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ARTICLE

Incidence of complications from indwelling pleural catheter for pleural effusion: A meta-analysis

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Abstract

Indwelling pleural catheter (IPC) is widely used in patients with pleural effusion (PE). This meta-analysis aimed to comprehensively summarize the clinical complication from IPC. We searched four large electronic databases (PubMed, EMBASE, MEDLINE, and Cochrane Library) for potentially relevant studies and assessed the included studies' quality using the methodological index for nonrandomized studies' criteria. Extracted data were used to pool rates, and to conduct subgroup and meta–regression analyses. Forty-one studies involving a cumulative 4983 patients with 5650 IPCs were included in this meta-analysis. The overall incidence of IPC complications was 20.3% (95% confidence interval [CI]: 15.0–26.3). The top four complications were: overall infection incidence 5.7% (95% CI: 0.7–2.4); overall catheter abnormality incidence 4.4% (95% CI: 2.8–6.3); pain incidence 1.2% (95% CI: 0.4–2.4); and overall loculation incidence 0.9% (95% CI: 0.1–2.1). Subgroup and meta-regression analyses for overall complications and infections by country, PE site, and PE type demonstrated these factors did not contribute significantly to heterogeneity. Further subgroup analyses for infection of benign PE showed that the overall infection incidence (12.6% [95% CI: 8.1–17.8] vs 0.7% [95% CI: 0.0–4.5]) and empyema incidence (9.1% [95% CI: 5.3–13.8] vs 0.0% [95% CI: 0.0–2.3]) of patients with liver-related PE were significantly higher than that of patients with heart-related PE. Our meta-analysis showed reliable pooled incidences of IPC-related complications, with infection being the most common. These results serve to remind clinicians about the incidence of IPC-related complications and emphasize the importance of taking corresponding preventive and therapeutic steps.

Abbreviations: BPE, benign pleural effusion; CI, confidence interval; IPC, indwelling pleural catheter; MINORS, methodological index for non-randomized studies; MPE, malignant pleural effusion; PE, pleural effusion.

Shuyan Wang and Rui Zhang contributed equally to this work.

Study Highlights

WHAT IS THE CURRENT KNOWLEDGE ON THE TOPIC?

Indwelling pleural catheter (IPC) is widely used in patients with pleural effusion (PE). The incidence rates of these complications have not heretofore been comprehensively summarized.

WHAT QUESTION DID THIS STUDY ADDRESS?

This meta-analysis aimed to comprehensively summarize the clinical complication from IPC.

WHAT DOES THIS STUDY ADD TO OUR KNOWLEDGE?

The overall incidence of IPC complications was 20.3% for a cumulative 4983 patients with 5650 IPCs. The top four complications were: overall infection incidence 5.7%, overall catheter abnormality incidence 4.4%, pain incidence 1.2%, and overall loculation incidence 0.9%. The subgroup analyses for infection of benign PE showed that the overall infection incidence (12.6% vs. 0.7%) and empyema incidence (9.1% vs. 0.0%) of patients with liver-related PE were significantly higher than that of patients with heart-related PE.

HOW MIGHT THIS CHANGE CLINICAL PHARMACOLOGY OR TRANSLATIONAL SCIENCE?

These reliable results serve to remind clinicians about the incidence of IPC-related complications and the importance of taking corresponding preventive and therapeutic steps in the future clinical work.

INTRODUCTION

Pleural effusion (PE), excessive accumulation of fluid in the pleural cavity, is a common clinical problem. PE is often secondary to malignant or benign diseases; the former is called malignant pleural effusion (MPE) and the latter is benign pleural effusion (BPE).[1] The estimated prevalence in the United States was 19 per million for MPE and 157 per million for BPE, with corresponding charges per patients of $12,819.0 and $7977.0, respectively.[2,3] The reported common etiologies of PE included malignant neoplasm, parapneumonic pleural effusion and empyema, tuberculosis, chronic heart failure, and cirrhosis.[2–4] Sequelae of excessive effusions may include impaired gas exchange, pulmonary function, lung volume, and lung mechanics, and may contribute to significant dyspnea, cough, and chest discomfort.[5–7]

Indwelling pleural catheter (IPC) was developed to improve dyspnea and quality of life in patients with PE, especially in those with symptomatic PE.[4,8] IPC has many advantages over other PE therapies, including shorter hospital stay, fewer repeat pleural procedures, and a lower re-admission rate.[9–11] However, IPC also confers shortcomings that should not be ignored, including complications like infection, pain, catheter abnormality, and catheter tract metastasis.[12,13] The incidence rates of these complications have not heretofore been comprehensively summarized. Thus, this meta-analysis aimed to summarize the incidences of all IPC-related clinical complications in patients with PE, and to evaluate their clinical significances.

METHODS

Literature search

Four large electronic databases (PubMed, EMBASE, MEDLINE, and Cochrane Library) were searched for potentially relevant studies from inception through October 2021. The following were used as keyword search terms: “indwelling pleural catheter,” “pleurX catheter,” “pleural catheter,” “tunneled pleural catheter,” “malignant pleural effusion,” “benign pleural effusion,” “refractory nonmalignant effusion,” “tuberculous pleural effusion,” “tuberculous pleuritis,” “hepatic hydrothorax,” “nonmalignant pleural effusion,” and “heart failure.” In addition, the references of related reviews and meta-analyses were manually checked to identify additional potential studies. Two of the authors independently screened all potentially relevant titles and abstracts, and any disagreements were resolved by a third author.

Inclusion and exclusion criteria

A study was included if it: (1) included patients with a diagnosis of PE; (2) included more than 30 patients with

PE; and (3) documented the detailed complications of IPC. The exclusion criteria were: (1) duplicated data were reported by the same author, from the same institution; (2) the article was not published in English; (3) the article was a conference abstract, animal trial, review, guideline, case report, or case serials; and (4) the article reported the patients received both the talc pleural fixation and IPC simultaneously. The definitions of complications are in Appendix S1 and the category of different subgroups applied in the subgroup analyses are in Appendix S2.

Quality assessment

Study quality was assessed using the methodological index for nonrandomized studies (MINORS) criteria. MINORS is a valid instrument designed to assess the methodological quality of nonrandomized studies. It includes 12 items with a maximum score of 24 for comparative studies; the first eight items, with a maximum score of 16, are for noncomparative studies. Low, fair, and high quality are defined by scores of 0–7, 8–11, and 12–16, respectively, for noncomparative studies, and 0–11, 12–17, and 18–24, respectively, for comparative studies.[14] Two of the authors independently estimated the quality of each included study.

Data extraction

The following information was extracted: (1) basic information, including author name, publication year, country, patient age, sex, and follow-up period; (2) the etiology and type of PE and where the PE information was published; and (3) complication information, including the number of patients with complications, number of IPC placements, and number of complications.

Statistical analysis

We used the respective rates of each complication type, and their corresponding standard errors, to pool results using the Bayesian method for meta-analyses. The I^2 statistic and Q tests were performed to assess the impact of study heterogeneity on the pooled results. If significant heterogeneity was present ($p < 0.05$ or $I^2 > 50\%$), randomized effect models were applied; otherwise, fixed effect models were used. Subgroup and meta-regression analyses were used to explore the source of heterogeneity. Sensitivity analysis was conducted to determine the impact of removing studies one at a time on the pooled results. All analyses were performed using Stata software (version 14.0; https://www.stata.com/).

RESULTS

Study selection

As shown in Figure 1, 7486 relevant studies were initially identified, among which 82 were retained for further evaluation. We ultimately included 41 studies published between 1999 and 2021.[15–55] Table 1 shows basic study information and the results of the quality evaluations of the included studies.

Quality assessment

Fifteen comparative studies had MINORS scores from 14–21 and 26 noncomparative studies had MINORS scores from 8–12. These MINORS scores correspond to fair-to-high quality (Table 1).

Patient and IPC characteristics

The 41 included studies reported a cumulative 5650 IPCs from 4983 patients. Patient characteristics, including age, sex, country, PE etiology, and PE site, are presented in Table 2. Different types of IPCs are shown in Appendix S3.

Pooled IPC-related complication incidences

The pooled meta-analysis results are showed in Figure 2. The random-effects model showed significant heterogeneity ($I^2 = 95.996\%$, $p = 0.000$) and the pooled overall complication incidence was 20.3% (95% confidence interval [CI]: 15.0–26.3).

Among IPC-related complications, infection was the most common, with an overall pooled incidence of 5.7% (95% CI: 0.7–2.4) significant heterogeneity ($I^2 = 86.600\%$, $p = 0.000$). Reported infections included wound infection, pleural infection, cellulitis, and empyema, with respective pooled incidences of 0.4% (95% CI: 0.1–1.0), 0.6% (95% CI: 0.1–1.3), 0.9% (95% CI: 0.3–1.7), and 1.3% (95% CI: 0.6–2.2).

Catheter abnormality was the second most common complication, with a pooled overall incidence of 4.4% (95% CI: 2.8–6.3), and included catheter obstruction 1.5% (95% CI: 0.7–2.4), catheter malfunction 1.1% (95% CI: 0.6–1.8), and catheter leakage 0.6% (95% CI: 0.2–1.3).

Other lower-incidence complications included pain 1.2% (95% CI: 0.4–2.4), pneumothorax 0.3% (95% CI: 0.1–0.7), overall loculation 0.9% (95% CI: 0.1–2.1), symptomatic

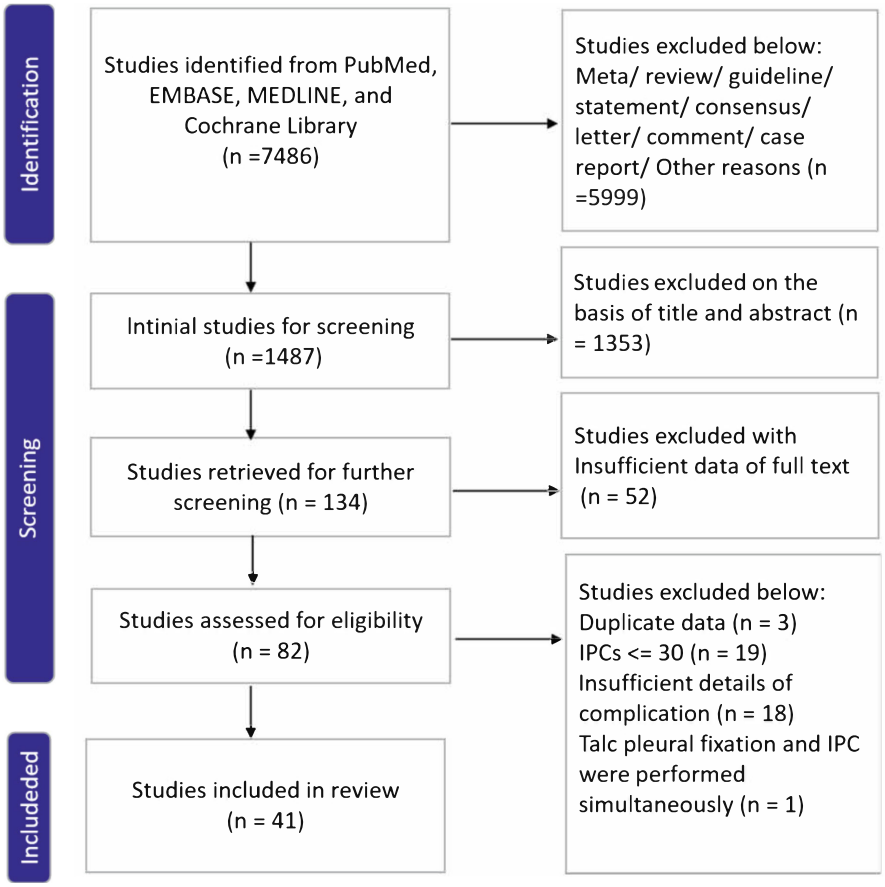

FIGURE 1 Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flow diagram shows study selection. IPC, indwelling pleural catheter.

loculation 0.8% (95% CI: 0.1–0.9), and worsening dyspnea 0.1% (95% CI: 0.0–0.3).

Other complications, including hemothorax, asymptomatic loculation, catheter metastasis, asymptomatic loculation, and serious adverse events had pooled incidence under 0.0%, and were thus extremely rare or negligible.

Subgroup analyses

Table S1 showed the baseline characteristics of different subgroups. The subgroup analyses showed that country, PE site, and PE type did not contribute significant heterogeneity to the incidences of overall complications or infections (Figure 3). We focused on the relationship between the etiology of BPE patients and infection condition, and the subgroup analyses showed that the overall infection incidence (12.6% [95% CI: 8.1–17.8] vs. 0.7% [95% CI: 0.0–4.5]) and empyema incidence (9.1% [95% CI: 5.3–13.8] vs. 0.0% [95% CI: 0.0–2.3]) of patients with liver-related PE were significantly higher than that of patients with heart-related PE with nonoverlapping 95% CI (Figure 4). Therefore, we believe that the etiology of benign BPE is a possible source of heterogeneity.

Meta-regression analyses

Meta-regression analyses for overall complications and infections were run to further clarify the impact of country, PE site, and PE type on pooled incidences and further identify heterogeneity sources. Figure 5a–c shows the meta-regression analysis results for overall complications, demonstrating that these factors did not make significant contributions to heterogeneity. Figure 5d–f shows the meta-regression analysis results for overall infection, which likewise did not account for significance.

Sensitivity analysis and publication bias

The pooled overall complication incidence values were assessed by removing each study one at a time to determine whether its removal led to significantly different values compared with the initial pooled values (Figure S1). As shown in Figure 6a, the funnel plot indicates significant publication bias by Egger's test ($t = 4.94$, $df = 39$, $p < 0.0001$). However, the trim and fill funnel plot show that the filled studies were distributed in the area with incidence less than 0, which is inconsistent with reality; the plot also suggests that a publication bias did not impact the pooled results (Figure 6b).

TABLE 1 Characteristics of included studies

Author (year)	Country	PE type	PE site	Follow-up time, months	Mean age, years	Male, *n*	Patients, *n*	IPCs, *n*	Complications, *n*	MINORS	Study type
Rajchgot (2021)	Canada	Malignant	Single	3	68	213	491	503	27	10	Noncomparative
Akram (2020)	Pakistan	Malignant	NR	25	50	31	102	NR	39	10	Noncomparative
Aujayeb (2020)	UK	Mix	NR	9	73	103	NR	168	22	9	Noncomparative
Frost (2019)	Germany	Malignant	Bilateral	19	65	130	395	448	60	12	Noncomparative
Messeder (2019)	UK	Malignant	Single	12	68	30	68	68	3	8	Noncomparative
Li (2019)	Canada	Benign	Bilateral	17	70	157	252	266	32	11	Noncomparative
Frost (2020)	Germany	Benign	Bilateral	76.5	69	32	54	62	15	10	Noncomparative
Porcel (2019)	Spain	Mix	Bilateral	21	73	181	308	336	129	18	Comparative
Shojaee (2018)	Multi-countries	Benign	Single	66	60	43	79	79	25	11	Noncomparative
Kniese (2018)	USA	Benign	NR	6	61	34	62	NR	25	11	Noncomparative
Muruganandan (2018)	Australia	Malignant	Single	6	66	41	87	87	78	17	Comparative
Thomas (2017)	Multi-countries	Malignant	NR	12	71	39	74	NR	30	17	Comparative
Faiz (2017)	USA	Malignant	Bilateral	8	60	103	172	173	22	9	Noncomparative
Raman (2017)	USA	Mix	Bilateral	12	53	NR	165	NR	20	17	Comparative
Hak (2016)	UK	Malignant	NR	6	66	NR	104	NR	15	16	Comparative
Skalski (2016)	USA	Mix	Bilateral	8.7	66	62	74	83	8	16	Comparative
Penz (2014)	UK	Malignant	Single	13	67	23	52	52	29	21	Comparative
Christopher (2015)	USA	Malignant	Bilateral	28	65	65	91	97	15	16	Comparative
Rial (2015)	Spain	Malignant	Bilateral	10	75	31	55	57	4	11	Noncomparative
Casal (2015)	USA	Malignant	NR	11	61	106	NR	260	58	18	Comparative
Krishnan (2015)	USA	Benign	Bilateral	5	74	20	37	44	0	11	Noncomparative
Ost (2014)	USA	Malignant	Single	14.5	60	100	266	266	31	11	Noncomparative
Freeman (2014)	USA	Benign	Single	6	69	17	40	40	1	14	Comparative
Lorenzo (2014)	Spain	Malignant	Single	2	66	30	51	51	10	12	Noncomparative
Rogier (2013)	Dutch	Malignant	Bilateral	10	57	19	45	50	14	12	Noncomparative
Srour (2013)	Canada	Benign	Single	24	79	22	38	43	13	9	Noncomparative
Fysh (2012)	Australia	Malignant	Bilateral	12	69	25	34	37	13	19	Comparative
Bertolaccini (2012)	Italy	Malignant	Bilateral	10	59	58	90	97	10	11	Noncomparative

TABLE 1 (Continued)

Author (year)	Country	PE type	PE site	Follow-up time, months	Mean age, years	Male, *n*	Patients, *n*	IPCs, *n*	Complications, *n*	MINORS	Study type
Hunt (2012)	USA	Malignant	NR	0.5	66	21	59	NR	3	15	Comparative
Suzuki (2011)	USA	Malignant	Bilateral	10	63	148	335	418	20	10	Noncomparative
Chalhoub (2011)	USA	Mix	Single	5	76	31	64	64	1	14	Comparative
Cases (2009)	Spain	Malignant	Bilateral	22	67	30	63	NR	8	12	Noncomparative
Bazerbashi (2009)	UK	Malignant	NR	14	66	80	125	NR	28	11	Noncomparative
Efthymiou (2009)	UK	Malignant	NR	1	NR	NR	116	116	66	10	Noncomparative
Liang (2008)	China	Mix	NR	0.5	64	93	133	NR	16	14	Comparative
Sioris (2008)	Finland	Malignant	Bilateral	24	63	24	51	53	12	10	Noncomparative
Schneider (2008)	Germany	Mix	Bilateral	13	64	52	100	107	15	9	Noncomparative
Warren (2008)	USA	Malignant	Bilateral	13	NR	NR	202	231	18	10	Noncomparative
Tremblay (2006)	Canada	Malignant	Bilateral	36	64	124	223	250	63	12	Noncomparative
Murthy (2006)	USA	Mix	Bilateral	13	60	27	58	63	4	10	Noncomparative
Putnam (1999)	USA	Malignant	Single	7.4	60	36	94	94	12	19	Comparative

Abbreviations: IPCs, the numbers of placement of indwelling pleural catheter; MINORS, methodological index for nonrandomized studies; the multi-countries was defined as the composition of at least two different countries; NR, not reported; PE, pleural effusion.

TABLE 2 Baseline characteristics of patients and IPCs

	Subgroups	Patients number, $n = 4983$ (100%)	IPCs, $n = 5650$ (100%)
Mean age,[a] *n* (%)	> = 65	2784 (55.86%)	3278 (58.02%)
	<65	2083 (41.80%)	2215 (39.20%)
Sex,[b] *n* (%)	Male	2381 (47.78%)	—
	Female	2369 (47.54%)	—
Country, *n* (%)	Australia	121 (2.43%)	124 (2.19%)
	Canada	1004 (20.15%)	1062 (18.80%)
	China	195 (3.91%)	195 (3.45%)
	Dutch	45 (0.90%)	50 (0.88%)
	Finland	51 (1.02%)	53 (0.94%)
	Germany	549 (11.02%)	617 (10.92%)
	Italy	90 (1.81%)	97 (1.72%)
	Pakistan	102 (2.05%)	102 (1.81%)
	Spain	477 (9.57%)	507 (8.97%)
	United Kingdom	633 (12.70%)	633 (11.20%)
	United States	1917 (38.47%)	2057 (36.41%)
	Multi-countries	153 (3.07%)	153 (2.71%)
Etiology[c]	Lung cancer	1445 (29.00%)	—
	Breast cancer	841 (16.88%)	—
	Mesothelioma	292 (5.86%)	—
	Other cancer	1571 (31.53%)	—
	Heart failure	252 (5.06%)	—
	Liver failure	226 (4.54%)	—
	Other benign diseases	355 (7.12%)	—
PE-location	Left or right side	1198 (24.04%)	1210 (21.42%)
	Mix bilateral	2544 (51.05%)	2806 (49.66%)
	Not reported	1241 (24.90%)	1246 (22.05%)

Abbreviations: IPCs, the numbers of placement of indwelling pleural catheter; PE, pleural effusion.

[a]Two studies did not report the mean age.

[b]Four studies did not report the gender type.

[c]Three studies did not report the detailed etiology of malignant PE and four did not report the detailed etiology of benign PE.

Thus, the meta-analysis results are relatively stable and reliable.

DISCUSSION

PE places a significant burden on medical and societal resources.[1–6] IPC can effectively alleviate PE symptoms and is widely administered.[4,8] However, it also confers non-trivial complications which have not previously been fully described. Thus, we focused herein on the cumulative, meta-analysis-based evidence of clinical IPC complication incidences.

The resulting overall complication incidence was 20.3% among a cumulative 5650 IPCs in 4983 patients with either MPE or BPE. Krishnan et al. reported the lowest overall complication incidence (0.0%), whereas Muruganandan et al. reported the highest (89.6%).[25,33] We further analyzed the differences among studies reporting low (range 0.0–7.8%) and high (range 40.3–89.6%) complication incidences, revealing that the former were more likely to report use of home drainage post-IPC, regular follow-up strategies, and detailed follow-up evaluations.

In addition, Avula et al. reported a relatively high overall complication incidence of 30.6% in their meta-analysis of 269 total patients with hepatic hydrothorax[56] and the meta-analysis by Kheir et al. of three randomized trials showed a comparable rate of 24.0% among 171 patients with MPE.[57] Zahid et al. reviewed 78 patients with MPE to show an IPC-related complication

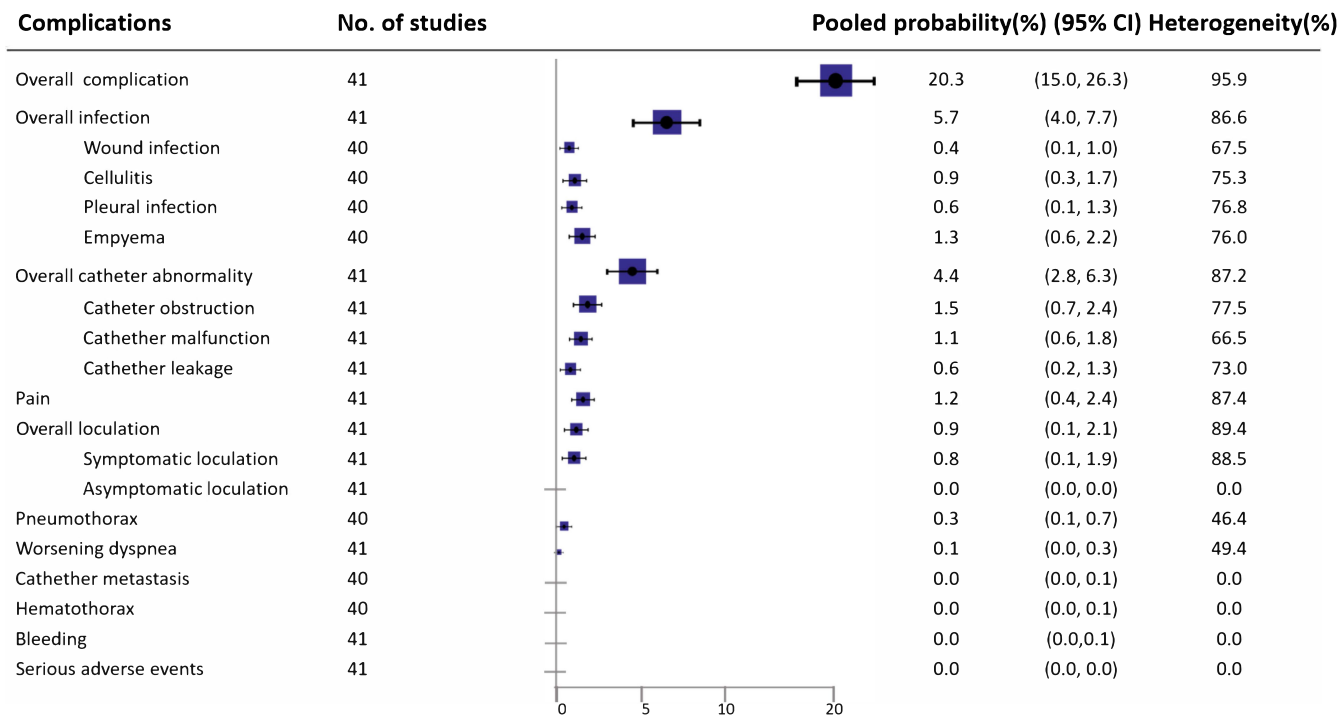

FIGURE 2 Forest plot shows the pooled results of different complications related to indwelling pleural catheter (IPC). CI, confidence interval.

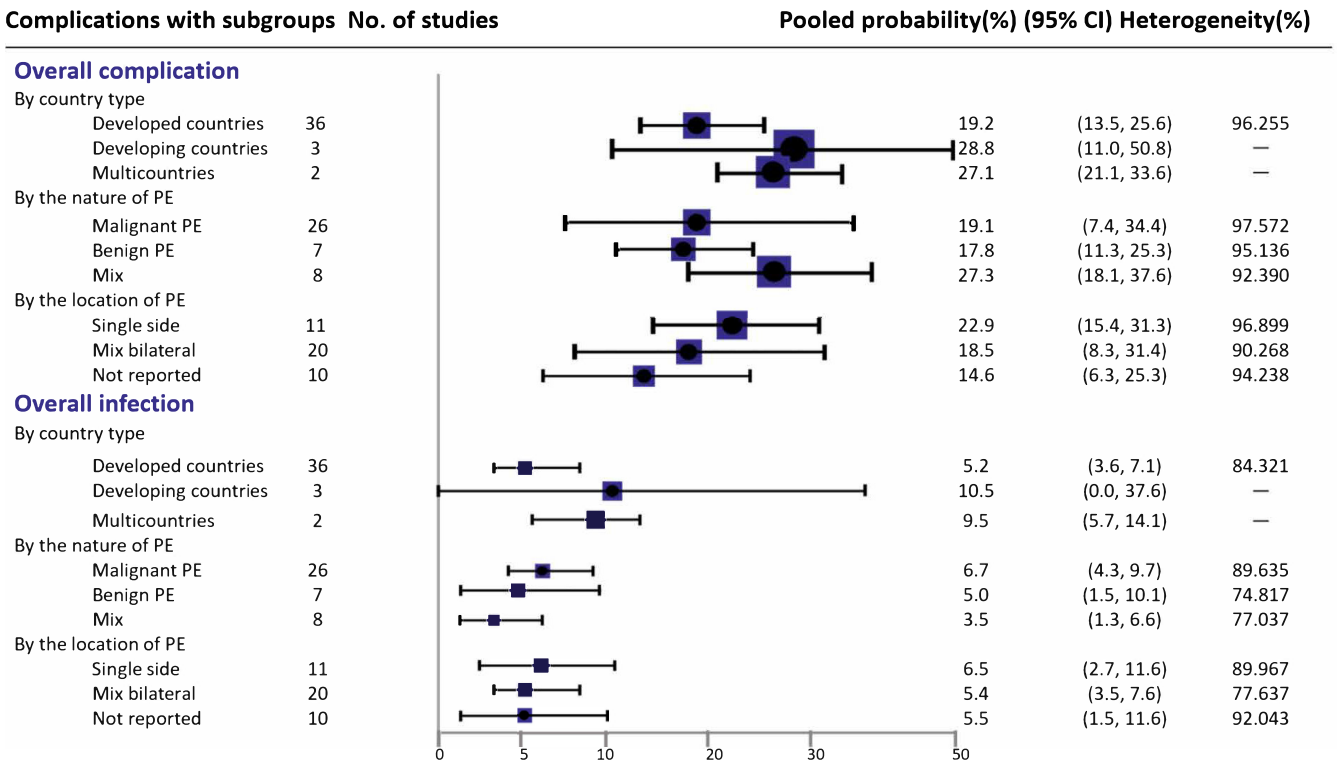

FIGURE 3 Forest plot shows the subgroup analyses results of overall complication and overall infection. CI, confidence interval; PE, pleural effusion.

incidence of 22.0%.[58] Therefore, our study, which included a large number of patients with MPE or BPE, showed more reliable, and relatively lower, overall complication incidence.

Infection was the most common complication herein (5.7%), including wound infection (0.4%), pleural infection (0.6%), cellulitis (0.9%), and empyema (1.3%). Patil et al. showed a higher rate of wound infection (2.7%) and

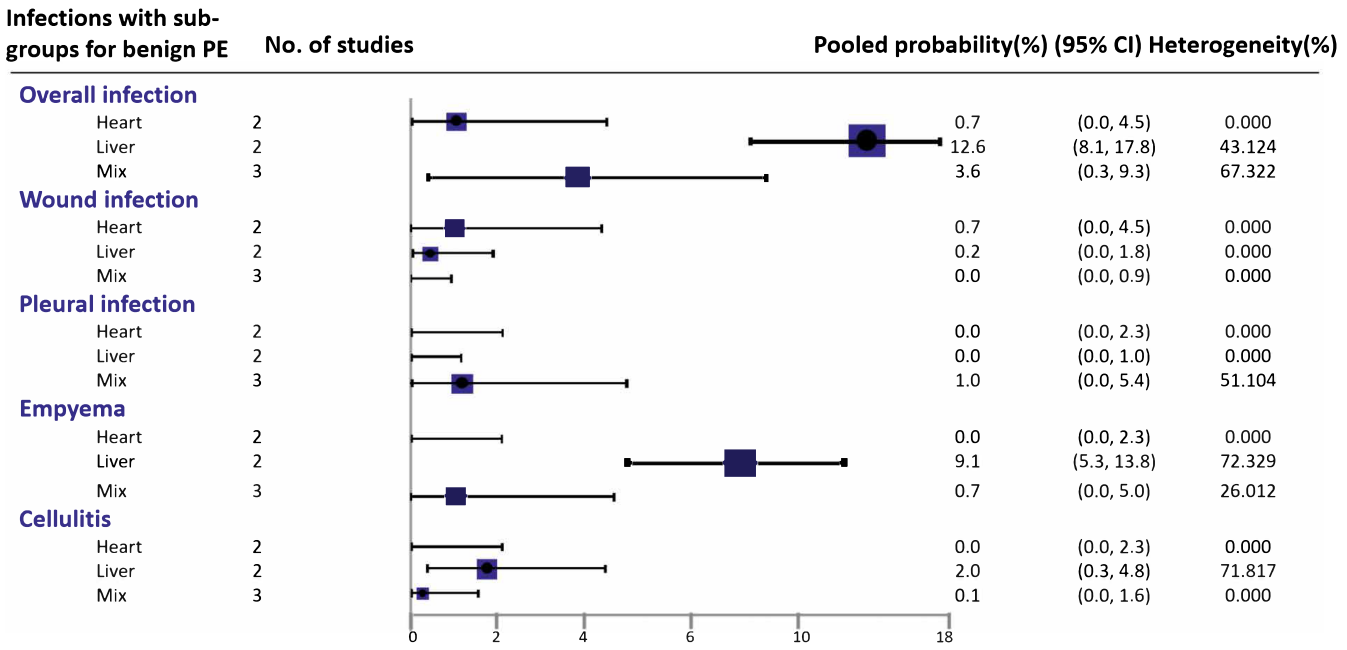

FIGURE 4 Forest plot shows the subgroup analyses results of different type of infection for patients with BPE. BPE, benign pleural effusion; CI, confidence interval; PE, pleural effusion.

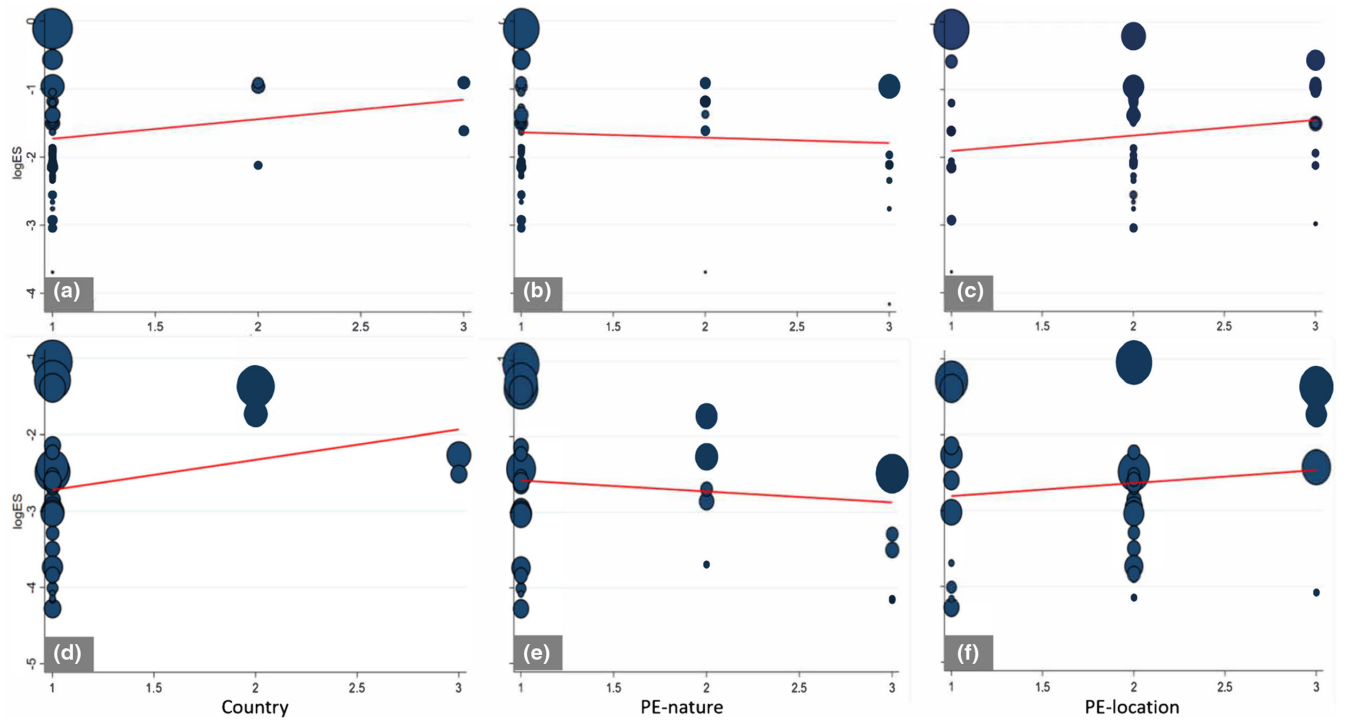

FIGURE 5 Bubble plot shows the meta-regression results of studies on overall complication by country (a), PE-nature (b), PE-location (c), and on overall infection by country (d), PE-nature (e), PE-location (f). PE, pleural effusion.

empyema (2.3%) in their meta-analysis of 325 patients with BPE.[11] In another meta-analysis of 246 patients with MPE, Iyer et al. demonstrated markedly higher rates of pleural infection (4.1%) and cellulitis (6.9%).[10] Our subgroup analysis also found the overall infection incidence (12.6% vs. 0.7%) and empyema incidence (9.1% vs. 0.0%) of patients with liver-related PE were significantly higher than that of patients with heart-related PE. Due to the limitation of the small number of studies (2 for liver-related and 2 for heart-related), more studies are needed in the future to confirm the previous conclusion and the relationship between BPE etiology and infection condition.

In this study, we extracted data of the median time ranging from 7 (5–10) days to 98 (23–291) days from IPC

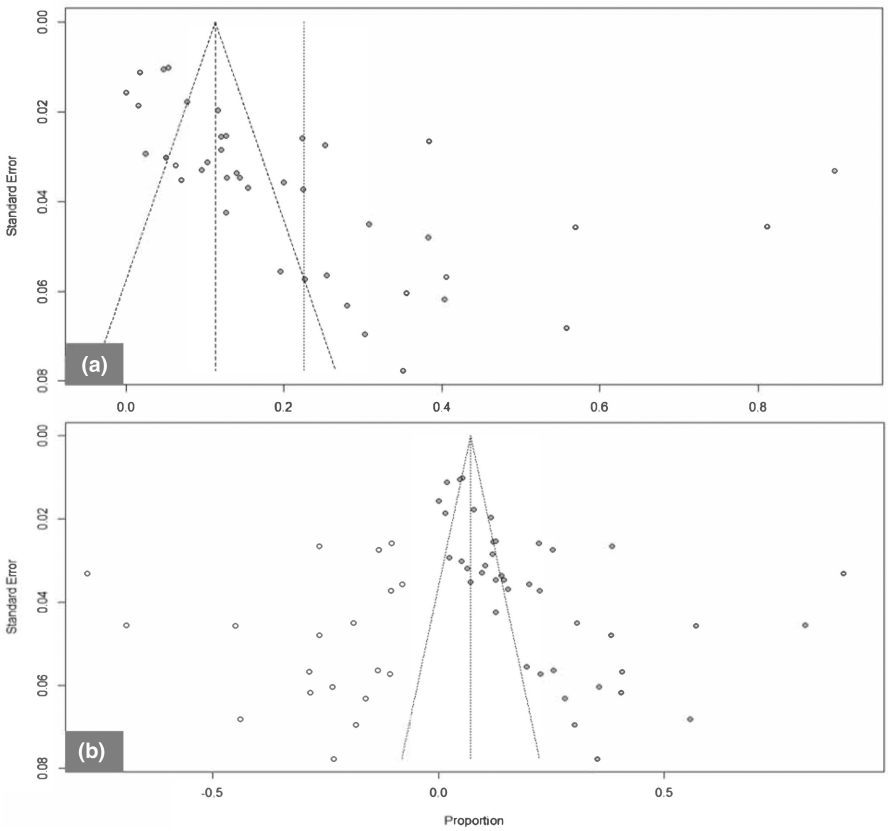

FIGURE 6 Publication bias assessment of all studies on overall complication (a). Funnel plot shows the potential publication bias (b). Trim and fill funnel plot shows that the publication bias did not change the pooled result.

insertion to infection in four studies. In addition, the reported median time was 41 (interquartile range 19–87) days, and neither antineoplastic therapy nor immunocompromised state increased the risk of IPC-related infection according to a multicenter study of 1408 IPCs among 1318 patients with MPE.[59] These investigators' conclusions were consistent with those of Mekhaiel et al.[60]

Methods to prevent and effectively treat postoperative infection, in addition to primary disease management, are high priorities. Zhao et al. studied 128 patients with MPE under focused preventive interventions, including maintaining an aseptic field throughout the surgical process, educating patients about normative IPC use, monitoring wound conditions, and regularly changing wound dressing and drainage bags; these significantly reduced IPC-related infection incidence from 13% to 5%.[61] In addition to these preventive measures, Gilbert et al. assessed 201 patients with MPE or BPE to show that use of prophylactic antibiotics decrease infection incidence to 2.2%.[62] However, we assert that the need for prophylactic antibiotics should be confirmed with large sample studies, in light of growing drug resistance from improper antibiotic uses. Infections should be treated early enough to avoid clinical aggravation. In cases of wound infection and cellulitis, oral empirical antibiotics, wound disinfection, and dressing changes without catheter removal are usually included in clinical management. Without timely treatment, wound infection and cellulitis can become pleural infection, empyema, or systemic infection.[63] Yet, in those with pleural infection or empyema, intravenous empiric antibiotics (after obtaining adequate blood and pleural fluid cultures) and adequate IPC drainage are commonly used. Antifibrinolytic therapy is sometimes required to insure smooth drainage. Fitzgerald et al.'s multicenter study addressed the safety of antifibrinolytic drugs for IPC-related infections, revealing that 82% of 39 patients with IPC-related pleural infection were successfully treated, with no major morbidity or mortality, with tPA (2.5–10 mg) and DNase (5 mg).[64] Further, Altmann et al. concluded that intrapleural fibrinolytic therapy is associated with both reduced need for surgical intervention and reduced IPC failure, without increasing mortality among patients with IPC-related pleural infection and empyema.[65] Regardless, we should attend to the problem of infection, as it accounts for a high proportion of IPC-related complications; this includes appropriate post-placement care and early identification and management of infection, to avoid systemic infection or more serious conditions.

Catheter-related abnormalities included catheter obstruction (1.5%), malfunction (1.1%), and leakage (0.6%). When a catheter has poor drainage, determining the cause is the first priority. If the problem is position, case-by-case tube adjustment or removal may be needed. If the lumen is blocked by embolus, antifibrinolytic therapy should be used, pending the outcome of normal saline irrigation. Emboli usually contain fibrin

and blood components; as such, alteplase is ideal due to its high fibrin affinity and selectivity, and short halflife.[66] The trial by Wilshire et al. reviewed 37 pleural catheter obstructions with alteplase (2–5 mg) without complication during or following.[67] Vial et al. studied 97 patients with MPE and nondraining IPC who received intrapleural tPA; 86% had restored patency after the first tPA dose. Among those who re-occluded, a second tPA dose restored patency in 72%. Those investigators reported complications in five cases (2 hemothoraces and 3 infections), among whom all were treated successfully without developing more serious events.[68]

Our pooled incidence of pain was 1.2%. When pain occurs, clinicians usually slow or stop drainage and prescribe analgesics, as necessary.[69] Pain may also be related to trauma from the catheter insertion into the recruitment lung.

Loculation (incidence 0.9% herein) included symptomatic (0.8%) and asymptomatic (0.0%). In such cases, antifibrinolytic therapy is usually used without complication. Thomas et al. showed pleural fluid drainage augmentation in 93% of 66 patients; dyspnea improvement was found in 83%, and only 3% had nonfatal pleural bleeding after antifibrinolytic therapy for IPC-related symptomatic loculations.[70] Lan et al. described an older woman with high bleeding risk in whom the lowest reported dose of 0.5 mg tPA was used to successfully treat loculation from IPC without bleeding.[71] We suggest that older patients, or those with poor tolerance, should specifically have treatment initiation for symptomatic loculation at a small dose.

Our meta-analysis also showed that the incidence of pneumothorax (0.3%), hemothorax (0.0%), worsening dyspnea (0.1%), tumor metastasis along the catheter (0.0%), and serious adverse events (0.0%) were very-low-to-negligible.

Our study was not without limitations. First, our pooled results generally had a high level of heterogeneity, for which we were unable to identify a clear source. This may have been related to the wide population range we included across studies. Second, we included only English language articles, which may have led to selection bias.

CONCLUSION

Our meta-analysis shows reliable pooled incidences of IPC-related complications, with infection occurring most commonly. The quantitative results herein serve to emphasize that clinicians should be aware of the incidences of IPC-related complications and apply corresponding preventive and therapeutic steps.

AUTHOR CONTRIBUTIONS

S.W. and R.Z. wrote the manuscript. Y.S., L.C., and F.W. designed the research. S.W., R.Z., J.Q., C.W., and X.H. performed the research. S.W. and J.Q. analyzed the data.

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CONFLICT OF INTEREST

The authors declared no competing interests for this work.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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