ORIGINAL ARTICLE

Surgical management and longterm follow-up of non-parasitic hepatic cysts

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Abstract

Background: Despite the increasing use of laparoscopic techniques, the optimal surgical approach for cystic liver disease has not been well defined. This study aims to determine the optimum operative approach for these patients.

Methods: Data were identified from the Lothian Surgical Audit, case note review and general practitioner contact. Patients were contacted and asked to complete the SF-36 questionnaire on quality of life.

Results: A total of 102 patients (67 with simple cysts, 31 with polycystic liver disease [PCLD], four with cystic tumours) underwent 62 laparoscopic deroofings, 15 open deroofings, 36 resections and one liver transplant between June 1985 and April 2006. The median follow-up was 77 months (range 3–250 months). Morbidity and recurrent symptom rates after laparoscopic surgery were greater in PCLD patients compared with simple cyst patients, at 31% (four patients) vs. 15% (seven patients) and 85% (11 patients) vs. 29% (24 patients), respectively. Four patients with simple cysts and eight with PCLD required further surgery. All patients with simple cysts had comparable quality of life after surgery. Patients with recurrent symptoms after surgery for PCLD had a significantly better quality of life following laparoscopic deroofing than after resection.

Conclusions: Most simple cysts can be managed laparoscopically, but there is a definite role for open resection in some patients. Open deroofing is the preferred approach for a dominant cyst pattern in PCLD, whereas resection is necessary for diffuse cystic disease.

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Introduction

Non-parasitic cystic disease of the liver occurs in up to 5–10% of the population, with a sharp rise in incidence with age.[1] The pathogenesis is related to the type of cyst. Simple cysts may be solitary or multiple, are lined by cuboidal epithelium and are believed to arise from the abnormal development of intrahepatic bile ducts in utero.[2] Polycystic liver disease (PCLD) is an autosomal dominant disease characterized by mutations on two genes on chromosome 19.[3] Patients with PCLD may also have cysts in other

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organs, particularly the kidneys. Neoplastic cysts (benign biliary cystadenomas and biliary cystadenocarcinomas) are acquired, but the cause is unknown. Traumatic cysts are also acquired and result from bile leakage from an injured intrahepatic bile duct after trauma.

The majority of patients with non-parasitic hepatic cysts are asymptomatic and the cysts may be found incidentally at laparotomy or with abdominal imaging. However, 5% of patients are symptomatic[4] and present with non-specific symptoms such as pain, nausea, vomiting, early satiety or heartburn. Rarely, cysts can present as a result of complications such as haemorrhage,[5] rupture,[6] infection,[6] torsion,[7] portal hypertension,[8] malignancy[9] and

obstructive jaundice.[10] In symptomatic or complicated cases it is usual to intervene and the procedures available include percutaneous aspiration with ethanol injection, laparoscopic deroofing, open deroofing, hepatic resection and transplantation. There is considerable controversy as to which procedure is preferable.[11] Laparoscopic deroofing was first reported in 1991,[12] and most studies seem to agree that it is the treatment of choice for simple cysts. However, recurrence rates vary greatly, from 0%[13] to 25%.[14] Other studies have suggested that open deroofing and resection are better operations.[15,16] There is no accepted best approach for the treatment of patients with PCLD. In these patients, laparoscopic deroofing leads to recurrence rates of 60%[17] to 100%,[18] whereas resection and transplantation have lower recurrence rates,[18] but are associated with significantly higher morbidity rates.[19] Moreover, the different surgical interventions have never been correlated with postoperative quality of life. The aim of this study was to evaluate all patients who underwent operative procedures for liver cysts in a specialist centre and to determine the most favourable operative approach in terms of morbidity, recurrence and quality of life.

Materials and methods

All patients who underwent operations for non-parasitic hepatic cysts were identified from the Lothian Surgical Audit[20] and the department's own prospective database. The case notes, radiology reports, operation notes, pathology reports and blood results were reviewed retrospectively for all patients. Patient gender, age at first operation, presenting symptoms, preoperative blood results and final pathology were documented. All patients who fulfilled the diagnostic criteria for PCLD (chromosome 19 mutations) were included in this subgroup for analysis. In the vast majority of patients, the diagnosis was established prior to referral to the surgical team. All other patients were labelled as having simple cysts. The number and location of the cysts and the size of the dominant cyst were recorded. The type and duration of the operation, complications, length of postoperative stay and follow-up were also documented. Patients were contacted by telephone to enquire about recurrent symptoms and were sent an adapted

SF-36 questionnaire, as a health survey and quality of life assessment.[21–23] The answers were scored using a scoring system developed by RAND Health (http://www.rand.org/health/surveys_tools/mos/mos_core_36item.html; RAND Corp., Cambridge, UK), which ranges from 0 to 3600, with a higher score indicating a better quality of life.

Data were analysed using SPSS Version 13.0 (SPSS, Inc., Chicago, IL, USA). Statistical tests included the Kruskal–Wallis test, Mann–Whitney U-test, chi-squared and Fisher's exact test. Values are given to the nearest whole number except for P-values, which are given to three significant figures.

Results

Between June 1985 and April 2006, 102 patients with liver cysts underwent 114 surgical procedures. Demographic data, size of the dominant cyst, cyst location(s) and lobar distribution according to type of disease are presented in Table 1. A total of 99 patients (97%) were symptomatic; the frequency of presenting symptoms is documented in Table 2. The remaining three asymptomatic patients underwent surgery for associated pathology (two had liver metastases and one had a rapid increase in the size of the cyst and required cholecystectomy for symptomatic gallstones). In this series, 63 patients (62%) with simple cysts had multiple cysts (more than three). Liver function tests were abnormal in almost one-third of patients (in 21 patients [32%] with simple cysts and in nine patients [29%] with PCLD). Twenty-one of the 31 patients (68%) with PCLD also had kidney cysts.

Twelve patients in the simple cysts group underwent one or more attempts at percutaneous aspiration at a median of 6.5 months prior to surgery, whereas nine patients in the PCLD group underwent attempted aspiration of the dominant cyst at a median of 6 months prior to surgery. Operative details and related postoperative morbidity are shown in Table 3. Two patients with simple cysts who underwent laparoscopic deroofing had further surgery (one open deroofing and one resection) and two patients who had open deroofing underwent a further open deroofing (one) and a resection (one). In the PCLD group, seven resections were carried out as a secondary procedure (two

Table 1 Demographic data, size of cyst and location of the dominant cyst in 102 patients who underwent operations for non-parasitic hepatic cysts

Demographics	Simple cysts (n = 67)	PCLD (n = 31)	Cystadenoma (n = 3)	Cystadenocarcinoma n = 1
Median age, years (range)[a]	60 (29–84)	49 (33–85)	39 (38–40)	52
Sex, M : F[a]	8 : 59	2 : 29	0 : 2	0 : 1
Median size, cm (range)[a]	11 (2–30)	10 (4–18)	12.7 (9.4–16)	
Bilateral location, %	23	100	10	
Right hemiliver, %	25	0	100	
Left hemiliver, %	14	0	0	
Unknown, %	38	0	0	

[a]No statistical significant differences
PCLD, polycystic liver disease; M, male; F, female

Table 2 Presenting symptoms in 102 patients who underwent operations for non-parasitic hepatic cysts

Symptom	Simple cysts (*n* = 67)	PCLD (*n* = 31)	Cystadenoma (*n* = 3)	Cystadenocarcinoma (*n* = 1)
Pain (%)	55 (82)	29 (94)	3 (100)	3 (100)
Bloating (%)[a]	16 (24)	17 (56)	0	0
Nausea (%)	15 (22)	10 (34)	0	0
Vomiting (%)	5 (8)	4 (13)	0	0
Early satiety (%)	12 (18)	10 (34)	1 (33)	0
Fatigue (%)	12 (18)	10 (34)	0	0
Shortness of breath (%)	7 (11)	6 (19)	0	0
Palpable mass (%)[a]	22 (33)	24 (78)	0	0
Heartburn (%)	0	0	1 (33)	0
Asymptomatic (%)	3 (4)	0	0	0

[a]Denotes statistical significant differences between simple cysts and PCLD, $P < 0.005$
PCLD, polycystic liver disease

Table 3 Operative details in patients with non-parasitic hepatic cysts. Data are given as median (range)

Pathology	Operation	*n*	Operation time, mins	Postoperative stay, days	Morbidity, *n* (%)
Simple cysts	Laparoscopic deroofing	48	75 (40–170)	3	7 (15)
	Open deroofing	11	90 (40–120)	8	3 (30)
	Resection	12	155 (90–295)	10	5 (42)
PCLD	Laparoscopic deroofing	13	105 (40–180)	4	4 (31)
	Open deroofing	11	110 (60–150)	12	4 (40)
	Resection	21	217 (90–360)	17	9 (43)
	Transplant	1	494	26	1 (100)
Cystadenoma	Laparoscopic deroofing	1	Unknown	1	0
	Resection	2	255	13	0

PCLD, polycystic liver disease

after open deroofing and five following laparoscopic deroofing). One patient who underwent an initial laparoscopic deroofing had a subsequent open deroofing followed by resection. One patient who underwent laparoscopic deroofing was found on pathological examination of the cyst wall to have a cystadenoma and subsequently underwent a major hepatic resection. All procedures were performed without any operative or perioperative mortality. The 34 resections included 28 hepatectomies, four left lateral sectionectomies and one segment III resection. Laparoscopic cholecystectomy was performed in 18 patients who underwent laparoscopic deroofing. The only transplant procedure in this series was carried out as a combined liver and kidney transplant.

Operative times for laparoscopic deroofing and open deroofing were comparable ($P = 0.560$). However, the operative time was significantly longer for resection ($P < 0.016$) compared with either laparoscopic or open deroofing (Table 3). These findings were similar in patients with simple cysts and those with PCLD. A laparoscopic approach translated into a shorter postoperative stay for simple cystic disease and PCLD ($P < 0.05$), whereas open deroofing and resection resulted in comparable lengths of postoperative stay ($P = 0.600$).

Overall, laparoscopic deroofing was associated with postoperative complications in 10 patients (16%). These included: pyrexia ($n = 2$); chest infection ($n = 2$); bile leak ($n = 2$); pleural effusion ($n = 1$); pneumothorax after central line insertion ($n = 1$); deep vein thrombosis and pulmonary embolism ($n = 1$) and myocardial infarction ($n = 1$). Complications after open deroofing included five chest infections and one pleural effusion. Fourteen patients developed complications after resection, including: pleural effusion ($n = 7$); bile leak ($n = 2$; one persistent); chest infection ($n = 2$); pyrexia ($n = 1$); prolapsed omentum at the drain site ($n = 1$), and pancreatitis ($n = 1$). The persistent bile leak required a hepaticojejunostomy 8 months later. Post-transplant complications included a chest infection complicated by MRSA (multiple-resistant *Staphylococcus aureus*), respiratory failure, gross peripheral oedema and post-traumatic stress disorder. Correlations between morbidity, type of cyst and type of surgical procedure are shown in Table 3. There were no statistical differences between procedures according to type of cyst.

The median follow-up was 77 months (range 3–250 months). Seventy-four patients were contacted by telephone and interviewed about symptom recurrence. Data for the remaining patients were obtained from the last follow-up letters. Table 4

Table 4 Recurrence following initial surgery in patients with non-parasitic hepatic cysts

Pathology	Operation	n	Patients with recurrent symptoms, n (%)	Time to recurrence, months	Patients who had further surgery, n (%)
Simple cysts (n = 67)	Laparoscopic deroofing	48	14 (29)	19	2 (4)
	Open deroofing	11	4 (36)	6	2 (18)
	Resection	12	3 (27)	12	0
PCLD (n = 31)	Laparoscopic deroofing	13	11 (85)	25	6 (46)
	Open deroofing	11	6 (55)	12	3 (27)
	Resection	21	10 (48)	28	0
	Transplant	1	0	N/A	0
Cystadenoma (n = 3)	Laparoscopic deroofing	1	0	N/A	1 (100)
	Resection	2	50	5	0

PCLD, polycystic liver disease; N/A, data not available

shows the proportion of patients with recurrent symptoms and time to recurrence after initial surgery.

Laparoscopic deroofing was associated with a significantly higher rate of symptom recurrence in PCLD patients compared with those with simple cysts (11 [85%] vs. 14 patients [29%]; $P = 0.001$, two-tailed chi-square). Furthermore, when compared with open deroofing or resection in the PCLD group, laparoscopic deroofing was associated with the highest rate of symptomatic recurrence, although this did not reach statistical significance. However, recurrent symptoms were less severe than those prior to the initial surgery according to patient responses in the follow-up questionnaire.

Overall, symptom recurrence was markedly reduced in the 39 patients who had fewer than three cysts compared with the 63 patients with three or more cysts (14% vs. 42%; $P = 0.02$, two-tailed chi-square). Only four of the 67 patients who underwent surgery for simple cysts required further surgical intervention, compared with nine of the 31 patients with PCLD ($P = 0.011$, two-tailed chi-square). Ninety SF-36 questionnaires (88%) were mailed out because nine patients were deceased and no contact addresses were available for the remainder. Sixty-four (71%) were returned (three patients were unable to complete the questionnaire). Overall, for patients with simple cysts there were no statistical differences in quality of life according to type of surgery (ANOVA, $P = 0.605$), although the more complex the procedure, the higher the mean score (Fig. 1A). Similarly, there was no statistical difference in quality of life by type of surgery among PCLD patients (ANOVA, $P = 0.700$), but the mean scores showed an opposite trend (Fig. 1B). However, the quality of life of patients with PCLD who had recurrent symptoms after laparoscopic deroofing was significantly better than that of patients who underwent resection, as confirmed by higher physical (Student's t-test, $P = 0.010$) and psychological scores (Student's t-test, $P = 0.006$).

Discussion

Because of the low incidence of symptomatic hepatic cysts in the general population, there has been no consensus on the optimal
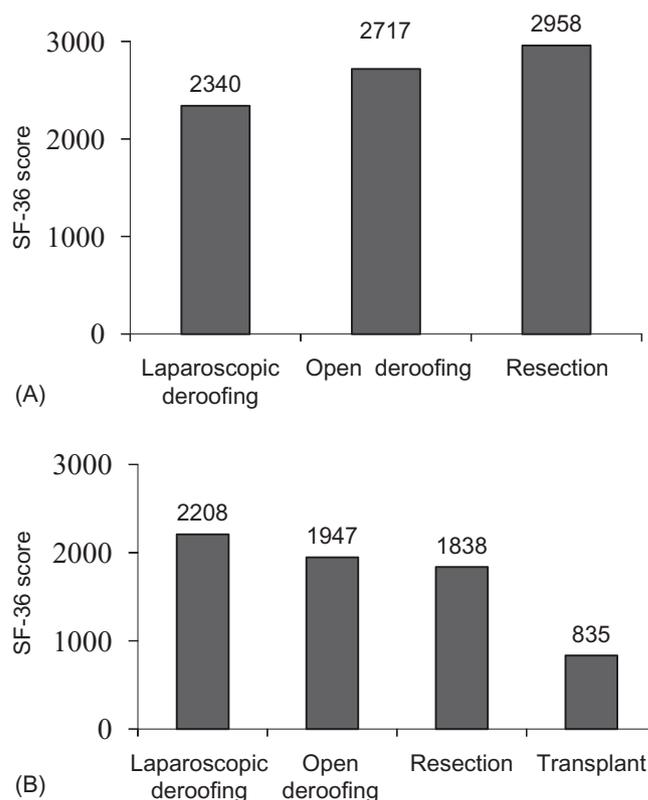

Figure 1 Quality of life scores following surgery for (A) simple cysts and (B) polycystic liver disease

approach to management of cystic liver disease and therefore patients are managed on an individual basis. Several studies have attempted to address this problem, but numbers of patients and lengths of follow-up have varied significantly and results are sometimes conflicting. The current study aims to address this issue from a single-centre perspective with experience from the second largest series of non-parasitic hepatic cysts in the literature.

In the management algorithm for patients with cystic disease, the clinician must be certain of the diagnosis and determine the

precise indication for surgery. It is widely accepted that symptoms are non-specific and the diagnosis is one of exclusion, which involves ruling out other significant pathology. Even so, concurrent pathology, such as gallstone disease, may be present; in this series, four patients (4%) were found to have co-existing gallstones. In the current series, almost one-third of patients had abnormal liver function tests. This association was one of the reasons for intervention in patients with small simple or PCLD cysts. An additional concern is the presence of malignancy. Although the radiological characterization of cyst pathology before surgery is generally accurate, a high index of suspicion for the presence of a neoplastic cyst should be maintained. This differentiation is even more difficult for simple cysts presenting with intra-cyst haemorrhage and with unusual radiological appearances, which could be mistaken for cystadenomas. The one case of mistaken radiological diagnosis of a cystadenoma in the present series supports the role for routine pathology examination of the cyst wall. If the presence of a cystadenoma is confirmed after the initial surgery, formal resection is required.

The second key question concerns the type of intervention, as several options are available. The choice may reflect the type and extent of cystic disease as well as the expertise and technology available locally. Percutaneous drainage and ethanol injection are increasingly used in some centres for patients with smaller simple cysts. The results are mixed and there appears to be a high recurrence rate. In the current series, 21 patients (12 with simple cysts and nine with PCLD) underwent attempted aspiration – in some cases combined with alcohol sclerosis – prior to referral. These patients had undergone repeated interventions with limited relief of symptoms. There seems to be little rationale for performing aspiration alone other than in an attempt to establish whether a specific cyst is symptomatic. Aspiration used in combination with instillation of alcohol may be of value in patients with significant co-morbidity or in those with a single small cyst which is symptomatic. However, this study did not seek to address the role of cyst aspiration and ethanol injection as the combination is not common practice at present in our centre.

In the current era of minimally invasive surgery, laparoscopic deroofing appears to be the preferred initial approach in most centres for the treatment of simple cysts.[24–26] However, others prefer resection as the primary surgery and report no recurrence and a 17% morbidity rate.[16] This study, however, had few patients and its follow-up period was too short to allow for the drawing of meaningful conclusions regarding symptomatic recurrence. In the current series, a laparoscopic approach was associated with a 15% morbidity rate, a short postoperative stay and a low re-operation rate compared with open deroofing. Furthermore, symptom recurrence occurred sooner after open deroofing than after laparoscopic deroofing. These results highlight some of the intrinsic benefits of minimally invasive surgery. In the current study, all open deroofing procedures were performed prior to 1999, since when the preferred approach for simple liver cysts has been a laparoscopic procedure.

It is important to highlight the presence of a group of patients in whom hepatic resection was the primary intervention. This was associated with similar postoperative morbidity rates but a 0% re-operation rate, lower symptom recurrence rate and longer time to recurrence compared with open deroofing. These findings challenge the suggestion that open deroofing is suitable as a second-line treatment[15] and, in fact, resection should be the preferred management choice in a selected group of patients in whom a laparoscopic technique is not feasible because of a multitude of cysts or their location(s). For example, a centrally located large cyst or a large posterior cyst may recur despite apparently adequate laparoscopic or open deroofing because the roof may reconstitute as the left and right hemilivers of the liver appose. Because of this tendency to recurrence, these cysts may be better managed by resection than by deroofing.

Several techniques to prevent cyst recurrence have been advocated, including the placement of omentum in the residual cavity or the ablation of the residual cyst lining. The utility of these methods is questionable and none were used in the current series.

In patients with PCLD, the choice of initial surgical technique is even more controversial as a result of the size and distribution of the cysts as well as the severe distortion in liver anatomy. Since 1999, our unit has tended towards a laparoscopic approach in the vast majority of simple cyst patients, but open deroofing or resection remained the primary approaches in PCLD and only a small number of patients have undergone laparoscopic deroofing, even after this date. In an attempt to rationalize the treatment, Gigot et al.[27] proposed a classification based on preoperative computed tomography (CT) scanning and suggested that therapy should be tailored to the type of disease. However, this classification is not widely used by radiologists and, therefore, the lack of uniform radiology reporting in the present series did not allow us to analyse the type of treatment and the Gigot staging. We should also point out that cyst size alone is of limited value when planning treatment strategy because multiple small cysts in a PCLD patient are as likely to require intervention as a large solitary cyst.

Laparoscopic deroofing has been increasingly used in PCLD, despite a high recurrence rate.[17,18,28] In this series, laparoscopic deroofing was the most successful operation in terms of operative time, length of postoperative stay and morbidity. However, 85% of those who underwent laparoscopic deroofing had recurrent symptoms and 46% of these patients underwent further surgery. Despite this, patients reported that recurrent symptoms were milder than symptoms prior to initial surgery, which translated into better physical and psychological quality of life scores compared with those collected after resection. However, any decision favouring laparoscopic deroofing should be carefully considered and should weigh the extent of disease, patient co-morbidity and the high risk of recurrence against the likely extent of improvement in symptoms. In patients with a dominant cyst pattern, a laparoscopic or open deroofing should be the preferred initial treatment, taking into account all of the above factors, whereas resection should be reserved for those with a diffuse cyst pattern.[28]

Resection in these patients is technically challenging, but, as the current data show, does not necessarily increase the risk; there is little difference between the two options in terms of morbidity, length of postoperative stay, symptom recurrence or quality of life. There appeared to be a lower re-operation rate and a longer time to recurrence in the resection group, which may well reflect the more extensive decompression of normal liver parenchyma achieved in these patients. Given the complexity of these patients, treatment should be carried out in specialist hepatobiliary units to ensure an adequate management algorithm for a successful outcome.

The role of transplantation in the management of PCLD could not be ascertained in the current study. However, there are patients with a diffuse disease pattern in whom there is a minimal amount of normal liver parenchyma associated with significant distortion of the liver anatomy. For these patients, transplantation may be the best course of action,[19] particularly if symptoms resulting from the size of the polycystic liver and associated with exhaustion, fatigue and cachexia are significant.

A treatment algorithm for the management of cystic liver disease is suggested in Fig. 2.

There are little data concerning the quality of life of patients who have undergone surgery for cystic liver disease. This study provides an insight into how patients perceive the effects of surgery during longterm follow-up. The SF-36 questionnaire revealed no significant differences in terms of quality of life

between any of the surgical procedures for simple cysts or PCLD. Although the results shown in Fig. 1 can be interpreted in many ways, no definite conclusions can be drawn because the small numbers in the analysis may be responsible for the lack of statistical significance. However, it was interesting to note that, in PCLD patients with recurrent symptoms, a more extensive initial procedure such as resection was associated with lower physical and psychological scores (i.e. lower quality of life scores) compared with those who had undergone laparoscopic deroofing. One might speculate that this may reflect patient disappointment after an initially high level of expectation that a more complex procedure might lead to better results. It should also be noted that the patient with PCLD may exhibit ongoing symptoms caused by renal involvement, which may be difficult to distinguish from the liver component. The challenges inherent in the management of cystic liver disease should be fully discussed with patients and the goals to be achieved with surgery should be identified on a case-by-case basis.

This study is limited because it did not include patients with cystic liver disease that was managed conservatively or using percutaneous methods, and conclusions are drawn in terms of symptom recurrence, rather than radiological recurrence. Many patients had no radiological follow-up, whereas others had only residual cysts on follow-up, as opposed to recurrence of the cysts which had been operated on. However, the significance of radiological recurrence in the context of no symptomatic recurrence
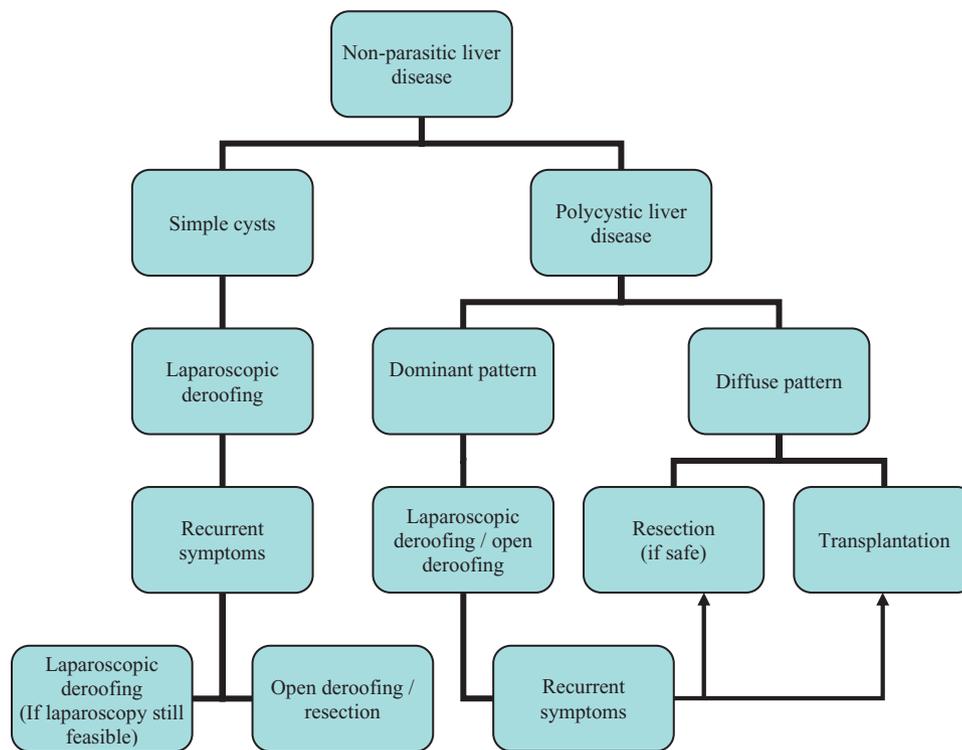

Figure 2 Management algorithm for non-parasitic liver cysts

remains to be determined. An in-depth analysis is difficult because of various factors and rigorous prospective evaluation may not be possible if patients fail on one type of intervention and require further procedures. Finally, because of the nature of the study, there was no baseline assessment of quality of life prior to the initial surgical intervention and therefore correlations between quality of life post-surgery and the extent of preoperative symptoms could not be assessed. The assessment presented here simply identifies the quality of life as perceived by patients at different time-points during follow-up.

In summary, the majority of simple liver cysts can be managed by a laparoscopic approach but there is a definite role for open resection in selected patients. In patients with PCLD, open deroofing is the preferred approach for a dominant cyst pattern, whereas hepatic resection or, indeed, liver transplantation may be necessary for disease with a diffuse cyst pattern. The management of non-parasitic cystic liver disease has evolved with the development of new surgical technologies, but remains challenging and offers a prospect of high recurrence rates. Treatment should be undertaken in specialist hepatobiliary units to ensure high rates of success.

Conflicts of interest
None declared.

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