Original Article

Percutaneous catheter drainage versus needle aspiration for liver abscess management: an updated systematic review, meta-analysis, and meta-regression of randomized controlled trials

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Background: Liver abscess is a life-threatening condition. Percutaneous catheter drainage (PCD) and percutaneous needle aspiration (PNA) are both minimally invasive techniques used to manage liver abscess. We aim to compare both techniques' efficacy and safety.

Methods: We performed a systematic review and meta-analysis involving randomized controlled trials (RCTs) from PubMed, Embase, Scopus, WOS, Cochrane, and Google scholar until July 22nd, 2022. We pooled dichotomous outcomes using risk ratio (RR) presented with a 95% confidence interval (CI) and continuous outcomes using mean difference (MD) with 95% CI. We registered our protocol with ID: CRD42022348755.

Results: We included 15 RCTs with 1,626 patients. Pooled RR favored PCD (RR: 1.21 with 95% CI: 1.11, 1.31, P<0.00001) in success rate and recurrence after six months (RR: 0.41 with 95% CI: 0.22, 0.79, P=0.007). We found no difference in adverse events (RR: 2.2 with 95% CI: 0.51, 9.54, P=0.29). Pooled MD favored PCD in time to clinical improvement (MD: −1.78 with 95% CI: −2.50, −1.06, P<0.00001), time to achieve 50% reduction (MD: −2.83 with 95% CI: −3.36, −2.30], P<0.00001) and duration of antibiotic needed (MD: −2.13 with 95% CI: −3.84, −0.42, P=0.01). We found no difference in the duration of hospitalization (MD: −0.72 with 95% CI: −1.48, 0.03, P=0.06). The results were heterogeneous for all the continuous outcomes which were all measured in days.

Conclusions: Our updated meta-analysis concluded that PCD is more effective than PNA in liver abscess drainage. However, evidence is still uncertain, and more high-quality trials are still required to confirm our results.

Keywords: Hepatic; catheter; drainage; needle; aspiration

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Introduction

Liver abscess is a pus-filled encapsulated mass in the liver parenchyma caused by a trauma or infection; bacterial, fungal, or parasitic microorganisms spread via the portal circulation (1,2). The most common type of liver abscess is bacterial, with Klebsiella pneumonia and Escherichia coli as the primary pathogenic microorganisms, followed by amebic liver abscesses (3-5). Cryptogenic abscesses, with unknown etiology, also represent about 20% of liver abscess (1,3). The incidence of liver abscess varies from 1.0 to 3.6 per 100,000 in Western nations (5), but it may rise up to 17 per 100,000 in Asia (6). Liver abscess is a life-threatening disease with a fatality rate of up to 15% to 19% (7-9). However, earlier diagnosis, and minimally invasive therapy advancement have significantly reduced liver abscess-associated mortality (7).

The management of patients with liver abscess should be personalized. It is critical to have the right antibiotics and sufficient drainage. The Abscess pathogenesis, clinical features, and patient overall status should be considered during the management. Generally, both antibiotic intervention and sufficient drainage are essential for managing liver abscess (1,3,10). The selected antibiotics should be effective against the most prevalent pathogens and until cultural results appear, empirical treatment should be started. Therefore, antibiotic treatment should include a combination of an aminoglycoside with either clindamycin or metronidazole or a beta-lactam antibiotic with an anaerobic covering (3,4,10).

Drainage of liver abscess may be achieved percutaneously (ultrasound or computed tomography guided) or surgically (via laparoscopic or open approach) (4,10). Anesthesia risk, the existence of a primary intra-abdominal pathology, the procedure's success rate, and practitioner's experience should be considered when making a treatment decision (10). Some studies reported that percutaneous drainage is preferred to surgical drainage for different reasons (11-13). Hence, in the absence of urgent surgical considerations such as peritonitis, percutaneous image-guided drainage is recommended as the first-line therapy. Large, multiloculated abscesses and those accompanied by accompanying biliary disease may benefit from surgical drainage (11). Surgical drainage is still recommended for inaccessible abscesses, numerous lesions that cannot be adequately handled percutaneously, and abscesses that do not respond to less invasive techniques (11).

Percutaneous US-guided drainage can be performed using catheter drainage (PCD) or needle aspiration (PNA). PCD is generally accepted as a safe and successful treatment option for liver abscess when combined with antibiotics. Some experts advocate repeated PNA over PCD because it is simpler to execute, less aggressive, less hazardous for post-procedure septicemia, and less costly (14).

However, published studies are conflicting and inconsistent about the best method for liver abscess drainage. A previously published systematic review and meta-analysis showed the superiority of PCD over PNA in some aspects, however, the data were derived from only five randomized controlled trials (RCTs) (15). Therefore, we conducted this systematic review and meta-analysis to update the synthesized evidence to evaluate the best approach for liver abscess drainage; PCD or PNA. We present the following article in accordance with the PRISMA reporting checklist (available at https://atm.amegroups.com/article/view/10.21037/atm-22-4663/rc).

Highlight box

Key findings

- PCD is more effective than PNA in liver abscess drainage leading to a better success rate, faster resolution, decreased need for antibiotics, and similar safety data.

What is known and what is new?

- Both antibiotic intervention and sufficient drainage are essential for managing liver abscesses. Drainage could be done percutaneously or surgically. Percutaneous image-guided drainage is recommended as the first-line therapy.
- However, published studies are conflicting and inconsistent about the best method for liver abscess drainage.
- We aim to evaluate the best approach for liver abscess drainage; PCD or PNA.

What is the implication, and what should change now?

- Future trials should report data for separate etiological diagnoses because our subgroup analysis favored PCD over PNA for pyogenic and amoebic abscesses and showed no difference for pyogenic only. We need to conduct more trials in different populations to decrease the limitation of our findings' generalizability.

Methods

Protocol registration

Our review protocol was prospectively submitted and published in PROSPERO with ID: CRD42022348755. We conducted a systematic review and meta-analysis mainly guided by the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement and the Cochrane Handbook of Systematic reviews and meta-analysis (16,17).

Data sources & search strategy

Web of Science, SCOPUS, EMBASE, PubMed, Google Scholar, and Cochrane Central were systematically searched by two reviewers (A.M. and M.T.) from inception until July 22, 2022. No search filters were used. The thorough search strategy and results are outlined in Table S1.

Eligibility criteria

We included only RCTs with the next PICO: population (P): patients with single or multiple, pyogenic or amebic liver abscesses; intervention (I): catheter drainage (C): needle aspiration; outcomes (O): principal outcomes of this study are to evaluate the success rate (clinical resolution of infection and radiological evidence of abscess resolution, either total disappearance or more than 50% decrease in the longest diameter before intervention for detailed definition check *Table 1*), duration of hospital stay, recurrence after six months and procedure-related adverse events. Secondary outcomes include time to clinical improvement (defined as relief of pain, absence of fever for 24 hours, absence of hepatic tenderness, and normalization of elevated leukocyte), time to achieve a 50% reduction in abscess cavity size, and duration of antibiotics needed. Animal studies, pilot studies, observational studies (cohort, case-control, cross-sectional, case series, and case reports), single-arm clinical trials, *in vitro*, book chapters, editorials, press articles, and conference abstracts were all ruled out from our analysis.

Study selection

After duplicates were removed using Covidence, two investigators (A.A. and M.E.) independently evaluated the titles and abstracts of the retrieved articles (33). Then, they checked the full texts of the relevant records for the previously mentioned eligibility criteria. To resolve any disagreements, a third reviewer (A.M.) was invited.

Data extraction

Using a pilot-tested extraction form, four reviewers (A.A., H.A., O.A., and M.E.) independently extracted the next data from the eligible articles: study characteristics (year of publication, country, maximum number of needle attempts, study design, total participants, type, and size of the abscesses, used antibiotics, and follow up duration). Baseline information includes (age, sex, number of patients in each group, number and location of abscesses, different clinical features including (fever, rigors, jaundice, and right hypochondrial pain), and different comorbidities including (diabetes, colitis, biliary stones, cholangitis and history of gastrointestinal surgeries. Efficacy outcomes data (the success rate, duration of hospital stay, recurrence after 6 months, procedure-related adverse events, time to clinical improvement, time to achieve a 50% reduction in abscess cavity size, and duration of antibiotics needed). Disagreements were resolved through discussion.

Risk of bias and quality assessment

Guided by The Cochrane Collaboration's tool for assessing the risk of bias in randomized trials, four reviewers (A.A., H.A., O.A., and M.E.) independently assessed the included studies for risk of bias (ROB) (34), the assessed domains include random sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessment, incomplete outcome data, selective reporting, and other bias. Disagreements were resolved by consensus. For the quality of evidence assessment, two reviewers (M.T. and B.A.) adopted the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) working group guidelines (35,36). Our findings on the quality of evidence were explained, documented, and included in each outcome's reporting. Any disagreements were handled via consensus.

Statistical analysis

Data synthesis was carried out with RevMan v5.3 software (37). We pooled dichotomous outcomes using risk ratio (RR) presented with the corresponding 95% confidence interval (CI) and continuous outcomes using mean difference (MD) with 95% CI. We used the

Table 1 Summary characteristics

Study ID	Study design	Country	Total participants	Type of abscess pyogenic amebic or both	Size of abscess (cm)	Used antibiotics	Maximum number of needle aspirations	Needle caliber and type	Catheter caliber and type	Follow-up duration	Success rate definition
Abusedera *et al.* 2014 (18)	RCT	Egypt	88	Pyogenic	>2	Cefazoline 1 g/12 h and Augmentin 1.2 g/8 h IV and with Metronidazole (500 mg IV or 500 mg orally three times a day)	Three	18 Gauge trocar needle	Plastic based catheter	6 months	Clinical and sonographic resolution
Ahmed *et al.* 2021 (19)	RCT	India	543	Amoebic and pyogenic	>5	Ceftriaxone 1 g 12 hourly and metronidazole 500 mg 6 hourly	Three	16–18 Gauge long needle	14 French pigtail	6 months	N/A
Bansel *et al.* 2015 (20)	Double blinded RCT	India	121	Amoebic and pyogenic	>5	NA	NA	16–18 Gauge spinal needle	28 French catheter	6 months	N/A
Batham *et al.* 2016 (21)	RCT	India	50	Amoebic and pyogenic	≥5	Cefazolin 1g IV b.i.d. injection, Metronidazole 750 mg IV every t.i.d. injection, Gentamicin 80 mg IV b.i.d. and chloroquine 600 mg for 2 days (600 mg is total dose for a day which is given in 2 divided doses and not 600 mg q.i.d.) followed by 300 mg for 19 days (given in 2 divided doses)	Three	16 Gauge comet tail needle	8–14 French multiple	6 months	Clinical and sonographic resolution
Gajera *et al.* 2022 (22)	RCT	India	50	Amoebic and pyogenic	>5	Ceftriaxone 1 g 12 hourly and metronidazole 500 mg 6 hourly	NA	16–18 Gauge long needle	14 French pigtail catheter with sharp trocar	6 Months	N/A
Gupta *et al.* 2011 (23)	RCT	India	82	Amoebic	>10	Intravenous metronidazole was continued for at least 10 days and until fever had subsided for at least 48 h; this was followed by oral metronidazole 40 mg/kg/day in three divided doses for the next 3 weeks	Three	16 Gauge disposable trocar needle	Trocar with a 14 French multi-sidehole pigtail catheter	2 years	Clinical and sonographic resolution
Hanumathappa *et al.* 2016 (24)	RCT	India	30	Amoebic and pyogenic	>5	Metronidazole 1 g IV every t.i.d., injection Ceftriaxone 1 g IV b.i.d.	Three	18 Gauge spinal needle	12–14 paediatric ICD tube	4 months	Clinical and sonographic resolution
Kulhari *et al.* 2019 (25)	RCT	India	190	Amoebic and pyogenic	>5	NA	NA	16–18 Gauge	12 French pigtail catheter	6 months	Clinical and sonographic resolution
Rajak *et al.* 1998 (26)	RCT	India	50	Amoebic and pyogenic	NA	Broad spectrum antibiotics, including an aminoglycoside (cloxacillin at 150 mg/kg per day IV and gentamicin at 4.5 mg/kg per day IV) with metronidazole (500 mg IV or 800 mg orally three times a day) and chloroquine	Two	18 Gauge needle	8-I 2 French pigtail or Malecot drainage catheter	Range, 8–37 weeks; mean, 20 weeks	Clinical and sonographic resolution
Singh *et al.* 2009 (27)	RCT	India	72	Amoebic and pyogenic	>10	Ceftriaxone 1 g, gentamicin 1 mg/kg and metronidazole 7.5 mg/kg, each administered three times a day was given	Three	16 Gauge disposable trocar needle	14 French multi-sidehole pigtail catheter	4 months	Clinical and sonographic resolution
Singh *et al.* 2019 (28)	RCT	India	66	Amoebic and pyogenic	>3	NA	Three	18 Gauge disposable trocar needle	12 French pigtail	6 months	Sufficient drainage without surgical drainage leading to infection resolution and discharge from hospital
Singh *et al.* 2013 (29)	RCT	India	60	Amoebic and pyogenic	>5	Injection Metronidazole 750 mg IV every t.i.d., injection, Cefazolin 1 g IV b.i.d., injection, Gentamicin 80 mg IV b.i.d., and chloroquine 600 mg for 2 days (600 mg is total dose for a day which is given in 2 divided doses and not 600 mg q.i.d.) followed by 300 mg for 19 days (given in 2 divided doses)	Three	23 Gauge needle	12 French pigtail catheter	6 months	Clinical and sonographic resolution
Surya *et al.* 2020 (30)	RCT	India	100	Amoebic and pyogenic	>5	Intravenous ceftriaxone 1 g, gentamicin 1 mg/kg and metronidazole 7.5 mg/kg, each administered three times a day. Intravenous antibiotics were continued for 10 days or for at least 48 h, followed by appropriate oral antibiotics for the next 4 weeks	Two	18 Gauge disposable trocar needle	12 French pigtail catheter	6 months	Clinical and sonographic resolution
Yu *et al.* 2004 (31)	RCT	China	64	Pyogenic	>3	Ampicillin 500 mg 6 hourly, cefuroxime 750 mg 8 hourly, and metronidazole 500 mg 8 hourly	Three	18 Gauge disposable trocar needle	8 French multi-sidehole pigtail catheter	Biweekly until completion of oral antibiotics without evidence of recurrent infection	Sufficient drainage without surgical drainage leading to infection resolution and discharge from hospital
Zerem *et al.* 2007 (32)	RCT	Bosnia and Herzegovina	60	Pyogenic	>3	IV cefazolin 1 g three times a day and gentamicin 1 mg/kg three times a day for 10 days	Three	18 Gauge disposable trocar needle	8 French multiple sidehole pigtail catheter	6 months	Clinical and sonographic resolution

Clinical resolution of infection and ultrasound evidence of abscess resolution, either total disappearance or more than 50% decrease in the longest diameter before intervention. RCT, randomized controlled trials; NA, not available; PCD, percutaneous catheter drainage; PNA, percutaneous needle aspiration; N, number.

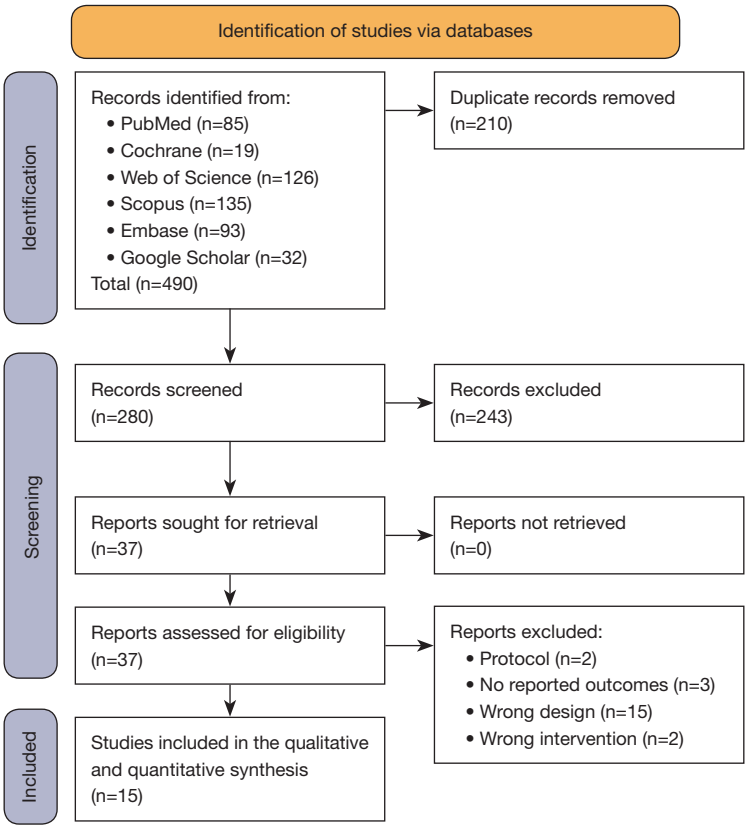

Figure 1 PRISMA flow chart of the screening process, which included searches of databases, and other sources.

I-square and Chi-square tests to examine heterogeneity; the Chi-square test determines if there is substantial heterogeneity, while the I-square determines the magnitude of heterogeneity. A substantial heterogeneity (for the Chi-square test) is defined as an alpha level below 0.1, according to the Cochrane Handbook (chapter nine) (16), while the I-square test is interpreted as follows: (0–40%: not significant; 30–60%: moderate heterogeneity; 60–90%: considerable heterogeneity). We utilized the random-effects model if the I-squared test was more than 50%. We performed a sensitivity analysis in case of significant heterogeneity to investigate the source of heterogeneity. Moreover, we made funnel plots to reveal publication bias for the success rate and duration of hospital stay outcomes, and we also tried to quantify publication bias by using the Egger test of intercept (38) via Comprehensive Meta-analysis Software (39). Also, we performed a subgroup analysis built on the type of the abscess, catheter caliber, and needle caliber. Finally, we conducted a meta-regression built on the weighted mean of both abscess size and volume.

Results

Search results and study selection

We identified 490 records after databases searching, then 210 duplicates were excluded. Title and abstract screening excluded 243 irrelevant records. We moved to full-text screening with 37 articles, 22 articles were excluded. Finally, 15 articles met our inclusion criteria (18-32). The prisma flow chart of the detailed selection process is demonstrated in *Figure 1*.

Characteristics of included studies

We included 15 trials with a total of 1,626 participants who were randomized to either PCD (n=824) or PNA (n=802). Further included trials' characteristics are presented in *Table 1*. Age was variable between included studies but mostly fell within the range of 16 to 70 years old. There was a male predominance in our study, 1,626 patients (79%) were males, and the right lobe of the liver was more

likely to be affected. Detailed baseline characteristics of the participants are presented in *Table 2*. Furthermore, microbiological diagnosis is clarified in *Table 3*.

Risk of bias and quality of evidence

We assessed the quality of the included studies according to the Cochrane risk of bias tool (34), as shown in *Figure 2*. All of the included trials had a low risk of random sequence generation bias except Abusedera *et al.* 2014 (18), Bansal *et al.* 2015 (20), Gajera *et al.* 2022 (22), Hanumathappa *et al.* 2016 (24), Kulhari *et al.* 2019 (25), and Rajak *et al.* 1998 (26) with an unclear risk of selection bias. All the included studies had a low risk of allocation concealment bias except Abusedera *et al.* 2014 (18), Ahmed *et al.* 2021 (19), Batham *et al.* 2016 (21), Bansal *et al.* 2015 (20), Gajera *et al.* 2022 (22), Hanumathappa *et al.* 2016 (24), Kulhari *et al.* 2019 (25), and Rajak *et al.* 1998 (26) with an unclear risk.

Moreover, all included trials had an unclear risk of performance and detection biases except in Bansal *et al.* 2015 (20), as the studies were of the surgical type, so blinding was hard. Also, all of the included trials had a low risk of attrition bias. Furthermore, all included trials had an unclear risk of reporting bias except Singh *et al.* 2009 (27), Singh *et al.* 2013 (29), and Singh *et al.* 2019 (28), which had low risk. Finally, all of the included trials had a low risk of other bias except Ahmed *et al.* 2021 (19), Bansal *et al.* 2015 (20), Batham *et al.* 2016 (21), Gajera *et al.* 2022 (22), Hanumathappa *et al.* 2016 (24), and Singh *et al.* 2013 (29). Author judgments are furtherly clarified in Table S2.

Using the GRADE system, all the included primary outcomes yielded moderate to very-low quality evidence. Details and explanations are clarified in *Table 4*.

Primary outcomes

Success rate

The pooled RR favored PCD (RR: 1.21 with 95% CI: 1.11, 1.31, P<0.00001) (very-low quality evidence) (*Figure 3A*, *Table 4*). The pooled studies were heterogenous (P<0.00001, I-square =77%). Therefore, we conducted a sensitivity analysis to investigate the source of heterogeneity; however, heterogeneity was not settled by sensitivity analysis (Table S3). Meta-regression analysis based on abscess size showed significant decrease in success rate with increasing the abscess size [b =–0.0343, standard error (SE) =0.0091, P=0.0002] (Figure S1). However, pus volume was not associated with decreased success rate (b =–0.0005, SE =0.0017, P=0.7592) (Figure S2). Moreover, we conducted a subgroup analysis based on the following:

(I) Abscess type: the test of subgroup differences was not significant (P=0.73) (Figure S3);
(II) Needle size: the test of subgroup differences was not significant (P=0.34) (Figure S4);
(III) Catheter size: the test of subgroup differences was not significant (P=0.42) (Figure S5).

Finally, we visually detected publication bias (Figure S6), and Egger's test was significant (P=0.00469).

We calculated the overall failure rate in both groups, where the overall failure in the PCD group was 25/784 (3.2%), the overall failure in the PNA group was 116/762 (15.22%), further details are given in the Table S4.

Recurrence after 6 months

The pooled RR favored PCD (RR: 0.41 with 95% CI: 0.22, 0.79, P=0.007) (moderate-quality evidence). The pooled studies were homogenous (P=0.35, I-square =9%) (*Figure 3B*, *Table 4*).

Procedure-related adverse events

We found no statistically significant difference between the PCD group and the PNA group (RR: 2.20 with 95% CI: 0.51, 9.54, P=0.29) (low-quality evidence) (*Figure 3C*, *Table 4*). The pooled studies were homogenous (P=0.98, I-square =0%).

We calculated the overall mortality that was 6/784 (0.77%) in the PCD group and 4/762 (0.52%) in the PNA group, further details are given in the Table S4.

Duration of hospitalization

We found no statistically significant difference between the PCD group and the PNA group (MD: –0.72 with 95% CI: –1.48, 0.03, P=0.06) (low quality evidence) (*Figure 3D*, *Table 4*). The pooled studies were heterogenous (P=0.0007, I-square =70%). Therefore, we conducted a sensitivity analysis to investigate the source of heterogeneity; however, heterogeneity was not resolved by sensitivity analysis (Table S3). Moreover, we conducted a subgroup analysis based on the following:

(I) Abscess type: the test of subgroup differences was not significant (P=0.53) (Figure S7);
(II) Needle size: the test of subgroup showed no differences (P=0.17) (Figure S8);
(III) Catheter size: the test of subgroup showed no differences (P=0.46) (Figure S9).

Finally, we did not visually detect publication bias

Table 2 Baseline characteristics

Study	Number of patients in each group		Age (years), mean (SD)		Gender (male), N (%)		Comorbidities, N (%)								Clinical features, N (%)								No. of abscess solitary: multiple, N (%)		Localization Rt, Lt, B, N (%)	
							Diabetes		Biliary stones		Cholangitis		History of gastrointestinal surgery		Rt. hypo pain		Rigors, chills		Fever		Jaundice					
	Needle	Catheter	Needle	Catheter	Needle	Catheter	Needle	Catheter	Needle	Catheter	Needle	Catheter	Needle	Catheter	Needle	Catheter	Needle	Catheter	Needle	Catheter	Needle	Catheter	Needle	Catheter	Needle	Catheter
Abusedera *et al.* 2014 (18)	43	45	Range [18–37]	Range [20–71]	32 (74.4)	33 (73.3)	24 [56]	25 [55]			NA				43 [100]	45 [100]	NA		42 [98]	42 [93]	NA		S: 33 [77], M: 10 [23]	S: 37 [82], M: 8 [18]	Rt: 26 (60.5), Lt: 13 (30.3), B: 4 (9.3)	Rt: 27 [60], Lt: 13 (28.9), B: 5 (11.1)
Ahmed *et al.* 2021 (19)	271	272	35 [16–78], median (range)		8:1 male: female		43 [8]		65 [12]		54 [10]		NA		456 [84]		NA		483 [89]		103 [19]		NA	NA	Rt: 413 [76], Lt: 43 [8], B: 87 [16]	
Bansel *et al.* 2015 (20)	52	69	Range [20–60]		110 [90]						NA				102 [84]		30 [25]		117 [97]		NA		S: 15 (12.4), M: 106 (87.6)		Rt: 99 [82], Lt: 15 [12], B: 7 [6]	
Batham *et al.* 2016 (21)	25	25	Range [15–65]		43 [86]						NA				46 [92]		15 [30]		43 [86]		NA		NA		NA	
Gajera *et al.* 2022 (22)	25	25	Range [18–61]		32 [64]						NA										NA					
Gupta *et al.* 2011 (23)	40	42	43 (16.5)	42.5 (15.75)	29 [72]	33 (78.6)	19 (47.5)	22 (52.4)	10 [25]	10 (23.8)	5 (12.5)	6 (14.3)	7 (17.5)	10 (23.8)	37 (92.5)	40 (95.2)	5 (12.5)	9 (21.4)	31 (77.5)	35 (83.3)	13 (32.5)	12 (28.6)	S: 34 [85], M: 6 [15]	S: 37 [88], M: 5 (11.9)	Rt: 31 (77.5), Lt: 2 [5], B: 7 (17.5)	Rt: 34 [80], Lt: 2 (4.7), B: 6 (14.3)
Hanumathappa *et al.* 2016 (24)	15	15	Range [16–58]		26 (86.6)						NA				30 [100]		NA		30 [100]		3 [10]		S: 23 [75], M: 7 [25]		Rt: 24 [80], Lt: 3 [10], B: 3 [10]	
Kulhari *et al.* 2019 (25)	95	95	NA		158 (83.15)						NA				89 (93.7)	91 (95.8)	48 (50.5)	47 (49.47)	87 (91.5)	86 (90.52)	10 (10.5)	13 (13.7)	S: 66 (69.5), M: 29 (30.5)	S: 74 (77.9), M: 21 (22.1)	Rt: 74 (77.9), Lt: 15 (15.8), B: 6 (6.3)	Rt: 81 (85.3), Lt: 13 (13.7), B: 1 (1.1)
Rajak *et al.* 1998 (26)	25	25	35.44 [2–72], mean (range)	35.6 [4–65]	19 [76]	19 [76]					NA				25 [100]	25 [100]	NA		25 [100]	23 [92]	3 [12]	3 [12]	S: 18 [72], M: 7 [28]	S: 20 [80], M: 5 [20]	Rt: 17 [68], Lt: 3 [12], B: 5 [20]	Rt: 17 [68], Lt: 4 [16], B: 4 [16]
Singh *et al.* 2009 (27)	36	36	42±18	40±7.15	25 (75.75)	28 (77.77)	5 (14.4)	3 (8.3)	12 [33]	11 (30.5)	4 (11.1)	7 (19.4)	4 (11.1)	2 (5.5)	33 (91.7)	34 (94.4)	8 (22.2)	10 (27.8)	29 (80.5)	27 [75]	8 (22.2)	3 (8.3)	S: 28 [78], M: 8 [22]	S: 31 [86], M: 5 [14]	Rt: 29 (80.5), Lt: 1 (2.7), B: 16 (16.6)	Rt: 32 (88.9), Lt: 0 [0], B: 4 (11.1)
Singh *et al.* 2019 (28)	33	33	41±8.2	42±8.4	27 (81.81)	28 (84.8)	8 (24.4)	9 (27.3)			NA				NA				24 [73]	22 [67]	20 [61]	18 [55]	S: 28 [85], M: 5 [15]	S: 30 [91], M: 3 [9]	Rt: 24 [73], Lt: 6 [18], B: 3 [9]	Rt: 25 [76], Lt: 3 [9], B: 5 [15]
Singh *et al.* 2013 (29)	30	30	Range [16–58]		53 (88.3)						NA				56 [93]		17 [28]		53 [88]		NA				NA	
Surya *et al.* 2020 (30)	50	50	Range [22–74]		88 [88]						NA				28 [56]	34 [68]	26 [52]	28 [56]	38 [76]	44 [88]	20 [40]	18 [36]	S: 44 [88], M: 6 [12]	S: 48 [96], M: 2 [4]	Rt: 38 [76], Lt: 6 [12], B: 6 [12]	Rt: 36 [72], Lt: 10 [20], B: 4 [8]
Yu *et al.* 2004 (31)	32	32	58.67±24.05	61±16.23	19 (59.4)	19 (59.4)	10 (31.3)	9 (27.3)	1 (3.1)	0 [0]	1 (3.1)	2 (6.2)	9 (27.3)	8 (24.8)	10 (31.3)	5 (15.6)	8 (24.8)	8 (24.8)	27 (84.4)	26 (81.3)	21 [42]	19 (59.4)	S: 27 [84], M: 5 [16]	S: 29 [90], M: 3 [10]	NA	
Zerem *et al.* 2007 (32)	30	30	52.1±3.4	50.3±5.4	12 [40]	12 [40]					NA				15 [50]	16 [53]	NA		24 [80]	21 [70]	NA		S: 28 [93], M: 2 [7]	S: 28 [93], M: 2 [7]	Rt: 16 (53.3), Lt: 13 (4.3), B: 1 (3.3)	Rt: 17 (56.7), Lt: 11 (36.7), B: 1 (6.6)

Rt, right lobe; Lt, left lobe; B, both; S, single; M, multiple; NA, not available; SD, standard deviation; N, number.

Table 3 Microbiological diagnosis

Study ID	Microbiological diagnosis, %								
	Amoebic liver abscess	Pyogenic liver abscess							
		Klebsiella pneumoniae	*Escherichia coli*	*Staphylococcus aureus*	*Streptococcus milleri*	*Pseudomonas aeruginosa*	*Enterococcus*	Polymicrobes	Negative
Abusedera *et al.* 2014 (18)	0	25	17.1	15.9	N/A	10.2	N/A	9.1	22.7
Ahmed *et al.* 2021 (19)	62	53.1	20.1	11.2	5.6	3.5	3.3	3.2	N/A
Bansal *et al.* 2016 (20)	9.9				85.1				
Batham *et al.* 2016 (21)	58	8	12	4	N/A	4	N/A	N/A	72
Gajera *et al.* 2022 (22)	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Gupta *et al.* 2011 (23)	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Hanumathappa *et al.* 2016 (24)	N/A	6.6	20	3.3	N/A	N/A	N/A	N/A	70
Kulhari *et al.* 2019 (25)	64	10.5	18.4	1.1	N/A	2.1	N/A	N/A	68
Rajak *et al.* 1998 (26)		N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Singh *et al.* 2009 (27)	67	6.9	12.5	1.4	N/A	2.8	N/A	N/A	0
Singh *et al.* 2019 (28)	77				23				
Singh *et al.* 2013 (29)	58	10	13.3	3.3		3.3			
Surya *et al.* 2020 (30)	38				10				
Yu *et al.* 2004 (31)	0	31.3	4.7	1.6	N/A	N/A	N/A	11	40.6
Zerem *et al.* 2007 (32)	0	31.7	8.3	5	6.7	1.7	1.7	16.7	25

N/A, not available.

(Figure S10), and Egger's test was not significant (P=0.30961).

Secondary outcomes

Time to clinical improvement (days)

The pooled MD favored PCD (MD: −1.78 with 95% CI: −2.50, −1.06, P<0.00001) (very-low quality evidence) (*Figure 4A*, *Table 4*). The pooled studies were heterogenous (P<0.00001, I-square =90%). Therefore, we conducted a sensitivity analysis to investigate the source of heterogeneity; however, heterogeneity was not settled by sensitivity analysis (Table S5).

Time to achieve a 50% reduction in abscess cavity size (days)

The pooled MD favored PCD (MD: −2.83 with

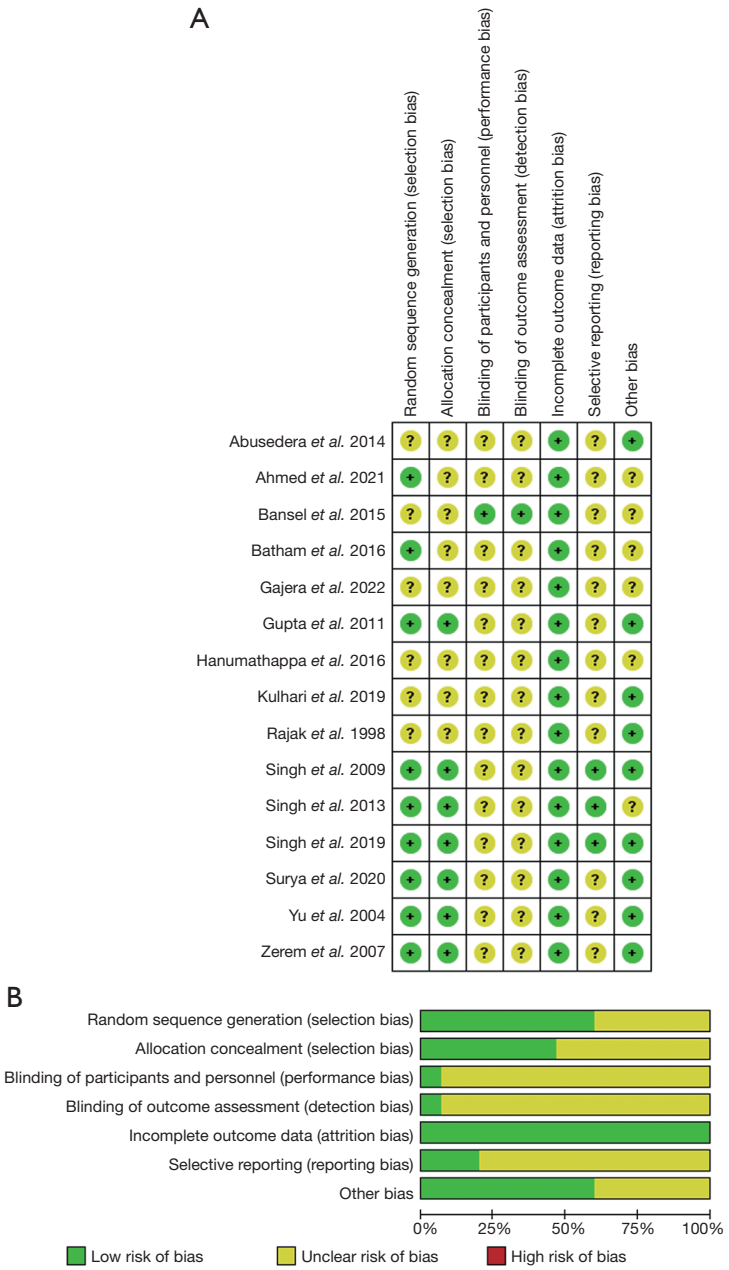

Figure 2 Summary of risk of bias [(A) review authors' judgments about each risk of bias item for each included study, (B) review authors' judgments about each risk of bias item presented as percentages across all included studies].

95% CI: −3.36, −2.30, P<0.00001) [very-low quality evidence (*Figure 4B*, *Table 4*)]. The pooled studies were heterogenous (P=0.0003, I-square =81%). Therefore, we conducted a sensitivity analysis to investigate the source of heterogeneity; however, heterogeneity was not resolved by sensitivity analysis (Table S5).

Duration of IV antibiotics (days)

The pooled MD favored PCD (MD: −2.13 with 95% CI: −3.84, −0.42, P=0.01) (very-low quality evidence) (*Figure 4C*, *Table 4*). The pooled studies were heterogenous (P<0.00001, I-square =93%). Therefore, we conducted a sensitivity analysis to investigate the source of heterogeneity; however,

Table 4 GRADE evidence profile

No. of studies	Certainty assessment						No. of patients		Effect		Certainty	Importance
	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Success rate	Placebo	Relative (95% CI)	Absolute (95% CI)		
Success rate												
13	Randomised trials	Serious[a]	Very serious[b]	Not serious	Not serious	Publication bias strongly suspected[c]	758/784 (96.7%)	629/762 (82.5%)	RR 1.21 (1.11 to 1.31)	173 more per 1,000 (from 91 more to 256 more)	⊕◯◯◯ (very low)	Critical
Recurrence after 6 months												
8	Randomised trials	Not serious	Not serious	Not serious	Serious[d]	None	12/493 (2.4%)	29/487 (6.0%)	RR 0.41 (0.22 to 0.79)	35 fewer per 1,000 (from 46 fewer to 13 fewer)	⊕⊕⊕◯ (moderate)	Critical
Procedure-related adverse events												
6	Randomised trials	Serious[e]	Not serious	Not serious	Serious[f]	None	5/218 (2.3%)	2/216 (0.9%)	RR 2.20 (0.51 to 9.54)	11 more per 1,000 (from 5 fewer to 79 more)	⊕⊕◯◯ (low)	Critical
Duration of hospital stay (days)												
9	Randomised trials	Not serious	Very serious[g]	Not serious	Not serious	None	631	611	–	MD 0.72 days fewer (1.48 fewer to 0.03 more)	⊕⊕◯◯ (low)	Critical
Time to clinical improvement (days)												
7	Randomised trials	Serious[h]	Very serious[i]	Not serious	Not serious	None	569	549	–	MD 1.78 days fewer (2.5 fewer to 1.06 fewer)	⊕◯◯◯ (very low)	Important
Time to achieve a 50% reduction in abscess cavity size (days)												
5	Randomised trials	Serious[j]	Very serious[k]	Not serious	Not serious	None	491	473	–	2.83 days fewer (3.36 fewer to 2.3 fewer)	⊕◯◯◯ (very low)	Important
Duration of IV antibiotics needed (days)												
5	Randomised trials	Not serious	Very serious[l]	Not serious	Serious[m]	None	403	403	–	MD 2.13 days fewer (3.84 fewer to 0.42 fewer)	⊕◯◯◯ (very low)	Important

[a], plausible bias likely to seriously alter the results; [b], considerable heterogeneity that could not be adequately explained; [c], we visually detected publication bias and Egger's test was significant; [d], low event rate; [e], Plausible bias likely to seriously alter the results; [f], low event rate; [g], considerable heterogeneity that could not be adequately explained; [h,j], explained by for "Plausible bias likely to seriously alter the results"; [i,k,l], explained by "considerable heterogeneity that could not be adequately explained"; [m], explained by "low event rate". CI, confidence interval; MD, mean difference; RR, risk ratio; IV, intravenous.

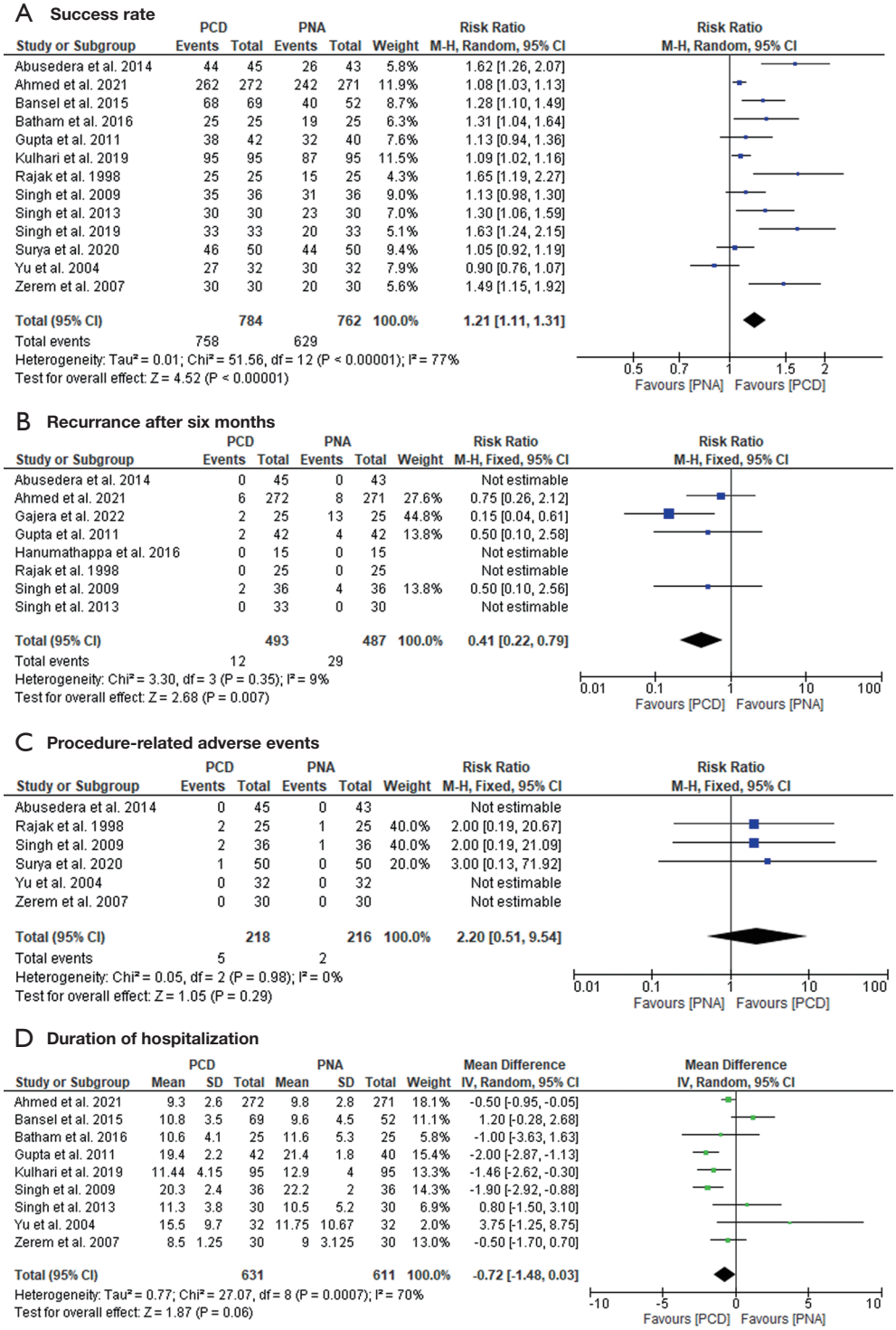

Figure 3 Forest plot of the primary outcomes [(A) success rate, (B) recurrence after 6 months, (C) procedure related adverse events, and (D) duration of hospitalization]. I^2, I-squared; CI, confidence interval; RR, risk ratio; df, degree of freedom.

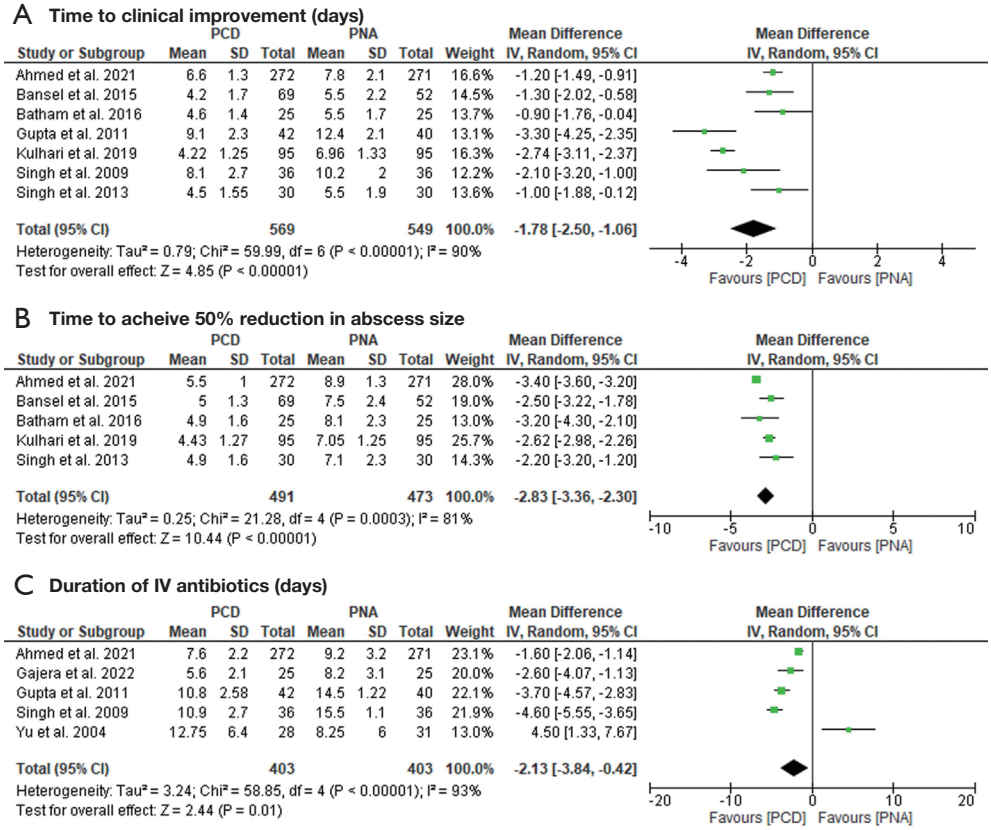

Figure 4 Forest plot of the secondary outcomes [(A) time to clinical improvement, (B) time to achieve 50% reduction in abscess size, and (C) duration of IV antibiotics]. I^2, I-squared; CI, confidence interval; df, degree of freedom.

heterogeneity was not resolved by sensitivity analysis (Table S5).

Discussion

Liver abscesses, either pyogenic or amoebic, remain a significant cause of morbidity and mortality in tropical countries (19). Morbidity and mortality are highly affected by several factors such as the presence of diabetes, which is accredited to low immunity, biliary disease, and type of organism, a recently published meta-analysis, Chan *et al.* concluded that klebsiella pneumoniae has lower mortality than non- klebsiella pneumoniae pyogenic liver abscess (40-42). Liver abscess has been even more common recently due to the increasing biliary interventions (20). Furthermore, the direct spread from biliary infection is a significant risk factor because the liver abscess is prevalent in 40 to 60 percent of gallstones or malignant biliary obstruction (43-45). Therefore, the liver abscess is now more common outside tropical countries, and deciding the best management approach is of great importance. In the current era of minimally invasive interventions, PCD and PNA are both considered the gold standard of care; however, which approach is better is still a matter of debate. Hence, we conducted this meta-analysis to compare the efficacy and safety of PCD versus PNA for liver abscess management. Our review showed that PCD is superior to PNA regarding success rate, recurrence after 6 months, time to clinical improvement, time to achieve 50% reduction, and duration of antibiotics administration. Moreover, adverse event rates were similar between PCD and PNA; however, no significant difference was observed regarding hospitalization duration.

Radiology plays a key role in determining the prognosis of pyogenic liver abscess (46,47), multiple loculi within the abscess, and increased size of the abscess were all predictors for percutaneous drainage failure (48,49). And to add in, there is no consensus in the literature on the degree of gas

formation impact on the clinical outcomes (50-52). The size of the abscess is a decisive factor for the prognosis and the management plan. It is more likely for larger abscesses to rupture, causing infection to spread in the peritoneal cavity, which may end up causing sepsis increasing morbidity and mortality, thus large and giant-sized abscesses may need prompt surgical intervention, but stratifying the intervention based on the size of the abscess is vague in the literature with no consensus on when exactly to choose surgical intervention over percutaneous drainage (49,53-55). Shelat *et al.* suggested that an abscess size of four cm or larger is the cut-off value for the need for PCD (55), and there is no consensus that an abscess larger than 10 cm is a strict indication for surgical intervention. However, surgical intervention is considered the favored intervention for patients with accompanied intraperitoneal pathology such as acute cholecystitis to allow cholecystectomy and drainage with the only absolute indication for surgery is rupture (49,56). Although abscess size plays a key role in the success rates, the clinical resolution, and which method to be used for drainage, it is not the only factor, as multiloculation, gas formation, and virulence of the causative organisms need to be implicated in the decision of the management plan (49).

Regarding success rate, PCD was superior to PNA. This can be explained by the following: first, catheter, especially those with wider caliber, provides continuous drainage of pus, preventing re-accumulation (19). Rapid re-accumulation of liver abscesses is a significant problem that can be due to the continuous inflammatory process after abscess evacuation and, in some cases, due to biliary communication (57). This hypothesis is supported by the results of our subgroup analysis emphasizing that catheter calibers 14 F and 12 F were associated with a significantly better success rate than PNA; however, 8 F catheter was not. Second, PCD is considered a better approach when dealing with large abscesses and thick pus viscous pus (57). The abscess size is considered a critical criterion in liver abscess management, and our meta-regression analysis showed that increasing abscess size is significantly associated with decreased success rate.

When dealing with a large liver abscess, on one hand, repeated needle aspirations with PNA is required. However, exposing patients to multiple needle aspirations within a short duration, from five to 14 days, is a traumatic and invasive procedure that might not be accepted by several patients being painful and distressing (28,57). Moreover, repeated needle aspirations are rarely successful. To clarify, Abusedera and El-Badry reported that the second and third aspiration was successful in only 19% and 5.5% of patients, respectively (18). Also, repeated aspirations were not successful in any case with multi-loculated abscess (18). On the other hand, the continuous drainage of PCD gives it a clear advantage over PNA preventing re-accumulation, which can be more significant in large abscesses because they produce a greater amount of pus compared with smaller abscesses which its day-to-day accumulation can be considered insignificant (28). Accordingly, PCD is a more effective approach, especially for large abscesses, which can decrease the risk of recurrence in the long term. This is supported by our findings that PCD significantly decreased the risk of recurrence after six months compared to PNA.

Despite the clear advantages of PCD over PNA, performing PCD requires more skill, surgical expertise, and nursing care than PNA (23,28). Also, catheter drainage is associated with patient discomfort, cellulitis at the puncture site, and catheter dislodgement (20). Furthermore, PNA still has some advantages over PCD, being a simpler, cheaper, and flexible technique that can be used to aspirate multiple small abscesses in a single procedure (15,23,26,28,29,31).

According to the increased success rate, PCD is expected to lead to more rapid resolution. This is supported by our analysis; PCD was associated with a significantly shorter time of clinical resolution, achieving a 50% reduction in abscess size and antibiotic administration. This is explained by the continuous drainage of PCD, leading to rapid abscess collapse and infection resolution, especially in the short term (29). However, the duration of hospitalization is similar for both techniques. This can be explained by the increased need for nursing care with PCD, thick pus which is not easy to be drained percutaneously, and multiple loculi within the abscess, which is a well-established element in PCD failure, despite its faster resolution results (58,59). Regarding safety, both techniques show similar safety findings when performed properly. Besides patient comorbidities, the experience and precision of the practitioner performing PCD or PNA decide the complications the patients might have after the procedure (28). However, Yu *et al.* 2004 reported five deaths (four after PCD and one after PNA) (31). Also, Singh *et al.* reported a perforated abscess after PCD, which led to sepsis and death (27). Furthermore, secondary bacterial contamination is still a serious concern after PCD; however, it is rarely reported (29).

In a previous systematic review, Cai *et al.* assessed PCD versus PNA for liver abscess drainage (15). Our results are in the same line as supporting PCD over PNA. Moreover, we clarified that PCD is associated with less incidence of

recurrence after six months and decreased duration of IV antibiotics administration.

Strengths and limitations

To the best of our knowledge, this is the most comprehensive meta-analysis synthesizing evidence from 15 RCTs on the safety and efficacy of PCD versus PNA for liver abscess drainage. Moreover, we conducted a thorough analysis, including meta-regression, sensitivity, and subgroup analysis; followed PRISMA guidelines (17); and followed GRADE group recommendations assessing the quality of evidence (36).

Our review has a few limitations. First, although we included 15 trials, 12 trials were conducted in India (19-30), one in Egypt (18), another in China (31), and another in Bosnia and Herzegovina (32). Therefore, the geographical distribution of our review population is limited, limiting the generalizability of our findings. Second, the antibiotic regimen varied among the included studies, as shown in *Table 1*; hence, it can significantly affect our findings. Third, we could not assess the success rate of PCD or PNA stratified by the etiological diagnosis because the included trials did not report data for separate histological findings and they attributed that to the histological diagnosis was tricky because most of the included trials were conducted in tertiary centers; therefore, patients had already been on antibiotics on admission. Fourth, all of the eligible studies showed an unclear risk of bias regarding multiple domains implying mal reporting of the included trials' methodology. Finally, some outcomes were associated with significant heterogeneity, and the GRADE assessment yielded low to very low-quality evidence in most of our outcomes, furtherly limiting the generalizability of our results.

Implications for clinical practice

For a single unilocular small abscess (<5 cm), both PCD and PNA can be clinically applicable, and the decision depends on patient preference, kit availability, and practitioner experience (15,28,31,32,60). However, for a single unilocular large abscess (>5 cm), PCD is preferred, given its continuous, uninterrupted drainage (60). For multiple or multilocular abscesses, the decision should be made on an individual basis, considering the number, size, and accessibility to abscesses, along with the expertise of the practitioner and the patient's comorbidities (60). However, PNA can be performed in case of multiple and small, easily accessible abscesses (15,23,26,28,29,31). Moreover, surgical intervention is still an option for cases with failed drainage after one week (60) or as an early intervention in patients with gas-forming abscesses and septic shock (61).

Implications for future research

Future trials should consider the following: first, following the CONSORT reporting guidelines for clinical trials (62) because the reporting of the included trials was mostly unclear, leading to uncertainty about the effect of different categories of bias on the trial's findings. Second, future trials should report data for separate etiological diagnoses because the results of our subgroup analysis showed conflicting data, favoring PCD over PNA for pyogenic and amoebic abscesses and showing no difference for pyogenic only. Third, a cost-effective analysis is still lacking in comparing the two procedures.

Conclusions

PCD is more effective than PNA in liver abscess drainage leading to a better success rate, faster resolution, decreased need for antibiotics, and similar safety data. However, evidence is still uncertain about this effect, and more high-quality multicentred trials are still required to ascertain our findings, especially in non-tropical countries.

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Footnote

Reporting Checklist: The authors have completed the PRISMA reporting checklist. Available at https://atm.amegroups.com/article/view/10.21037/atm-22-4663/rc

Peer Review File: Available at https://atm.amegroups.com/article/view/10.21037/atm-22-4663/prf

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://atm.amegroups.com/article/view/10.21037/atm-22-4663/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related

to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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