

BMJ Open Percutaneous catheter drainage versus percutaneous needle aspiration for liver abscess: a systematic review, meta-analysis and trial sequential analysis

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ABSTRACT

Objective To compare the effectiveness and safety of percutaneous catheter drainage (PCD) against percutaneous needle aspiration (PNA) for liver abscess.

Design Systematic review, meta-analysis and trial sequential analysis.

Data sources PubMed, Web of Science, Cochrane Library, Embase, Airiti Library and ClinicalTrials.gov were searched from their inception up to 16 March 2022.

Eligibility criteria Randomised controlled trials that compared PCD to PNA for liver abscess were considered eligible, without restriction on language.

Data extraction and synthesis Primary outcome was treatment success rate. Depending on heterogeneity, either a fixed-effects model or a random-effects model was used to derive overall estimates. Review Manager V.5.3 software was used for meta-analysis. Trial sequential analysis was performed using the Trial Sequential Analysis software. Certainty of evidence was evaluated using the Grading of Recommendations, Assessment, Development and Evaluation system.

Results Ten trials totalling 1287 individuals were included. Pooled analysis revealed that PCD, when compared with PNA, enhanced treatment success rate (risk ratio 1.16, 95% CI 1.07 to 1.25). Trial sequential analysis demonstrated this robust finding with required information size attained. For large abscesses, subgroup analysis favoured PCD (test of subgroup difference, $p < 0.001$). In comparison to PNA, pooled analysis indicated a significant benefit of PCD on time to achieve clinical improvement or complete clinical relief (mean differences (MD) -2.53 days; 95% CI -3.54 to -1.52) in six studies with 1000 patients; time to achieve a 50% reduction in abscess size (MD -2.49 days; 95% CI -3.59 to -1.38) in five studies with 772 patients; and duration of intravenous antibiotic use (MD -4.04 days, 95% CI -5.99 to -2.10) in four studies with 763 patients. In-hospital mortality and complications were not different.

Conclusion In patients with liver abscess, ultrasound-guided PCD raises the treatment success rate by 136 in 1000 patients, improves clinical outcomes by 3 days and reduces the need for intravenous antibiotics by 4 days.

PROSPERO registration number CRD42022316540.

STRENGTHS AND LIMITATIONS OF THIS STUDY

- ⇒ Our study used trial sequential analysis to synthesise the body of evidence demonstrating the role of percutaneous interventions in patients with liver abscess.
- ⇒ To determine the relationship between abscess size and treatment outcome, a comprehensive subgroup analysis and meta-regression was conducted.
- ⇒ Using the revised Cochrane risk-of-bias tool and the Grading of Recommendations, Assessment, Development and Evaluation system to evaluate the risk of bias and evidence certainty, respectively, is a distinguishing feature of our systematic review.
- ⇒ Eight of the 10 included studies were conducted in India, and the particularly low in-hospital mortality found in this meta-analysis suggest that the data may not be representative of liver abscess in general.
- ⇒ Another limitation of our study is the marginal insignificance of publication bias using Egger's test.

INTRODUCTION

Liver abscess is an intrahepatic infectious disease caused by amoeba or bacteria. The 1-month and intensive care unit mortality rates among patients with pyogenic liver abscesses can be as high as 7.4% and 28%, respectively.^{1 2} Most patients recover after receiving antibiotics, but some require image-guided percutaneous interventional therapy, which could considerably lower morbidity, mortality and the need for surgical intervention.^{3–5}

Percutaneous catheter drainage (PCD) and percutaneous needle aspiration (PNA) are the two primary ultrasound-guided percutaneous therapeutic methods used to treat liver abscesses. PNA represents intermittent needle aspiration, while PCD denotes the continuous use of indwelling pigtail catheters. Some studies have demonstrated a higher treatment success rate with PCD than with

PNA in the management of liver abscesses.^{6 7} However, some authors have also considered that needle aspiration is an easier, more cost-effective and equivalently efficient interventional therapy.^{8 9}

The best option among the two treatments for liver abscess remains inconclusive in different clinical conditions. The goal of this systematic review is to compare the efficacy and safety of ultrasound-guided PCD versus PNA for liver abscess management.

METHODS

This study is reported according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement and Cochrane Handbook for Systematic Reviews of Interventions.^{10 11} The study protocol is publicly available on PROSPERO. The details about amendments and the reasons for them are provided in the PROSPERO record.

Search strategy

Five databases, including PubMed, Web of Science, Cochrane (Cochrane Database of Systematic Reviews and Cochrane Central Register of Controlled Trials), Embase and Airiti Library, were independently searched by two reviewers (J-WL and C-TC) from their inception to 16 March 2022. In addition, ClinicalTrials.gov, a web-based study registry, was searched. We also performed a manual search of the reference lists of all retrieved articles and relevant reviews to identify additional eligible studies. There was no restriction on language, study type, publication period or publication status. The detailed search strategy is shown in online supplemental table S1.

Eligibility criteria

We included randomised controlled trials (RCTs) recruiting patients with uncomplicated or complicated liver abscesses and comparing ultrasound-guided PCD versus PNA. We excluded studies without a control group or those that only had medical therapy as a comparator. Trials without a detailed abstract, those that did not have its full text available and those that did not include a clinical outcome for the target group were also excluded.

Study selection

Two reviewers (J-WL and C-TC) screened the titles and abstracts for relevance, and then they independently decided which studies to include according to the eligibility criteria. There was no restriction on language, publication period or publication status. If any two studies were found to overlap, the publication with more cases was selected. Disagreements were resolved through discussion with a third reviewer (M-SH).

Outcomes

The primary outcome was the treatment success rate (see online supplemental table S2 for more details on the definition). The secondary outcomes were (1) in-hospital mortality rate; (2) time to achieve clinical improvement

or complete clinical relief; (3) number of patients with a >50% decrease in abscess size at the end of treatment; (4) time to achieve a 50% reduction in abscess size; (5) number of patients whose abscess disappeared at the end of treatment; (6) time to achieve total or near total resolution of the abscess; (7) length of hospital stay; (8) duration of intravenous antibiotic use; (9) sonographic resolution at 6 months; (10) recurrence within 6 months; (11) all procedure-related complications; (12) major procedure-related complications; and (13) number of patients requiring surgical intervention.

Data extraction

The data from individual studies were independently extracted by two reviewers (J-WL and C-TC) using a standardised data extraction form via Excel software (Microsoft, 2019 version). Disagreements were resolved through discussion with a third reviewer (DH-TY).

If the continuous variable outcomes of interest were not available in the retrieved study, we estimated the sample mean and SD using the sample size, median, range and IQR.¹² This meta-analysis included the calculated sample mean and SD, but the data were also examined to determine if they were skewed away from normality.^{12–15}

Risk of bias assessment

Two reviewers (J-WL and I-HL) independently used the revised Cochrane risk-of-bias tool (RoB 2.0) to assess the methodological quality of eligible studies (summarised in online supplemental table S3).^{16 17} The five domains for assessment are (1) bias arising from the randomisation process; (2) bias due to deviations from intended interventions; (3) bias due to missing outcome data; (4) bias in measurement of the outcome; and (5) bias in selection of the reported result. Regarding the risk involving these domains, each RCT was viewed and scored as (1) low risk of bias; (2) some concerns; or (3) high risk of bias. Disagreements were resolved by discussion with a third reviewer (T-FH).

Statistical analysis

Statistical analysis was performed using Review Manager V.5.3 software (Nordic Cochrane Centre).¹⁸ Binary variables were expressed as risk ratios (RRs) and 95% CIs. For studies with no event in one arm, a fixed value of 0.5 was added to the zero cells to avoid computational errors. The outcomes of studies with no event in either arm are displayed as 'Not estimable' in the forest plots, and these studies were excluded from the meta-analysis statistical estimate. Continuous variables were presented as the mean and SD, and they were assessed using weighted mean differences (MD) and respective 95% CIs.

Statistical heterogeneity across trials was assessed by both Cochran's Q test and the I^2 statistic. P values less than 0.1 and I^2 values greater than 50% were considered to represent statistical heterogeneity, and a random-effects model was used to estimate the variables. Meta-analysis was performed using a fixed-effects model if there was

no statistical heterogeneity. A *p* value less than 0.05 was considered statistically significant, and all statistical tests were two-sided.

Subgroup analysis of the primary outcome was performed based on the following subgroups: type of abscess pathogen; risk of bias; inclusion criteria for abscess size; and actual abscess size. To compare the actual mean abscess size among the included studies, we used abscess volume. If the included trial did not mention abscess volume, the abscess volume was estimated and computed using the following formula: estimated volume = $\frac{4}{3} \pi r^3 \sim 4.19 r^3$ (*r* representing radius). Subgroup analyses of the secondary outcomes with continuous variables were performed based on data skewness if the estimated data included in our meta-analyses were skewed away from normality.

For the primary outcome, trial sequential analysis was performed using the Trial Sequential Analysis V.0.9.5.10 Beta software (Copenhagen Trial Unit, Denmark).^{19 20} There are substantial risks of random error with cumulative meta-analyses.²¹ Conventional meta-analyses are susceptible to producing false positive and false negative results due to repeated significance testing as new trials are added and insufficient data size. In trial sequential analysis, the required data size was estimated, and the statistical significance threshold was modified to account for heterogeneity. Moreover, trial sequential monitoring limits were estimated.²² Trial sequential analysis may reduce the risk of random errors, assist researchers in estimating sample sizes for future trials and demonstrate robust evidence in meta-analyses.²³ Our study's hypothesis testing parameters included a two-sided test, an overall maximum type I error of 5%, and the O'Brien-Fleming alpha-spending function. The required sample size was based on a power of 80%, a relative risk reduction of 20%, and the incidence in the control arm (the PNA group) to determine the required information size. A diversity adjustment was also made based on the estimated ratio between the variance of the selected random effects model and the variance of the fixed effect.²⁴ Based on a previous systematic review, the relative risk reduction of 20% was estimated to be expected.²⁵ The O'Brien-Fleming function -spending function was applied to the inner wedge futility boundary to determine futility.

For the primary outcome, meta-regression was carried out using Comprehensive Meta Analysis V.3.0 software (Biostat, Englewood, New Jersey, USA). Sensitivity analysis for the primary outcome was performed using the leave-one-out method to further examine the robustness of the results and to identify the possible cause of heterogeneity. Egger's test and funnel plot were employed to determine publication bias.

Two reviewers (J-WL and T-FH) evaluated the certainty of evidence using the GRADE (Grading of Recommendations, Assessment, Development and Evaluation) system, which includes risk of bias, inconsistency, indirectness, imprecision and publication bias.²⁶ The certainty of evidence was classified as very low, low, moderate or high.

Disagreements were resolved by discussion with a third reviewer (H-MC).

Patient and public involvement

None.

RESULTS

Study selection

Online supplemental figure S1 shows the PRISMA flow-chart of this systematic review and the reasons for exclusion of illegible studies. Ten studies were identified using databases and registers, while five studies were identified using other methods. Four of the 15 studies were eliminated due to duplication. A total of 11 studies met the eligibility criteria in our review. One study, however, was disregarded because it revealed the inappropriate use of a 28-French pigtail catheter for PCD and an unusually high percentage of concurrent pyogenic and amoebic coinfection (85%).²⁷ Finally, a total of 10 studies involving 1287 individuals were included in our meta-analysis.^{6-8 28-34}

Study characteristics

Table 1 and online supplemental table S3 show the characteristics of the 10 included RCTs. Most of these studies involving young and middle-aged adults with mixed types of abscess pathogen were conducted in India. The definition of treatment success or failure in the different trials is provided in online supplemental table S2.

Risk of bias assessment

The complete assessment of the risk of bias in each trial is shown in detail in online supplemental figure S2 and online supplemental table S4. The main problems with the 10 trials involved the inability to blind participants and research staff. However, most studies provided a clear and comprehensive description of the protocol for the intervention operations as well as the schedule and duration of antibiotic administration. Non-adherence to the protocol was not mentioned in the trials. One study had an issue in selective reporting.⁷ Most of the study outcomes were reported as a range and a *p* value, without mention of a median or mean value. The SD or IQR was not provided in full. The overall risk of bias in nine studies (90%) was categorised as low or as some concerns.

Primary outcome

Treatment success rate

A total of 10 trials with 1287 randomised participants were included in the meta-analysis of success rate.^{6-8 28-34} The success rates in the PCD group and the PNA group were 96.3% and 84.7%, respectively. PCD therapy increased the success rate compared with PNA therapy (RR 1.16, 95% CI 1.07 to 1.25; *p* < 0.01) (figure 1). Statistically significant heterogeneity was observed among these trials (*I*² = 72%; *p* < 0.01).

Subgroup analysis

Subgroup analysis by inclusion criteria of abscess size revealed a trend of higher success rate of PCD versus

Table 1 Characteristics of the included studies

Author, year	Country	Sample size	Type of abscess pathogen (pyogenic vs amoeba vs indeterminate) (%)	Single abscess (PCD vs PNA) (%)	DM (%)	Initial antibiotic regimen	Size of drainage catheter (Fr)/ aspiration needle (G)	Maximal PNA attempts (times)	Abscess size (PCD vs PNA) diameter (cm) or volume (mL)
Rajak <i>et al</i> 1998 ⁷	India	50	Mixed (22 vs 40 vs 38)	80 vs 72	NA	Cloxacillin & gentamicin & metronidazole & chloroquine	8–12/18	NA	336 mL vs 222 mL
Yu <i>et al</i> 2004 ⁸	China	64	Pyogenic (100 vs 0 vs 0)	91 vs 84	30	Ampicillin & cefuroxime & metronidazole	8/18	NA	6.2 cm vs 5.6 cm
Zerem <i>et al</i> 2007 ⁶	Bosnia and Herzegovina	60	Pyogenic (100 vs 0 vs 0)	93 vs 93	28	Cefazolin & gentamicin	8/18	3	7.4 cm vs 7.4 cm
Singh <i>et al</i> 2009 ³¹	India	72	Mixed (67 vs 33 vs 0)	86 vs 78	11	Ceftriaxone & gentamicin & metronidazole	14/16	3	>10 cm
Gupta <i>et al</i> 2010 ²⁹	India	82	Amoeba (0 vs 100 vs 0)	88 vs 85	50	Metronidazole	14/16	3	>10 cm
Singh <i>et al</i> 2013 ³³	India	60	Mixed (23 vs 58 vs 12)	All 75	NA	Metronidazole & cefazolin & gentamicin & chloroquine	12/18	3	302 mL vs 249 mL
Singh <i>et al</i> 2019 ³²	India	66	Mixed (23 vs 77 vs 0)	91 vs 85	26	NA	12/18	3	7.8 cm vs 7.7 cm
Kulhari <i>et al</i> 2019 ³⁰	India	190	Mixed (24 vs 64 vs 12)	78 vs 70	NA	NA	12/16–18	3	293 mL vs 291 mL
Surya <i>et al</i> 2020 ³⁴	India	100	Mixed (10 vs 38 vs 52)	96 vs 88	NA	Ceftriaxone & gentamicin & metronidazole	12/18	2	8.4 cm vs 7.4 cm
Ahmed <i>et al</i> 2021 ²⁸	India	543	Mixed (37 vs 62 vs 1)	NA	8	Ceftriaxone & metronidazole	14/16–18	3	>5 cm

DM, diabetes mellitus; Fr, French; G, gauge; NA, not available; PCD, percutaneous catheter drainage; PNA, percutaneous needle aspiration.

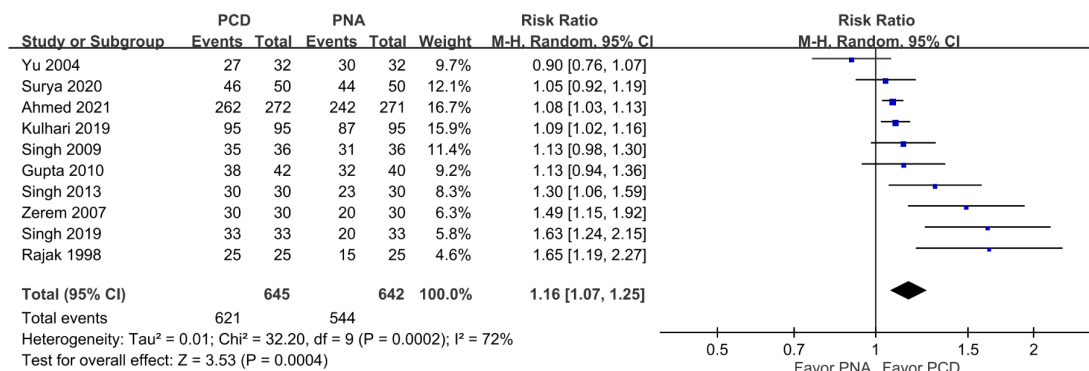


Figure 1 Forest plots showing the effect of percutaneous catheter drainage (PCD) and percutaneous needle aspiration (PNA) on success rate.

PNA for large abscess size (test of subgroup difference, $p < 0.001$) (online supplemental figure 3A).

A comparison of estimates of the pooled intervention effect based on the type of abscess pathogen revealed no subgroup difference in any of the subgroups examined (test of subgroup difference, $p = 0.96$) (online supplemental figure 3B). Based on the revised Cochrane ROB 2.0, subgroup analysis by study quality revealed a similar preference for PCD over PNA (online supplemental figure 3C).

Subgroup analysis by actual mean abscess size revealed that PCD was significantly more successful than PNA for mean abscess sizes greater than 6 cm in diameter or 113 mL in volume (test of subgroup difference, $p = 0.03$)

(figure 2). Abscess size was found to be a predictor of success rate in univariable meta-regression analysis using a random-effects model ($p = 0.04$). The proportion of subjects with a solitary abscess ($p = 0.84$), involvement of bilateral hepatic lobes ($p = 0.94$) and diabetes mellitus ($p = 0.90$) had no effect on univariable meta-regression analysis of study characteristics.

Sensitivity analysis

The sensitivity analysis of the primary outcome, which excluded data from each included study, had no effect on the overall significance of the results (online supplemental figure S4).

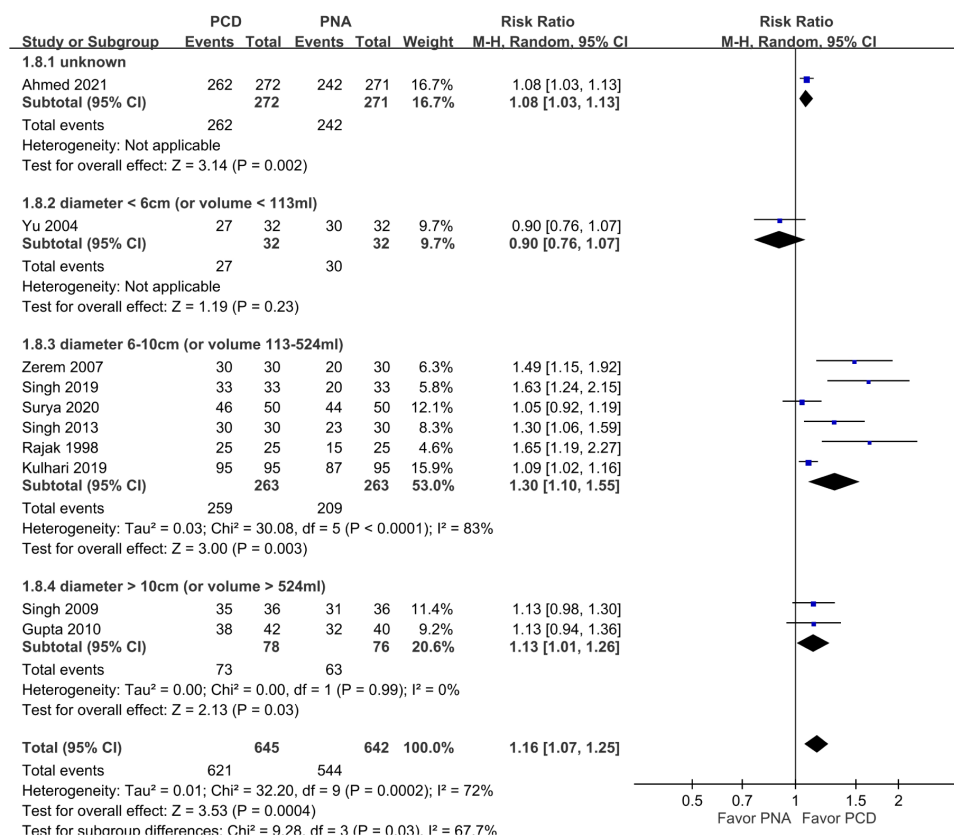


Figure 2 Forest plots showing subgroup analysis of success rate between percutaneous catheter drainage (PCD) and percutaneous needle aspiration (PNA) based on actual mean abscess size.

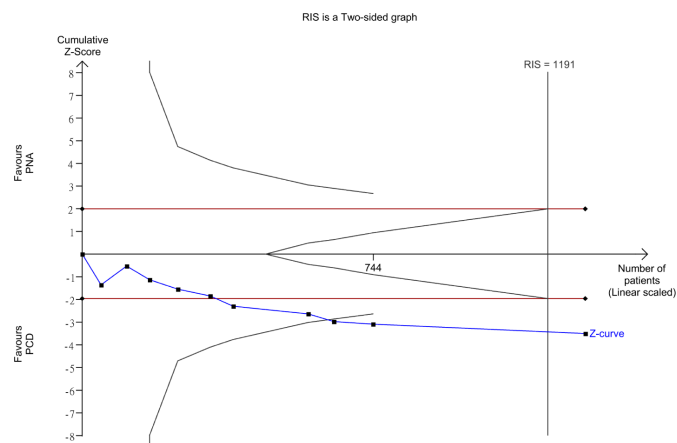


Figure 3 Trial sequential analysis of percutaneous catheter drainage (PCD) versus percutaneous needle aspiration (PNA) for success rate. The blue line (Z-curve) shows the cumulative meta-analysis adding the results of individual trials based on the year of publication. The horizontal red line represents the conventional boundary with a 5% level of significance. The monitoring boundary (black sloping lines) shows the significance level after adjusting for the cumulative analysis. The black vertical line shows the required information size (RIS). After diversity adjustment, the estimated information size required was 1191 participants.

Trial sequential analysis

According to the incidence in the control arm of 84.7%, power of 80%, type I error of 5% and relative risk reduction of 20%, trial sequential analysis with a random-effects model revealed the relative risk of 1.16 (95% CI 1.04 to 1.29; $I^2=72\%$, diversity $D^2=83\%$, $p<0.001$). The cumulative Z-curve crosses both the traditional and trial sequential monitoring boundaries in favour of PCD, with the 1191 subjects of required information size obtained (figure 3).

Publication bias

The funnel plot of SE versus log RR for success rate revealed a slightly asymmetrical distribution by visual inspection (online supplemental figure S5). Egger's regression intercept test showed no statistical significance of publication bias ($p=0.07$).

Certainty of evidence

Because of the potential risk of bias and the heterogeneity, we downgraded the primary outcome of the 10 included studies from high to low certainty of evidence. However, the combined data from three low-risk studies revealed that PCD had a positive effect without heterogeneity. As a result, we gave the success rate evidence for the three high-quality studies a high certainty rating (table 2).

Secondary outcomes

In-hospital mortality rate

The pooled in-hospital mortality of 10 studies in the PCD and PNA groups was 0.9% and 0.6%, respectively.^{6–8 28–34} There was no significant difference in in-hospital mortality between the two groups (RR 1.35; 95% CI 0.46 to 4.01; $p=0.59$). The heterogeneity was not significant ($I^2=18\%$;

$p=0.30$) (online supplemental figure S6). The certainty of evidence was low.

Clinical improvement

A pooled analysis of six studies indicated a statistically significant effect of PCD on the time to achieve clinical improvement or complete clinical relief (MD -2.53 days; 95% CI -3.54 to -1.52; $p<0.01$), with significant heterogeneity ($I^2=94\%$; $p<0.01$). A subgroup analysis based on the skewness of the data revealed a preference for PCD over PNA (online supplemental figure 7A).^{28–33} The certainty of evidence was high.

Data from five trials show that PCD shortened the time to achieve a 50% reduction in abscess size (MD -2.49 days; 95% CI -3.59 to -1.38; $p<0.01$) with significant heterogeneity ($I^2=91\%$; $p<0.01$). A subgroup analysis based on the skewness of the data also revealed a similar preference for PCD over PNA (online supplemental figure 7B).^{7 28 30 32 33} The certainty of evidence was moderate.

There was no significant difference in the time to achieve total or near total resolution of the abscess, the number of patients with a >50% decrease in abscess size and the number of patients whose abscess disappeared at the end of treatment between the two groups (online supplemental figure 8A–C).

Sonographic resolution at 6 months was provided by one trial, which indicated a beneficial effect of PCD with an RR of 1.12 (online supplemental figure 8D).²⁸ The certainty of evidence was moderate.

Duration of therapy

Eight studies of 1171 patients examined the length of hospital stay.^{6 8 28–31 33 34} There was no significant difference between the groups (MD -0.18 days; 95% CI -1.62 to 1.25; $p=0.80$). The heterogeneity was significant ($I^2=92\%$; $p<0.01$) (online supplemental figure 9A). The certainty of evidence was low.

Four trials including 763 participants provided a continuous outcome on the duration of intravenous antibiotic use.^{28 29 31 32} The combined results showed that PCD reduced the time with considerable heterogeneity ($I^2=94\%$; $p<0.01$) (MD -4.04 days, 95% CI -5.99 to -2.10) (online supplemental figure 7C). The evidence had a moderate degree of certainty.

Recurrence

Seven studies with 920 patients were included in this meta-analysis for recurrence of liver abscess within 6 months.^{6 7 28 29 31–33} There was no significant difference (RR 0.62; 95% CI 0.29 to 1.33; $p=0.22$) and no heterogeneity ($I^2=0\%$; $p=0.87$) (online supplemental figure 7D). The certainty of evidence was moderate.

Complications

Meta-analysis from six studies that assessed all procedure-related complications showed a higher but non-significant risk among patients treated with PCD compared with those treated with PNA (RR 2.51, 95% CI 0.86 to 7.34; $p=0.09$), without heterogeneity ($I^2=0\%$; $p=0.44$) (online

Table 2 GRADE summary of findings

Outcome	Studies (n)	Patients (n)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Absolute effect with 95% CI	Certainty
Treatment success rate of all trials	10	1287	Serious*	Serious†	Not serious	Not serious	None	136 more per 1000 (from 59 more to 212 more)	⊕⊕ Low
Treatment success rate of trials with low risk	3	202	Not serious	Not serious	Not serious	Not serious	None	203 more per 1000 (from 68 more to 360 more)	⊕⊕⊕⊕ High
In-hospital mortality rate	10	1287	Serious*	Not serious	Not serious	Serious‡	None	2 more per 1000 (from 3 fewer to 19 more)	⊕⊕ Low
Time to achieve clinical improvement or complete clinical relief	6	1000	Not serious	Not serious	Not serious	Not serious	None	MD 2.53 lower (3.54 lower to 1.52 lower)	⊕⊕⊕⊕ High
Time to achieve a 50% reduction in abscess size	5	772	Serious*	Not serious	Not serious	Not serious	None	MD 2.49 lower (3.59 lower to 1.38 lower)	⊕⊕⊕ Moderate
Time to achieve total or near total resolution of the abscess	4	693	Serious*	Serious†	Not serious	Serious†	None	MD 1.15 higher (1.27 lower to 3.56 higher)	⊕ Very low
Number of patients with >50% decrease in abscess at the end of treatment	1	60	Not serious	NA	Not serious	Serious‡	NA	99 more per 1000 (from 114 fewer to 488 more)	⊕⊕⊕ Moderate
Number of patients whose abscess disappeared at the end of treatment	1	60	Not serious	NA	Not serious	Serious‡	NA	234 more per 1000 (from 18 fewer to 711 more)	⊕⊕⊕ Moderate
Sonographic resolution at 6 months	1	543	Serious*	NA	Not serious	Not serious	NA	77 more per 1000 (from 0 fewer to 167 more)	⊕⊕⊕ Moderate
Length of hospital stay	8	1171	Not serious	Serious†	Not serious	Serious‡	None	MD 0.18 lower (1.62 lower to 1.25 higher)	⊕⊕ Low
Duration of intravenous antibiotic use	4	763	Not serious	Not serious	Not serious	Not serious	Publication bias strongly suspected§	MD 4.04 lower (5.99 lower to 2.1 lower)	⊕⊕⊕ Moderate
Recurrence within 6 months	7	920	Not serious	Not serious	Not serious	Serious‡	None	13 fewer per 1000 (from 25 fewer to 12 more)	⊕⊕⊕ Moderate
All procedure-related complications	6	871	Not serious	Not serious	Not serious	Serious‡	None	14 more per 1000 (from 1 fewer to 58 more)	⊕⊕⊕ Moderate

Continued

Table 2 Continued

Outcome	Studies (n)	Patients (n)	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Absolute effect with 95% CI	Certainty
Major procedure-related complications	8	662	Serious*	Not serious	Not serious	Serious†	None	0 fewer per 1000 (from 0 fewer to 0 fewer)	⊕⊕ Low
Number of patients requiring surgical intervention	8	1171	Not serious	Not serious	Not serious	Serious‡	None	9 fewer per 1000 (from 22 fewer to 15 more)	⊕⊕⊕ Moderate

*Less than 50% of studies with low overall risk of bias, or more than 25% of studies with high overall risk of bias.
†Moderate or considerable heterogeneity (heterogeneity p value<0.1 and I²>50%).
‡Total number of participants less than optimal information size, and relative wide 95% CI.
§Egger's test p value<0.05.
GRADE, Grading of Recommendations, Assessment, Development and Evaluation; MD, mean difference; NA, not assessable; No, number; RCT, randomised controlled trial; RR, risk ratio.

supplemental figure 9B).^{6-8 28 29 31} The certainty of evidence was moderate.

In the eight studies that reported major procedure-related complications, there was no evidence of a difference between the two groups for this outcome (RR 3.00, 95% CI 0.13 to 71.02; p=0.50) (online supplemental figure 9C).^{6-8 30-34} The certainty of evidence was low.

Eight studies with a total of 1171 participants evaluated the number of patients requiring surgical intervention.^{6 8 28-31 33 34} Compared with PNA, the pooled effect for PCD showed a small but non-significant effect (RR 0.77, 95% CI 0.42 to 1.40; p=0.39) without heterogeneity (I²=0%; p=0.57) (online supplemental figure 9D). The certainty of evidence was moderate.

DISCUSSION

This meta-analysis included 10 randomised trials that compared ultrasound-guided PCD to ultrasound-guided PNA for liver abscess. PCD was associated with increased treatment success rate, a shorter time to achieve clinical improvement or complete clinical relief, a shorter time to achieve a 50% reduction in abscess size, increased sonographic resolution at 6 months, a shorter duration of intravenous antibiotic use and a non-significant increase in all procedure-related complications.

Five studies (306 participants) were included in a prior systematic review and meta-analysis published in 2015 to evaluate the effects of percutaneous treatment methods.²⁵ Because of its higher treatment success rate (RR 0.81, 95% CI 0.66 to 0.99), quicker time to achieve clinical relief (standardised mean difference (SMD) 0.73, 95% CI 0.36 to 1.11) and quicker time to achieve a 50% reduction in abscess size (SMD 1.08, 95% CI 0.64 to 1.53), PCD was found to be a more effective strategy than PNA in the meta-analysis. Our study revealed comparable results with the potential to reduce the length of intravenous antibiotic use. Additionally, five RCTs that were not included in the prior systematic review were included in our investigation. We further conducted a trial sequential analysis of the cumulative meta-analysis to investigate the risk of type I error. Information size estimation was coupled with an adjusted level of statistical significance. Our trial sequential analysis demonstrated that once the required information size was attained, the cumulative Z-curve crossed both the low alpha-spending and the trial sequential monitoring boundaries. Our trial sequential analysis proved the robustness of this meta-analysis, in which sufficient quality of evidence for the PCD effect has also been shown.

In terms of PCD treatment efficacy, complications and clinical improvement, two additional recently published meta-analyses yielded similar results to our study.^{35 36} Based on abscess size and pus volume, Mahmoud *et al* performed meta-regression analysis.³⁶ Our meta-regression analysis supported their conclusion regarding the association between abscess size and treatment efficacy. Moreover, our meta-regression analysis revealed that solitary abscess,

bilateral lobe involvement and diabetes mellitus had no impact on the success rate of treatment. In addition, our subgroup analysis revealed that the abscess diameter and size cut-off values favoured PCD. Lastly, a distinctive feature of our meta-analysis is that we conducted trial sequential analysis, which demonstrated the robustness of PCD's success rate.

The primary outcome of our meta-analysis revealed significant heterogeneity. Risk of bias, type of abscess pathogen and abscess size were taken into consideration for subgroup analyses. The heterogeneity seen for the success rate was greatly reduced by the inclusion criteria of abscess size. The success rate of PCD was significantly greater than that of PNA for abscesses larger than 6 cm in diameter or 113 mL in volume, according to subgroup analysis by the actual mean abscess size. In a meta-regression for treatment success, abscess size was found to be a predictor of success rate. Two studies concluded that PCD is superior to PNA for the treatment of liver abscesses larger than 10 cm in diameter.^{29 31} According to Rajak *et al*, it is challenging to completely drain large abscesses with only a few aspiration efforts.⁷ Ahmed *et al* claimed that a large abscess cavity (>150 mL), the presence of biliary communication and a thick pus consistency were the reasons for a failed PNA intervention.²⁸ Unlike intermittent needle aspiration, percutaneous catheter placement provides continuous drainage without the complications of incomplete evacuation and pus reaccumulation. Therefore, PCD was deemed more effective than PNA, particularly for large or pus-filled abscesses.^{6 7}

PCD therapy is associated with a higher treatment success rate and rapid clinical and radiological improvement (a shorter time to achieve clinical improvement or complete clinical relief, a shorter time to achieve a 50% reduction in abscess size and a shorter duration of intravenous antibiotic use). In our study, there was no significant difference in the length of hospital stay or time to achieve total or near total resolution. In three included trials, however, the PCD group had larger abscesses and longer hospital stays than the PNA group.^{8 33 34} A larger abscess size and longer time to achieve total or near total resolution of the abscess were also observed in the PCD group of three included trials.^{7 33 34} A large abscess at admission implied an extended hospital stay and a poor prognosis.³⁷ Consequently, it is possible that our study underestimated the benefit of PCD on these outcomes, and additional studies may be required in the future to demonstrate PCD's other clinical benefit.

Some studies claimed that patients who underwent a failed PNA were treated by open or laparoscopic surgical drainage.^{28 29 31 32 34} These patients had to undergo surgery due to inadequate drainage, persistent sepsis, ruptured liver abscess, peritonitis and gallbladder stones.^{8 28 29 31 34} However, the patients who experienced PNA treatment failure were converted to PCD treatment in some trials but were not added to the PCD group.^{6 7 28 30 33 34} This strategy may reduce the chance of requiring surgery. Consequently, PCD, when used as a rescue for PNA, had

no effect on the number of patients requiring surgical intervention in our study.

Another finding of our investigation was the non-significant increase in all procedure-related PCD complications. In our study, the overall complication rates for PCD and PNA procedures were 2.5% and 0.9%, respectively. This finding was consistent with the results of previous research.^{7 9 28} According to Vakamacawai *et al* (PCD 5.7% vs PNA 0%), Ahmed *et al* (PCD 2.2% vs PNA 0%) and Rajak *et al* (PCD 8.0% vs PNA 4.0%), there was a relative increase in the risk of all complications in the PCD group compared with the PNA group.^{7 9 28} The larger diameter of the drainage catheter used to treat PCD is a possible explanation. However, the requirement for frequent aspiration in the PNA group may also raise concerns regarding the rate of complication, particularly for large abscesses. In our study, major procedure-related complications were not significantly different between the two groups, and both interventions were safe treatment modalities for liver abscess.^{5 25 38 39} Our result served as a reminder to clinical healthcare professionals to remain vigilant for procedure-related complications. The optimal number of participants has not been reached for this outcome, and the 95% CI is relatively large. Due to the significant limitations in the domain of imprecision, we lowered the GRADE certainty rating.

In our meta-analyses, we included skewed data of continuous variables for secondary outcomes. A subgroup analysis based on the skewness of the data revealed that, according to the central limit theorem, there was no subgroup difference between the two groups in terms of the time to achieve complete or near-complete abscess resolution ($p=0.10$). Subgroup analyses based on the skewness of the data also revealed a preference for PCD over PNA in terms of the time to achieve clinical improvement or complete clinical relief and the time to reduce the abscess size by 50%. Therefore, the addition of skewed data had no impact on the treatment effect.

Our study also has several limitations. First, eight of the 10 included studies were conducted in India,^{7 8 28–34} and the particularly low in-hospital mortality found in this meta-analysis suggests that the data may not be representative of liver abscess in general. In terms of the geographical distribution of studies about liver abscess, the top-producing countries were the USA, Taiwan and India. In the case of amoebic liver abscess, Indian researchers led scientific production.⁴⁰ Second, liver abscesses are generally caused by pyogenic, amoebic or mixed infections. However, most included trials reported the combined results of pyogenic, amoebic and mixed infections.^{7 28 30–34} Only two studies included purely pyogenic liver abscesses, and another study included purely amoebic liver abscesses.^{6 8 29} Therefore, we performed a subgroup analysis based on the type of abscess pathogen, and the results revealed no subgroup difference in the success rate. Third, Egger's regression intercept showed borderline insignificance of publication bias (p value=0.07). Nevertheless, we performed

a thorough literature search to identify all relevant published and unpublished research, with the initial search result encompassing more than 7000 studies from six databases. Web of Science, Cochrane Library, Embase and ClinicalTrials.gov were used to search for grey literature and unpublished studies, including conference proceedings, official publications, meeting abstracts and trial registers. Local studies composed in Chinese were searched using the Airiti Library. Additionally, manual searches were performed in the review papers and reference lists. Fourth, our subgroup analyses often contained a very small number of studies, and it is questionable if the defining variable for the subgroup is truly the pivotal characteristic.

CONCLUSION

Our meta-analysis based on RCTs about ultrasound-guided therapy for liver abscess revealed that, compared with PNA, the PCD was the more effective modality, providing a higher treatment success rate, quicker clinical improvement, shorter duration of intravenous antibiotic use and non-significantly increased all procedure-related complications. For abscesses larger than 6 cm in diameter or 113 mL in volume, subgroup analysis favoured PCD. Trial sequential analysis demonstrated the robustness of our findings. Future research into the complications associated with these two types of interventions could be considered.

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