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Laparoscopic drainage of cryptogenic liver abscess

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Abstract

Background To retrospectively compare the outcomes of percutaneously drained and laparoscopically drained liver abscesses.

Methods Eight-five consecutive patients with radiological evidence of liver abscess were treated at National University Hospital of Singapore from 2005 to 2011. Multivariable logistic regression was used to identify failures of intervention. This was defined as persistent objective signs of sepsis. Complications, length of antibiotic therapy, and hospital stay were recorded but not used as indicators for failure of intervention. A propensity score analysis was used to adjust for possible confounders.

Results Twenty-seven (40.3 %) patients in the percutaneous group did not respond to primary intervention compared to 2 patients (11.1 %) in the laparoscopic group ($p = 0.020$). Two patients within the percutaneous group died from progression of sepsis despite intervention. In the multivariate model with propensity score, laparoscopic drainage had a protective effect against failure compared to percutaneous drainage of liver abscess (odds ratio [OR], 0.03; 95 % confidence interval [CI], [0–0.4]; $p = 0.008$). There were no differences in complications related to the intervention ($p = 0.108$). Mean duration of antibiotics ($p = 0.437$) and hospital stay ($p = 0.175$) between the groups was similar.

Conclusions Laparoscopic drainage of cryptogenic liver abscesses should be considered as an option for drainage of liver abscess.

Keywords Laparoscopic drainage · Liver abscess · Percutaneous drainage · Sepsis

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Liver abscess is a potentially lethal clinical problem, with mortalities ranging 6–14 % even if treated [1]. The causes and microbiological agents of pyogenic liver abscesses differ between the East and West [2]. In the East, liver abscesses are predominantly cryptogenic, whereas in the West, they are associated with biliary abnormalities or malignancy [3].

Compared to the United States and Central Europe, liver abscesses in Korea and Taiwan are associated with *Klebsiella pneumoniae* [4, 5], particularly in patients with diabetes [6]. *Klebsiella pneumoniae*–associated abscesses appear to have a more benign natural history compared to other bacteria [7]. In the West, the predominant bacteria recovered in liver abscesses were *Escherichia coli, Staphylococcus,* and *Streptococcus* [8–10].

Treatment of liver abscesses has evolved in recent times, shifting from open surgical drainage described by Oschner et al. in 1938 to percutaneous drainage in current modern times [11]. Percutaneous drainage is seen as simple and noninvasive compared to open surgical drainage. Open drainage of liver abscesses has been associated with significant morbidity and mortality [12]. Despite the popularity of percutaneous

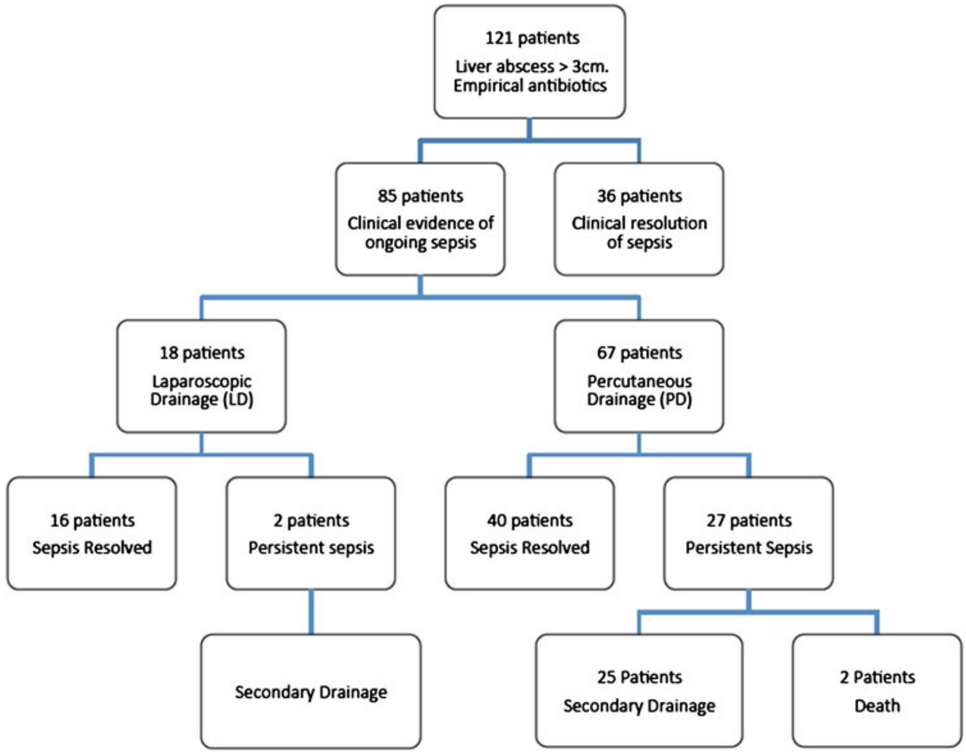

Fig. 1 Work flow of 121 patients with liver abscess at a single institution

drainage, proponents of surgical drainage contend that complete drainage with favorable clinical outcomes is only achievable with open procedures [13, 14]. To date, no randomized controlled trials exist comparing the two methods, although in many centers surgical drainage is often only offered after failure of conservative measures.

Laparoscopic drainage provides an interesting intermediary: a minimally invasive technique with potentially better abscess drainage [15, 16]. No comparisons between laparoscopic and percutaneous drainage have yet been carried out. Therefore, the objective of this study was to compare the outcomes of percutaneously drained and laparoscopically drained abscesses.

Methods

Study population

This retrospective study included 121 consecutive patients admitted to the National University Hospital, Singapore, with radiological evidence of liver abscesses between January 1, 2005, to February 28, 2011. These patients were retrieved from admissions to both the medical and surgical units with a diagnosis of liver abscess. Comprehensive review of patients' case notes and computerized medical records were carried out. NHG Domain Specific Review Board (DSRB) approval (reference DSRB-D/09/224) was received before retrospective chart review.

Inclusion criteria included patients age over 18 years with liver abscesses measuring more than 3 cm at the widest dimension and clinical evidence of infection (presence of fever, raised white cell count, and increased C-reactive protein level). Patients were excluded if they were found to have had previous biliary intervention or liver transplantation. In addition, patients with clinical resolution of sepsis before drainage intervention were also excluded ($n = 39$). Final analysis was carried out on 85 patients.

Treatment

Blood samples were taken and cultured before patients began therapy with a broad-spectrum empirical antibiotic. The choice of antibiotics was ceftriaxone 1 g twice daily and metronidazole 500 mg three times a day based on local microbiology.

At 24–72 h from admission, in the presence of persistent fever or rising inflammatory markers, each patient was subjected to a drainage procedure determined by the physician's preference. This was either percutaneous drainage under radiological guidance or laparoscopic drainage under general anesthesia (Fig. 1).

In our hospital, all percutaneous drainage of liver abscess is performed under radiological guidance. Typically a 5F, 185 mm UNI-well (Angiomed, Karlsruhe, Germany) needle was used. Via the Seldinger technique, a PTFE 0.035-inch J-tip fixed core guide wire is passed into the cavity and the tract dilated with a 6–8F vessel dilator before the insertion of a 6–8F Navarre (Bard Nordic, Sweden) locking pigtail drainage catheter or a soft drain pigtail. The drain is secured and connected to open drainage. The patency of the catheter is maintained with daily flushing of 20 mL of normal saline.

In the laparoscopic approach, the standard method adopted is the positioning of the patient in a French position after induction of general anesthesia. This is followed by insertion of a 10 mm Hassan port under direct vision in the transumbilical position. Further 5 mm ports were inserted at the midclavicular line on either side of the optic port. Using a 5 mm optic camera, a 10 mm laparoscopic ultrasound probe was used to locate the abscess. Under ultrasound guidance, the surface of the abscess is scoured with hook diathermy. Upon entering the cavity, a suction catheter is used to completely deloculate and drain the abscess. After this, a 10F soft tube drain is placed within the cavity and brought out through the enlarged 5 mm port site. The patency of the drain is similarly flushed with normal saline daily. All drains are removed if the drainage is less than 30 mL over a 24-hour period.

Study variables

Variables collected included patient demographics, abscess characteristics, and treatment data and outcome.

Patient demographic variables included age, gender, and American Society of Anesthesiology (ASA) grade, together with diabetes mellitus status, admission white cell count, and C-reactive protein levels. Abscess characteristics included the location of abscess (either right or left lobe), size, locularity (multilocularity was defined as the presence of one or more septation within a single abscess), and number; presence of rupture; and microbiology data. Treatment consisted of the type of drainage procedure.

Length of antibiotic therapy was calculated from the time of intervention to the end date. Antibiotic therapy was continued over 4 to 6 weeks; its cessation was based on continued clinical and biochemical resolution of sepsis. All drains were removed if total drainage totaled less than 30 mL over 24 h. Hospital stay duration was calculated from the time of intervention to the time of discharge.

The primary end point was failure of drainage therapy at 72 h. Failure was defined as persistent fever (temperature ≥37.5 °C) and/or presence of persistently raised white cell count ($\times 10^9$/L) and C-reactive protein (mg/L) at 72 h from time of drainage, resulting in a need for a secondary drainage procedure or resulting in death. Death from sepsis included events occurring within 30 days of the diagnosis or during the same hospital admission. Secondary end points included complications related to the procedure, length of hospital stay, and duration of antibiotic therapy. Complications from the procedure were not considered failures of intervention.

Statistical analysis

Student's *t*-tests were performed to compare continuous variables; Chi square tests were performed to compare categorical variables. A propensity score was initially used to balance demographics and abscess characteristics, which were distributed unequally between the surgery and no-surgery groups [17]. A propensity score was calculated for each patient. The score expressed the patient's probability of undergoing laparoscopic versus percutaneous drainage, given their demographics and abscess characteristics. Because the probability of surgery in clinical practice depends on the surgeon's and patient's decision, predictors that were most likely to influence this decision and ultimate outcome were identified. These variables included age; gender; initial white cell count and C-reactive protein values; size, location, multilocularity, and presence of preprocedure abscess rupture; ASA grade; and diabetes status. The variables were entered into a multivariable logistic regression model as predictors with laparoscopic drainage of abscess as the outcome. From this model, the expected probability of surgery for each patient, given his or her clinical variables, was estimated. Patients were subsequently grouped into deciles on the basis of their propensity score to ensure that within each stratum, comparisons were made for patients with a similar expected probability of having surgery and, to a larger extent, a similar distribution of confounders.

We proceeded to restrict the analysis to patients with an overlapping propensity score, and a logistic regression model was applied for this restricted sample ($n = 75$) to determine predictors of failure of the procedure, defined as persistent sepsis requiring a secondary procedure or death. We also performed an analysis showing the association between the procedure and the risk of complication as well as length of antibiotic therapy and hospital stay. Variables that were not included in propensity analysis were included in the multivariate analysis. Microbiology results and complications were variables not included in the propensity score because we thought they would not affect the surgeon's decision to operate. From these estimates, odds ratios (ORs) with 95 % confidence intervals (CIs) were computed. The 95 % CI for ORs not including 1 was considered statistically significant. All statistical analysis was performed by SPSS software, version 17 (SPSS Inc., Chicago, IL, USA).

Results

Eighty-five patients had clinical evidence of persistent sepsis at 24–72 h. Eighteen patients received laparoscopic drainage and 67 received percutaneous drainage (Table 1). The mean age in the percutaneous group was 53.6 ± 15.6 years and in

Table 1 Clinical characteristics of 85 patients with radiologically confirmed liver abscesses

Characteristic	PD ($n = 67$)	LD ($n = 18$)	p
Age (years)	53.6 ± 15.6	59.2 ± 17.7	0.195
Gender			
Male	40 (78.4 %)	11(61.1 %)	
Female	27 (21.6 %)	7 (38.9 %)	0.914
ASA grade			
1	55 (82.1 %)	6 (33.3 %)	
2	8 (11.9 %)	8 (44.4 %)	
3	4 (6.0 %)	4 (22.3 %)	<0.001
Diabetes mellitus status	38 (56.7 %)	9 (50.0 %)	0.661
C-reactive protein (mg/L)	190.3 ± 117.0	165.3 ± 140.3	0.442
White cell count (10^9/L)	16.9 ± 6.6	15.50 ± 4.6	0.405

PD percutaneous drainage, *LD* laparoscopic drainage

Data are presented as mean ± standard deviation or *n* (%)

ASA American Society of Anesthesiologists

Table 2 Abscess characteristics of 85 patients with radiologically confirmed liver abscesses

Characteristic	PD ($n = 67$)	LD ($n = 18$)	p
Size of liver abscess (cm)	7.6 ± 2.4	7.6 ± 3.3	0.933
Multilocularity	63 (94.0 %)	17 (94.4 %)	0.947
Abscess location			
Right lobe	52 (77.6 %)	10 (55.6 %)	
Left lobe	15 (22.4 %)	8 (44.4 %)	0.077
Presence of preprocedure rupture	2 (3.0 %)	4 (22.2 %)	0.005
Microbiology			
Klebsiella spp.	45 (67.2 %)	7 (38.9 %)	
Escherichia coli	3 (4.5 %)	0 (0 %)	
Enterococcus faecalis	2 (3.0 %)	3 (16.7 %)	
Amoeba	5 (7.5 %)	3 (16.7 %)	
Other	22 (32.8 %)	11 (61.1 %)	0.029
No bacterial growth	12 (17.9 %)	5 (27.8 %)	

PD percutaneous drainage, *LD* laparoscopic drainage

the laparoscopic group; 59.2 ± 17.7 years. In both groups, the vast majority of patients were men: 78.4 % in the percutaneous group versus 61.1 % in the laparoscopic group. Thirty-eight patients (56.7 %) in the percutaneous drainage group had diabetes. This was similar in the laparoscopic drainage group, with 9 patients (50 %). Fifty-five percutaneously drained patients (82.1 %) were classified as ASA grade 1 compared to only 6 patients (33.3 %) in the laparoscopic group.

In both groups, the characteristics of the liver abscesses were similar, with a mean size of 7.6 cm ± 2.4 in the percutaneous drainage group and 7.6 cm ± 3.3 in the laparoscopic drainage group (Table 2). More than 94.0 % of abscesses were multilocular. In addition, 52 percutaneously drained patients (77.6 %) had abscesses located in the right lobe of the liver compared to only 15 patients (22.4 %) in the left lobe. This was similar in the laparoscopic drainage group: 10 patients (55.6 %) had abscesses in the right liver versus 8 (44.4 %) in the left. It is interesting to note that *Klebsiella* spp. were more commonly isolated in the percutaneously drained group (67.2 %) compared to any other bacteria (32.8 %). However, non-*Klebsiella* spp. bacteriology predominated in the laparoscopic drainage group (61.1 %) ($p = 0.029$). Only 3.0 % of pyogenic abscesses in the percutaneous group were ruptured at presentation compared to 22.2 % in the laparoscopic group ($p = 0.005$).

Primary outcomes

Overall, a total of 27 patients (40.3 %) in the percutaneous group experienced treatment failure compared to only 2 patients (11.1 %) in the laparoscopic patients ($p = 0.020$) (Table 3). Twenty-five patients in the percutaneous group eventually experienced resolution of sepsis after secondary procedures. Two deaths occurred in this group from progression of sepsis despite drainage. In contrast, 16 patients (88.9 %) in the laparoscopic group experienced resolution of sepsis after primary intervention. No deaths were reported among those who underwent laparoscopic drainage.

Secondary outcomes

In the percutaneous group, 9 patients (13.4 %) had intervention-related complications compared to 3 patients (16.7 %) in the laparoscopic group (Table 3). Two serious complications occurred in the percutaneous group. This included an inadvertent cannulation of the right portal vein. The drain was removed, and the patient did not experience any further adverse events. A second patient had an inadvertent diaphragmatic injury from the introducer needle traversing the lower most aspect of the diaphragm. However, no clinical pneumothorax was noted on subsequent radiographs. Both complications occurred under fluoroscopic guidance. One drain in the percutaneous group had to be replaced because of occlusion of the lumen resulting from its small caliber.

After laparoscopic drainage, three patients developed complications associated with general anesthesia. Two of the three patients experienced myocardial infarctions, one of which required coronary bypass surgery. The second patient was managed conservatively. Bile leak occurred in our third patient, which resolved spontaneously.

Table 3 Primary outcomes of 85 patients with radiologically confirmed liver abscess after primary intervention

Characteristic	PD ($n = 67$)	LD ($n = 18$)	p
Failure of primary interventional procedure[a]	27 (40.3 %)	2 (11.1 %)	0.020
Complication from procedure	9 (13.4 %)	3 (16.7 %)	
Cannulation of portal vein	1	0	
Diaphragmatic injury	1	0	
Bile leak	0	1	
Bleeding requiring transfusion	1	0	
Unintended dislodgement of drain	5	0	
Occlusion of drain requiring replacement	1	0	
Myocardial infarction	0	2	

PD percutaneous drainage, *LD* laparoscopic drainage

[a] Failure is defined as the presence of persistent sepsis (i.e., presence of ongoing clinical and biochemical evidence of infection) or death from sepsis despite intervention

Table 4 Secondary outcomes of 85 patients with radiologically confirmed liver abscesses after all drainage intervention

Characteristic	Univariate			Multivariate		
	Mean	95 % CI	p	Mean	95 % CI	p
Length of antibiotics (days)						
PD	46.0	33.0–59.1		45.5	41.5–49.4	
LD	43.6	29.7–57.4	0.678	41.7	31.4–52.0	0.437
Length of hospital stay (days)						
PD	23.6	16.4–30.9		15.3	12.6–17.9	
LD	18.2	10.5–25.8	0.100	11.2	5.7–15.7	0.175

PD percutaneous drainage, *LD* laparoscopic drainage

After multivariate analysis of both groups (Table 4), the mean length of antibiotic therapy in the percutaneously drained patients was similar, 45.5 ± 16.7 days versus 41.7 ± 22.3 days in the laparoscopic group. There was also no difference in the mean length of hospital stay between the two groups; 15.3 ± 10.9 days versus 11.2 ± 11.9 days.

Propensity scoring

The main differences between the two groups included the following: ASA status ($p < 0.001$), presence of preprocedure rupture ($p = 0.005$), microbiology ($p = 0.029$), and failure of primary interventional procedure ($p = 0.020$). The predictors for failures/outcomes of primary intervention pointed toward the type of primary intervention. In the multivariate analysis with propensity score, after adjusting for age, gender, ASA grading, diabetes mellitus, initial white cell count, C-reactive protein levels, abscess size, location, multilocularity, and presence of preprocedure abscess rupture, there appears to have been a protective effect from laparoscopic drainage against failure compared to percutaneous drainage (OR, 0.03; 95 % CI, 0.0–0.4; $p = 0.008$) (Table 5). In the restricted analysis with the overlapping propensity score, the laparoscopic group contained no events, and therefore a logistic regression analysis could not be applied. There were no differences in complications between the two interventions ($p = 0.108$).

Discussion

The literature provides much evidence against open surgical drainage compared to percutaneous drainage. Christein et al. [18] reported morbidities of up to 41 % and 15 % mortalities associated with open drainage, as did Mezhir et al. [19] from Memorial Sloan-Kettering Cancer Center. This may be a result of patient selection, as up to 40 % of their patients presented with septic shock. Septic shock with multiorgan failure has been shown to be associated with higher mortality [20]. Christein et al. offered open surgical drainage to acutely unwell patients as well as to patients with failed percutaneous drainage. Despite these studies, some series reported comparable mortality and morbidity rates. For instance, Tan et al. [14] reported much lower associated mortality for both procedures, at 2.8 % in the percutaneous group and 4.5 % in the surgical group. However, it is important to note that in their patient population, none of their patients was in septic shock.

The advantages of surgical drainage over percutaneous drainage must be recognized as an option in a subset of patients. Barakate et al. [21] identified factors that would predict failure of percutaneous drainage. These factors include multilocularity (OR, 15.8; 95 % CI, 4.8–52.4), associated abscess rupture (OR, 6.6; 95 % CI, 2.0–22.6), presence of biliary communication (OR, 5.4; 95 % CI, 1.2–24.3), elevated serum urea (OR, 6.2; 95 % CI 1.7–22.3), creatinine (OR, 6.2; 95 % CI, 1.7–22.3), and

Table 5 Analysis of failure of primary intervention with propensity score of liver abscesses by logistic regression model ($n = 85$)

Primary intervention	Univariate			Multivariate		
	Failure	Crude OR	*p*	Failure	Adjusted OR[b]	*p*
Drainage						
PD	27	1		27	1	
LD	2	0.2 (0.04–0.9)	0.033	2	0.03 (0.0–0.4)	0.008
Microbiology[a]						
2 or more		1			1	
1		0.5 (0.05–4.4)	0.502		0.5 (0.2–1.5)	0.233
Complication[a]						
No		1			1	
Yes		1.1 (0.9–11.4)	0.056		3.3 (0.8–13.7)	0.108

OR odds ratio, *PD* percutaneous drainage, *LD* laparoscopic drainage

[a] Variable not included in the propensity analysis

[b] Adjusted for age, gender, American Society of Anesthesiologists grade, diabetes status, initial white cell count and C-reactive protein levels, abscess size, location, locularity, and presence of preprocedure rupture in a propensity score analysis

total bilirubin (OR, 3.2; 95 % CI, 1.1–9.2). Multilocularity appears to be a predictor of failure in percutaneous drainage as a result of compartmentalization of the cavity into individual pockets [20]. Hope et al. [11] demonstrated a relationship between multilocularity in liver abscess with interventional success. In their study, liver abscesses was classified into three groups, I (small, <3 cm), II (large, >3 cm, unilocular), and III (large, >3 cm, multilocular). They found patients in either group I or II satisfactorily treated with antibiotics and percutaneous drainage, but patients with grade III abscesses did not experience resolution with these measures alone and required operative drainage.

Although comparisons between open and percutaneous drainage have been extensively carried out, none has directly compared percutaneous drainage with laparoscopic drainage. With advancements in minimally invasive surgical techniques, laparoscopic management of pyogenic liver abscess should be considered as an alternative procedure.

The overall findings in our study support laparoscopic drainage in the management of liver abscesses (Table 5). Because this is a retrospective study, we used propensity scoring as a method to remove bias from the management, which may ultimately affect the outcomes studied. A subgroup analysis demonstrating overlapping propensity scores demonstrated no treatment failures in the laparoscopic group. There were also no differences between the two groups in terms of length of antibiotic therapy and hospital stay.

We acknowledge that our study has weaknesses, including the nonrandomized design and the relatively small sample size. The surgeon's decision to operate was influenced by the underlying prognosis of the patient. In addition, the decision for either procedure was at the discretion of the primary doctor, which may explain to some degree the disparity in ASA grading between the two groups. These decisions are inherently difficult to capture and can potentially overestimate the so-called surgery effect. The propensity score method was used to minimize the effects of confounding arising from imbalances in known prognostic variables between the surgery and percutaneous group, thereby reducing the overestimation of the surgery effect. However, despite our best efforts, residual confounders may be unaccounted for.

We did note that a larger proportion of abscesses were located in the left liver in the laparoscopic group compared to the percutaneous group (44.4 % vs. 24.4 %), although this was statistically insignificant. Perhaps the better results seen the laparoscopic group are a direct correlation of a more benign abscess arising from the left liver versus the right. This has not been demonstrated in our study or in the literature. Further, 22.2 % of abscesses in the laparoscopic group were associated with preprocedure rupture compared to only 3 % in the percutaneous,group which may indicate that the abscesses in the laparoscopic group may be more liquefied and therefore more amendable to drainage. However, with the laparoscopic technique, an additional benefit provided by this technique includes the ability to provide adequate abdominal cavity washout, which may translate to better sepsis control. This will not be easily achievable by the percutaneous method.

Microbiology of the liver abscess was only available after aspiration had taken place. In eight of our patients, amoeba grew in culture. The mainstay of amoebic liver abscess is antibiotic therapy, specifically metronidazole. All patients with liver abscesses have been initially treated with this agent empirically; therefore, in patients whose disease fails to respond to antibiotic therapy, aspiration of the liver abscess is still indicated. Microbiology was not included in the propensity scoring and therefore did not directly affect failure of intervention.

After failed primary intervention, patients were treated with a secondary drainage procedure at the discretion of the physician. This was either a laparoscopic or percutaneous method; however, because of the large crossover, we did not include this in our analysis. The aim of our study was to compare source control between the two interventions at first intention. Shortening the period of sepsis perhaps reduces patient morbidity and mortality.

Although only minor complications existed in the percutaneous group compared to the two postoperative myocardial infarctions in the laparoscopic group (presumably contributed to by the general anesthesia), no deaths occurred in the laparoscopic group due to sepsis, whereas two such deaths occurred in the percutaneous group. Complications associated with interventions were not included in the propensity scoring and therefore did not affect failure of intervention.

In our study, we did not find any significant differences in the length of hospital stay or in antibiotic therapy. We think this is because we currently do not have a standardized protocol for the management of these patients; as a result, the length of hospital stay was at the discretion of the attending physician. Similarly, a 6-week course of antibiotics was typically applied for all patients regardless of type of drainage.

Nevertheless, with the information that we do currently possess, laparoscopic drainage of liver abscesses appears to offer several advantages, and although we cannot definitively claim the superiority of this method as a result of the retrospective nature of this study, laparoscopic drainage should be considered in the management of liver abscess. However, randomized controlled trials are needed to test the superiority of laparoscopic drainage.

Conflict of interest Liza Tan, Hui Jun Zhou, Mikael Hartman, Iyer Shridhar Ganpathi, Krishnakumar Madhavan, and Stephen Chang have no conflicts of interest or financial ties to disclose.

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