdomen was contaminated by cyst content after perforation. The duration of chemotherapy is the same in perforation and PAIR. Our success in perfusion is due to our observance of the rule of complete elimination of the cyst, the principal objective in the treatment of cyst. In other words, removing all the structures inside the cyst, rather than inactivating it, is an effective form of treatment. Surgery therefore remains the first choice treatment in our endemic region.

Surgical treatment was performed in case of superficial cysts, rupture or cysts with a major extrahepatic component, cysts close to vessels, and those with biliary involvement or suspicion thereof, irrespective of stage or diameter.

Since HCL is endemic in our region, and since presentations usually involve large and complicated cysts, the PAIR procedure is not generally appropriate. The low number of PAIR procedures in this study derives largely from patient preferences for surgery because of the pandemic and the nature of the cyst. One hundred thirty-five of the 225 patients were referred to the radiology department for PAIR. However, 43 of these were reported as unsuitable and were referred to the surgery department, where surgical treatment was applied with no complications. The reasons for unsuitability are shown in Table 2. Our high recurrence rate after PAIR encourages us to avoid conservative treatment.

However, we encountered no mortality or morbidity in the 133 operated patients in this study. There was also no recurrence, the most important post-operative complication, with only biliary fistula being observed. Some large-scale studies have reported lower morbidity with resectional surgery than with conservative procedures [8]. Our findings are consistent with those studies.

The most frequent complications of HCLs are infection and cyst rupture into the biliary tree [16]. Rupture into the choledocum was present before surgery in one of our patients. That patient was operated using ERCP, and no complication developed. Rupture into the small bile ducts is asymptomatic and most cases can be detected during surgery. Perioperative bile leakage was present in 21 of our 133 operated patients, and this was sutured using number 3/0 polypropylene. Postoperative biliary fistula developed in two of these patients.

Surgical procedures were performed on five patients with biliary involvement at cholangiography carried out prior to PAIR. Since no fistula was detected perioperatively in any of these cases, no additional fistula-oriented intervention was performed. Bile fluid emerged from the drain in two of the five patients in the postoperative period. Management of postoperative bile leakage often requires sphincterotomy and the use of invasive procedures such as stent-

ing or percutaneous drainage, which may be associated with morbidity and even mortality [8]. Endoscopic retrograde cholangiopancreatography (ERCP) was applied to three patients producing 200 cc of postoperative bile from the drain, to two who underwent fistula interventions during surgery, and to one suspected case during PAIR but in which no perioperative fistula was observed, while bile flow ceased spontaneously in two patients.

Biliary fistulas that do not close spontaneously or with ERCP can be easily detected without any procedure during open surgery due to their high flow rate. Both short- and long-term postoperative morbidity, bile leakage, and recurrence risks are significantly low in surgical treatment [17]. We do not therefore recommend any additional procedure for investigating biliary fistulas that are not seen perioperatively. Our open surgery biliary fistula rate is 0.015%. Abscess developed in two patients after surgery, and these were drained percutaneously.

We do not recommend the use of PAIR in types 4 or 5, due to the high rate of bile leakage and increased risk of severe post-operative complications. The aim must be to determine the most appropriate mode of treatment while causing minimal damage to healthy tissue. Surgery represents the gold standard in the treatment of HCL [12]. We recommend cystectomy as a surgical technique in endemic regions, since it is safe and entails minimal complications. However, it should definitely not be applied to superficial cysts, as the spread of the cyst material from the needle insertion site causes anaphylaxis and widespread cysts in the abdomen.

The most feared complication of percutaneous treatment of hydatid disease is fatal anaphylactic shock [18]. No fatal anaphylactic shock was observed in the present study, although reversible anaphylactic shock was encountered during open surgery in one case. Care must be taken during PAIR, and it should always be remembered that such complications may develop with either PAIR or open surgery in the treatment of hydatid cysts.

Less frequent complications include intraperitoneal rupture [16]. This may result in pressure necrosis due to trauma or relentless expansion of the hydatid cyst, leading to rupture into the peritoneal cavity, pleural cavity, or bile duct [8,16]. Rupture into the bile ducts was determined in one patient in our clinic, and intraperitoneal rupture in three. We think that spontaneous cyst development in three patients was the result of increased pressure within the cyst. Intraperitoneal rupture developed due to a fall in one patient. Hydatid cyst rupture should therefore always be considered in endemic regions, especially in patients presenting with abdominal pain as a result of trauma with a history of HCL. No symptoms other than abdominal pain were present in three patients presenting to our emergency surgery unit due to rupture. Such complications may not be caused if abdominal

exploration is well performed during surgery in cases operated due to rupture and when albendazole is administered at appropriate doses and time frames.

The length of hospital stay depends on the treatment selection. Stays of 1–4 days have been reported with the percutaneous approach and of 6–15 days for surgery [10]. Our patients undergoing PAIR were hospitalized for three days each. The mean length of stay with open surgery was 7.3 days. However, PAIR also entails such disadvantages as a high recurrence rate and rehospitalization for treatment.

Conclusion

The treatment of HCL must be selected on the basis of the stage, diameter, location, whether or not the cyst is complicated, and the patient's general condition. The absence of recurrence in surgical treatment, irrespective of the cyst characteristics, and recurrence being seen in PAIR despite patient selection, may be indicative of the superiority of surgery. In addition, chemotherapy use for 6–12 months after PAIR can reduce recurrence rates.

Availability of Data and Materials

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Author Contributions

YD, ASe, TO: Conception and design, acquisition of data, drafting of manuscript, supervision, and critical revision of the manuscript. YD, TO, ASO, KK: Conception, design and drafting of manuscript. YD, GO, HD: Prepared table and figures, analysed the data. All authors contributed to editorial changes in the manuscript. All co-authors have seen and approved the final version of the paper and have agreed to its submission for publication. All authors have participated sufficiently in the work and agreed to be accountable for all aspects of the work.

Ethics Approval and Consent to Participate

This retrospective chart review study involving human participants was in accordance with the ethical standards of the institutional and national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. The requisite approvals were received from Health Sciences University Adana City Training and Research Hospital the ethical committee (No:1935, Dated: 05.10.2022). Informed consent was obtained from all patients.

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Conflict of Interest

The authors declare no conflict of interest.

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