CHEST

Management of Benign Pleural Effusions Using Indwelling Pleural Catheters

A Systematic Review and Meta-analysis

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BACKGROUND: The indwelling pleural catheter (IPC), which was initially introduced for the management of recurrent malignant effusions, could be a valuable management option for recurrent benign pleural effusion (BPE), replacing chemical pleurodesis. The purpose of this study is to analyze the efficacy and safety of IPC use in the management of refractory nonmalignant effusions.

METHODS: We conducted a systematic review and meta-analysis on the published literature. Retrospective cohort studies, case series, and reports that used IPCs for the management of pleural effusion were included in the study.

RESULTS: Thirteen studies were included in the analysis, with a total of 325 patients. Congestive heart failure (49.8%) was the most common cause of BPE requiring IPC placement. The estimated average rate of spontaneous pleurodesis was 51.3% (95% CI, 37.1%-65.6%). The estimated average rate of all complications was 17.2% (95% CI, 9.8%-24.5%) for the entire group. The estimated average rate of major complications included the following: empyema, 2.3% (95% CI, 0.0%-4.7%); loculation, 2.0% (95% CI, 0.0%-4.7%); dislodgement, 1.3% (95% CI, 0.0%-3.7%); leakage, 1.3% (95% CI, 0.0%-3.5%); and pneumothorax, 1.2% (95% CI, 0.0%-4.1%). The estimated average rate of minor complications included the following: skin infection, 2.7% (95% CI, 0.6%-4.9%); blockage and drainage failure, 1.1% (95% CI, 0.0%-3.5%); subcutaneous emphysema, 1.1% (95% CI, 0.0%-4.0%); and other, 2.5% (95% CI, 0.0%-5.2%). One death was directly related to IPC use.

CONCLUSIONS: IPCs are an effective and viable option in the management of patients with refractory BPE. The quality of evidence to support IPC use for BPE remains low, and high-quality studies such as randomized controlled trials are needed.

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KEY WORDS: benign pleural effusion; indwelling pleural catheter; pleurodesis

ABBREVIATIONS: BPE = benign pleural effusion; CHF = congestive heart failure; HH = hepatic hydrothorax; IPC = indwelling pleural catheter; MPE = malignant pleural effusion

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Over the past decade, the indwelling pleural catheter (IPC) has become an attractive treatment option for the management of recurrent malignant pleural effusion (MPE).[1,2] Several case series have been published reporting the potential use of IPCs in the management of benign conditions such as congestive heart failure (CHF), hepatic hydrothorax (HH), renal failure, chylothorax, empyema, and so on.[3-13] Data regarding this approach are limited to retrospective cohort studies, case series, and case reports.[14,15] The aim of our paper is to review and analyze the published literature in this arena and to evaluate the efficacy and safety of IPC use in the management of patients with refractory non-MPE.

Methods

Search Methodology

A literature search was conducted using the electronic database engines PubMed, Cochrane database, EMBASE, and MEDLINE from January 2011 to January 2016 to identify published reports addressing outcomes in patients treated with an IPC for the treatment of pleural effusion due to benign conditions. The following words were used as the search keys: "indwelling pleural catheter," "PleurX catheter," "pleural catheter," "tunneled pleural catheter," "benign pleural effusion," "refractory nonmalignant effusion," "hepatic hydrothorax," "nonmalignant pleural effusion," "heart failure," and "congestive heart failure."

Study Eligibility

The studies were included in the analysis if they met the following inclusion criteria: (1) case series that used an IPC for the management of BPE regardless of the cause, (2) articles with reported follow-up, and (3) articles with reported outcomes. Retrospective cohort studies, case series, and abstracts presented at national meetings were included in this study. Articles were excluded if (1) there were not written in English, (2) no follow-up or outcomes were reported, or (3) they represented review articles, single case reports, and editorials. In retrospective cohort studies using multiple modalities for the treatment of both benign and malignant effusions, data from the cohort of patients who underwent either BPE alone or IPC alone, without chemical pleurodesis, were collected and analyzed. The quality of studies was assessed according to the Grading of Recommendations Assessment, Development, and Evaluation approach.[16] A Preferred Reporting Items for Systematic Reviews and Meta-Analyses flow diagram for details of the review process in the meta-analysis is shown in Figure 1.

Data Collection

The primary outcome was spontaneous pleurodesis with the resolution of pleural effusion and removal of the IPC with no need for additional pleural interventions. Any pleural punctures after the IPC placement were considered additional pleural procedures. Spontaneous pleurodesis was defined as a decrease in pleural fluid drainage to < 50 mL on three consecutive IPC drainage procedures, with no evidence of significant effusion on chest ultrasonography, chest radiography, or chest CT scan and no recurrence of pleural effusion after catheter removal. None of the included studies reported the use of ultrasonographic characteristics such as the absence of a gliding

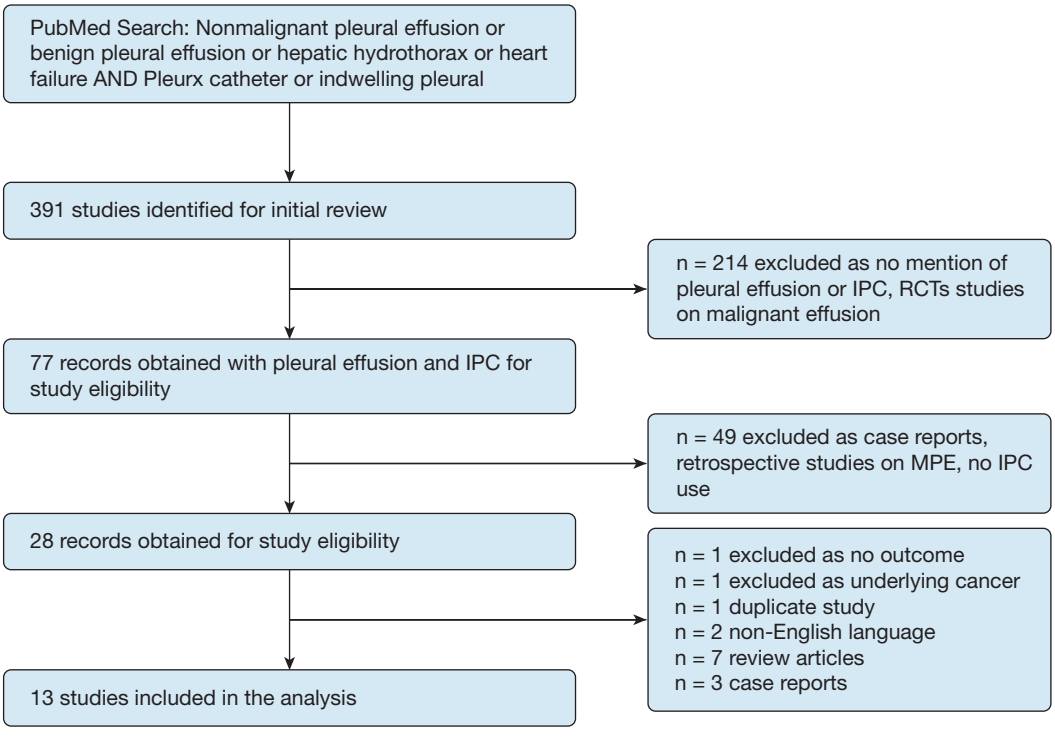


Figure 1 – *Preferred Reporting Items for Systematic Reviews and Meta-Analyses flowchart of included studies. IPC = indwelling pleural catheter; MPE = malignant pleural effusion; RCT = randomized controlled trial.*

sign to define true pleurodesis. All patients in the included studies underwent IPC placement for refractory BPE after being considered to have received optimal medical management.

The secondary outcomes included the time to pleurodesis, complication rates, and the number of patients requiring additional pleural procedures such as injection of a thrombolytic agent to treat a clogged IPC, antibiotic use, and replacement of the IPC. The safety of the IPC was assessed by the rate of complications. The complications were further divided into major and minor categories. Major complications were defined as ones that (1) required premature removal or replacement of the IPC, (2) produced serious infections such as empyema or sepsis, (3) produced pneumothorax, and (4) required additional invasive pleural procedures. Minor complications were defined as ones that did not require catheter removal and were managed conservatively without any invasive pleural intervention. The use of thrombolytic therapy to treat IPC blockage was considered a minor complication.

Statistical Analysis

The spontaneous pleurodesis and complication rates were summarized by studies using 95% CIs obtained using Jeffreys Prior method and displayed graphically using a forest plot. The results of the studies were combined in a meta-analysis using standard random-effects models, from which estimates of the average rates were obtained with 95% CIs. The models were also used to obtain 95% prediction intervals, which represent the range within which we would expect the rate of the new study to occur. The heterogeneity of the study outcomes was assessed using Q and I^2 statistics. The Q statistic evaluates the homogeneity assumption (ie, all studies have the same common rate), whereas the I^2 statistic represents the amount of variability in the meta-analysis attributed to study heterogeneity. There is a clear difference among the studies included in the analyses with multiple uncontrolled variables. The random-effects model was used because of the obvious heterogeneity.

Forest plots were presented to summarize the results. Every study that was included in the analysis represented a horizontal line. The center square represented the estimated effect, and the line represented the 95% CI. The combined effect of all the studies was similarly represented. Funnel plots were used to look for publication bias with the Egger test, which is a useful tool when conducting a meta-analysis. All analyses were conducted in SAS, version 9.4 (SAS Institute) at a significance level of .05.

Results

Based on the search criteria, we reviewed 391 records. Of the 391 records, only 30 papers were eligible for further review. Two studies were excluded because IPC was used in the management of cases with underlying hematologic malignancies and after lung transplantation.[17-19] Although the post-lung-transplantation pleural effusions were benign in nature, pleurodesis would be significantly affected by the thoracic surgery, and the role of the IPC in achieving pleurodesis is questionable. Therefore, we excluded this study from the analysis to avoid selection bias. We also excluded a study by Schneider et al[19] in which the IPCs were placed in malignant and nonmalignant effusions. In this study, the majority of nonmalignant effusions were of unclear cause, as 10 of the 12 patients were diagnosed with chronic inflammatory pleurisy. Additionally, the authors did not clearly define the complication rate of IPC placement between malignant and nonmalignant effusions, and therefore it was not possible to analyze the outcome. Also, most patients in this study underwent IPC placement as part of video-assisted thoracoscopic surgery, which can by itself affect the rate of spontaneous pleurodesis and complications.[19]

One abstract was excluded, as the same authors subsequently published a case series on a subset of their patients.[20] Another abstract by Imler et al[21] was excluded, as the authors described the placement of indwelling catheters in patients with refractory ascites or HH, but most catheters were placed in the peritoneal cavity, and the abstract did not reveal any IPC placement details such as pleurodesis and complication rates.[21] Three reports were found to be case reports and were excluded (Fig 1).[22-24]

Thirteen studies totaling 325 patients were included in the analysis. Eight of the 13 studies were published after 2010,[8-13,24-26] and seven of these were published as case series. Of the five studies published before 2010, two were case series[27,28] and three were abstracts (Table 1).[29-31]

All patients in the included studies were adults, with age ranging from 27 to 95 years. The majority of patients were men (175 patients [53.8%]). In all included studies, the IPC was used for BPE that was refractory despite optimal medical therapy. The causes of underlying effusion were cardiac causes (49.8%), hepatic disease (12.3%), chylothorax (3.4%), empyema (2.8%), inflammatory pleurisy (6.5%), renal disease (4.0%), yellow nail syndrome (1.5%), and others (19.7%), as shown in Table 2. Three hundred fifty IPCs were placed in 325 patients. Based on the available studies, it was difficult to estimate the duration of IPC in situ in all patients, because most of the included studies did not describe the mean time from IPC placement to a complication that required catheter removal. IPCs were inserted for symptom management, as a bridge to cardiac or liver transplantation, or for palliative purposes.

Spontaneous Pleurodesis

Of the 325 patients, 160 were reported to have spontaneous pleurodesis. The estimated average rate of

TABLE 1] Studies Included in the Analysis

Study/Year	Type of Study	Sample Size	Cause	Number of IPCs	Quality of Study
Majid et al[11]/2015	Retrospective cohort	23	Heart failure	28	⊕⊖⊖⊖ Very low due to risk of bias[a,b]
Krishnan et al[26]/2015	Case series	37	Multiple causes	44	⊕⊖⊖⊖ Very low due to risk of bias[b,c]
Potechin et al[12]/2015	Case series	8	ESRD	9	⊕⊖⊖⊖ Very low risk of bias[b]
Bhatnagar et al[8]/2014	Case series	57	Multiple causes	57	⊕⊖⊖⊖ Very low due to risk of bias[b,c]
Freeman et al[32]/2014	Retrospective cohort	40	Heart failure	40	⊕⊖⊖⊖ Very low due to risk of bias[b]
Srour et al[13]/2013	Case series	38	Heart failure		⊕⊖⊖⊖ Very low due to risk of bias[b]
DePew et al[10]/2013	Case series	11	Chylothorax	14	⊕⊖⊖⊖ Very low due to risk of bias[b]
Chalhoub et al[9]/2011	Retrospective cohort	23	Multiple causes	23	⊕⊖⊖⊖ Very low due to risk of bias[b]
Herlihy et al[27]/2009	Case series	5	Heart failure	5	⊕⊖⊖⊖ Very low due to risk of bias[a,c]
Kilburn et al[30]/2010	Abstract	8	Hepatic hydrothorax	8	⊕⊖⊖⊖ Very low due to risk of bias[b,c]
Borgeson et al[29]/2009	Abstract	22	Heart failure	23	⊕⊖⊖⊖ Very low due to risk of bias[b,c]
Murthy et al[28]/2006	Case series	11	Multiple causes	11	⊕⊖⊖⊖ Very low due to risk of bias[b,c]
Parsaei et al[31]/2006	Abstract	42	Multiple causes	45	⊕⊖⊖⊖ Very low due to risk of bias[b,c]

Grading of Recommendations Assessment, Development, and Evaluation Working Group grades of evidence were used: high quality = further research is very unlikely to change our confidence in the estimate of effect; moderate quality = further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate; low quality = further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate; very low quality = we are very uncertain about the estimate. ESRD = end-stage renal disease; IPC = indwelling pleural catheter.
[a]Clear evidence of selection bias.
[b]Methodology is case series.
[c]Missing information leading to information bias.

spontaneous pleurodesis was 51.3% (95% CI, 37.1%-65.6%) as shown in Figure 2. The rate of pleurodesis varied between studies and depending on the underlying cause. We conducted a subgroup analysis based on the cardiac and noncardiac causes of BPE. In the group with cardiac causes, spontaneous pleurodesis was achieved in 42.1% of cases (95% CI, 20.1%-64.1%) as shown in Figure 3. In the noncardiac group, spontaneous pleurodesis was achieved in 61.4% (95% CI, 45.3%-77.4%) as illustrated in Figure 4. When comparing cardiac and noncardiac causes of BPE, there was a nonsignificant difference between the groups (OR, 0.457; $P = .165$).

Time to Pleurodesis

The time to pleurodesis was reported in nine of the 13 studies. The meta-analysis could not be performed because five of nine studies[10-13,29] reported this outcome as median days, whereas the other four studies[8,9,25,26] reported the mean time to pleurodesis as shown in Table 3.

Additional Pleural Procedures

Eighty-four other pleural procedures were needed after insertion of IPCs, and they included therapeutic thoracentesis, diagnostic pleuroscopy, and catheter replacement.[8,10-13,25,27,31]

Hospital Readmission Rates

One of the important outcomes reported by the studies is the reduction in hospital stay and readmission rates. In a study by Freeman et al,[32] when compared with thoracoscopy and talc pleurodesis, patients with IPC insertion had a shorter hospital stay (mean of 2 days

TABLE 2] Patient Baseline Characteristics

Characteristic	Frequency (% of Patients)
Sex	
Male	175 (53.8)
Female	150 (46.2)
Side of effusion	
Right	135 (41.5)
Left	32 (9.8)
Both	17 (5.2)
Unknown	141 (43.4)
Cause	
Cardiac	162 (49.8)
Hepatic	40 (12.3)
Chylothorax	11 (3.4)
Empyema	9 (2.8)
Inflammatory pleurisy	21 (6.5)
Yellow nail	5 (1.5)
Renal disease	13 (4.0)
Other	64 (19.7)

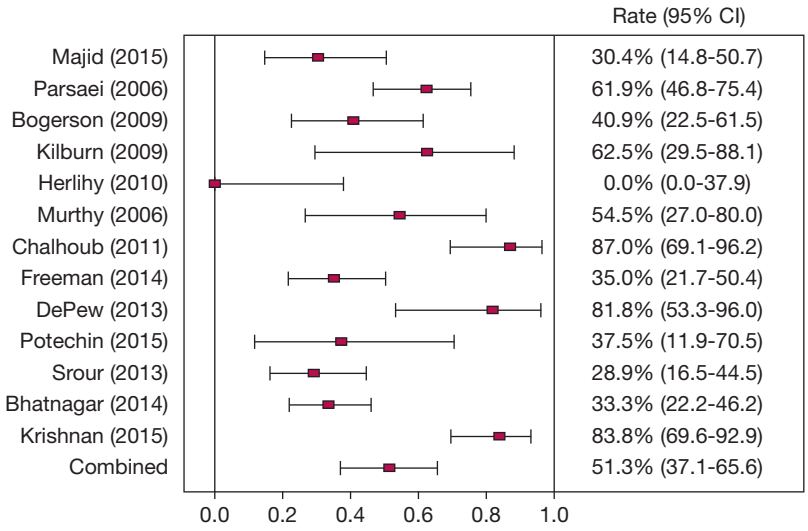
vs 6 days in the thoracoscopy group) and lower readmission rates (5% vs 23% in the thoracoscopy group), whereas other studies have shown a reduction in readmission rate due to pleural effusion,[20,26,29] as shown in Table 4.

Safety Outcomes

Regarding safety outcomes, the overall average rate of complications was 17.2% (95% CI, 9.8%-24.5%) (Table 5). The average rate of major complications included empyema, 2.3% (95% CI, 0.0%-4.7%); fluid loculation, 2.0% (95% CI, 0.0%-4.7%); IPC dislodgement, 1.3% (95% CI, 0.0%-3.7%); pleural fluid leakage, 1.3% (95% CI, 0.0%-3.5%); and pneumothorax, 1.2% (95% CI, 0.0%-4.1%). The average rate of minor complications included skin infection, 2.7% (95% CI, 0.6%-4.9%); blockage and drainage failure, 1.1% (95% CI, 0.0%- 3.5%); subcutaneous emphysema, 1.1% (95% CI, 0.0%-4.0%); and other, 2.5% (95% CI, 0.0%-5.2%). In subgroup analysis, the average rate of all complications in the group with cardiac causes was 16.1% (95% CI, 0.7%-31.6%), and it was 14.0% (95% CI, 6.8%-21.2%) in the group with noncardiac causes, with no significant difference between the groups.

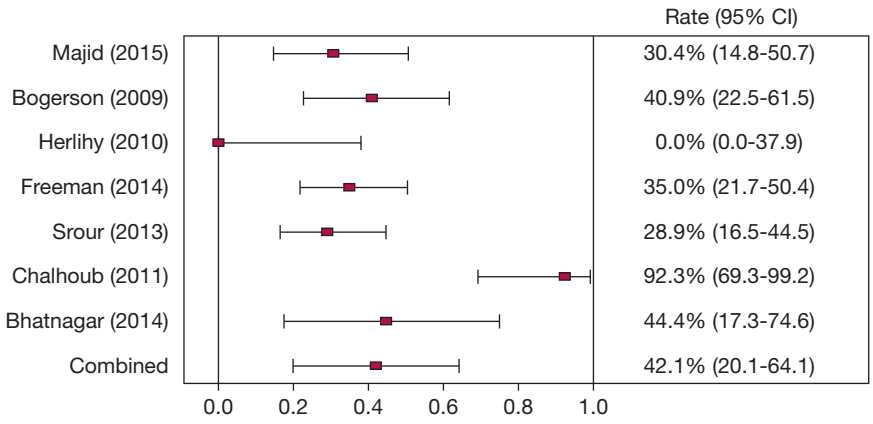
One of the major complications of IPC insertion is empyema. Overall, there were nine reported cases of empyema, and all were treated medically without any surgical intervention. Three of nine patients needed IPC removal, and one death was attributed to severe sepsis secondary to empyema.[27]

Most of the major and minor complications were treated conservatively. From the available data, 37 catheters were



	Estimated Average Rate (95% CI)	95% Prediction Interval	I^2	Q (*P* value)
Spontaneous Pleurodesis	51.3% (37.1-65.6)	(0.1%-100.0%)	87.2%	93.8 ($P < .001$)

Figure 2 – *Forest plot of estimated rate of spontaneous pleurodesis.*



	Estimated Average Rate (95% CI)	95% Prediction Interval	I^2	Q (*P* value)
Spontaneous Pleurodesis	42.1% (20.1-64.1)	(0.0%-100.0%)	88.4%	51.8 (*P* < .001)

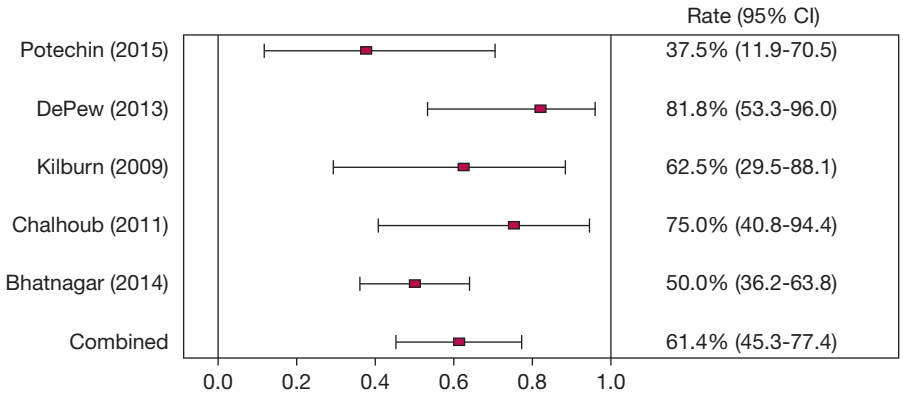
Figure 3 – *Forest plot of estimated rate of spontaneous pleurodesis in cardiac cases.*

removed secondary to complications. Complications that necessitated the removal of an indwelling catheter were loculation (three cases),[8,27] pleural fluid leakage (one case),[13] IPC dislodgement (one case),[12] and, as described earlier, empyema (three cases). Detailed information was reported from only eight of 37 catheter removals secondary to complications, leaving 29 catheters that were removed because of unspecified complications. Although there were six reported cases of pneumothorax secondary to IPC insertion, none of them required large-bore chest tubes.[13,28]

Among the minor complications, eight patients experienced insertion site local skin infection and were treated with topical antibiotics, with only one patient requiring systemic therapy.[8,9,23,25,28,31] Six patients had blockage and drainage failure, which were treated with tissue plasminogen activator injection.[8,10,29]

In studies that looked at electrolyte imbalances after IPC placement, there were no significant electrolyte abnormalities reported in patients with end-stage renal disease, heart failure, HH, and chylothorax.[9,10,12] Only two patients experienced renal failure, and one death was attributed to renal failure.[8]

There was clear heterogeneity in the included studies (retrospective cohort studies, case series, abstracts,



	Estimated Average Rate (95% CI)	95% Prediction Interval	I^2	Q (*P* value)
Spontaneous Pleurodesis	61.4% (45.3-77.4)	(13.2%-100.0%)	50.7%	8.1 (*P* = .087)

Figure 4 – *Forest plot of estimated rate of spontaneous pleurodesis in noncardiac cases.*

TABLE 3] Summary of Time-to-Pleurodesis Data

Study/Year	Sample Size	Cause	Patients Who Achieved Pleurodesis (No.)	Patients Who Achieved Pleurodesis (%)	Time to Pleurodesis (d)
Majid et al[11]/ 2015	23	Heart failure	7	30	66 (median)
Krishnan et al[26]/ 2015	37	Multiple causes	31	83.7	56.1 (mean, 19-140)
Potechin et al[12]/ 2015	8	ESRD	3	37.5	77 (median, 9-208)
Bhatnagar et al[8]/ 2014	57	Multiple causes	19	33.3	102 (mean)
Freeman et al[32]/ 2014	40	Heart failure	14	35	150 (mean)
Srour et al[13]/ 2013	38	Heart failure	11	28.9	66 (median)
DePew et al[10]/ 2013	11	Chylothorax	9	81.8	176 (median, 24-558)
Chalhoub et al[9]/ 2011	23	Multiple causes	20	86.9	110.8 (mean; SD, 41)
Borgeson et al[29]/ 2009	22	Heart failure	9	40.9	109 (median)

See Table 1 legend for expansion of abbreviations.

different underlying causes), which was statistically significant (I^2 = 84.1%). Based on the visual interpretation of the funnel plot, no significant publication bias was noted.

TABLE 4] Description of Readmission Rates and Reduction in Hospital Readmission After IPC Placement

Freeman et al[32]	Readmission rate in IPC group, 9 (5%) vs TP group 2 (23%) (P = .048)
Krishnan et al[26]	Admission rates dropped from 59 to 15 in patients with IPCs 1 y before and after IPC placement and from 42 to 6 in the 3 mo before and after IPC placement (P < .0001) In patients who achieved spontaneous pleurodesis, total admissions dropped from 60 to 9 in the 1 y before and after the IPC was removed and from 33 to 2 in the 3 mo before and after IPC removal (P < .0001).
Bogerson et al[29]	Rate of total hospitalizations dropped from 3.5 to 1.7 at 1 y after IPC placement (P < .02) and from 2.6 to 1.6 at 6 mo after IPC placement Rate of hospitalizations due to heart failure dropped from 2.3 to 0.6 at 1 y and from 1.7 to 0.5 at 6 mo after IPC placement (P < .02)

TP = thoracoscopic pleurodesis. See Table 1 legend for expansion of other abbreviations.

Discussion

The results of our analysis show that IPCs can be used effectively in the management of BPEs, with an estimated spontaneous pleurodesis rate of 51.3%, and could be considered in patients with refractory BPE for palliation. These results are similar to the meta-analysis conducted in a MPE population, which reported a spontaneous pleurodesis rate of 45%.[33] To our knowledge, this is the first meta-analysis that addresses the use of IPC in the management of BPE. We acknowledge that the major limitation of our study is that the reports included in this meta-analysis are non-randomized-controlled trials with low quality of evidence, but this is currently the best available data on this topic.

About 70% of patients with CHF have pleural effusion at some stage of their disease,[34] whereas 5% to 10% of patients with portal hypertension and 20% of patients receiving hemodialysis experience pleural effusion.[35,36] A small proportion of patients with heart failure experience pleural effusion despite receiving optimal medical care for their CHF. The treatment options for these patients are serial thoracenteses or surgical or chemical pleurodesis. Repeating thoracentesis entails multiple clinic or hospital visits, and this is challenging in cases in which the fluid is rapidly reaccumulating and in patients receiving anticoagulation therapy. Surgical or thoracoscopic pleurodesis has emerged as an option, but

TABLE 5] Estimated Rate of All Complications

Complication	Estimated Rate, % (95% CI)	95% Prediction Interval, %	I^2 (%)	Q (*P* Value)
Any complication	17.2 (9.8-24.5)	0.0-41.5	74.7	47.4 (.001)
Skin infection	2.7 (0.6-4.9)	0.3-5.1	0.0	4.4 (.974)
Empyema	2.3 (0.0-4.7)	0.0-5.0	0.0	1.3 (.591)
Loculation	2.0 (0.0-4.7)	0.0-5.0	0.0	3.3 (.993)
Dislodgement	1.3 (0.0-3.7)	0.0-4.0	0.0	3.1 (.994)
Pneumothorax	1.2 (0.0-4.1)	0.0-4.4	0.0	6.2 (.906)
Blockage/drainage failure	1.1 (0.0-3.5)	0.0-3.8	0.0	4.4 (.976)
Leakage	1.3 (0.0-3.5)	0.0-3.8	0.0	.8 (1.000)
Subcutaneous emphysema	1.1 (0.0-4.0)	0.0-4.4	0.0	6.3 (.901)
Other complications	2.5 (0.0-5.2)	0.0-5.5	0.0	5.4 (.944)

regardless of the type of chemical used in pleurodesis, there is a potential risk of respiratory complications associated with sclerosing agents and the longer need for hospital stay due to the amount of fluid drainage and management of postpleurodesis pain.[25,37,38] Patients with HH are particularly difficult to manage. The treatment options for refractory HH are serial thoracenteses, transjugular intrahepatic portosystemic shunt, pleurodesis, thoracoscopic diaphragmatic defect repair, and liver transplantation. Some patients do not qualify for the transjugular intrahepatic portosystemic shunt procedure, and surgical pleurodesis for treatment in HH was disappointing and is currently limited to patients with no other treatment options.[39-41]

The rate of spontaneous pleurodesis was our primary efficacy outcome. The estimated average rate of spontaneous pleurodesis was 51.3% for all benign conditions. Although CHF was the most common cause of BPE (49.8%) in our study, the estimated average rate of spontaneous pleurodesis in the cardiac cases was lower (42.1%) than in the noncardiac cases (61.4%), but the difference was not statistically significant. The exact mechanism of how IPC insertion leads to spontaneous pleurodesis is not known,[42] so it is hard to explain the difference in the rate of spontaneous pleurodesis among cardiac and noncardiac pleural effusions. One possible mechanism could be a low-grade inflammatory reaction that develops in response to the catheter acting as a foreign body in the pleural space.[9] However, the placement of IPCs for MPE was not associated with any changes in systemic inflammatory markers.[43]

Concerning symptomatic improvement, Srour et al[13] and Potechin et al[12] showed an improvement in dyspnea using the transitional dyspnea index score, whereas other studies reported a subjective improvement in dyspnea among the majority of the patients.[20,31] Along with symptomatic improvement, IPC use produced a reduced length of hospital stay and a reduction in readmission rates, which are relevant clinical outcomes. These results indicate that patients with IPCs had less dyspnea as well as improved symptoms; they also stayed out of the hospital. Thus, IPC is a viable option for palliation in selected patients with refractory BPE.

Based on our systematic review, our results concur with a previous study by Chalhoub et al[9] that showed a longer IPC duration (110 days vs 36 days) in patients with BPE when compared with MPE. The longer duration of IPC in benign effusions may be because patients with benign effusion have a longer survival compared with patients with MPE, many of whom die with an IPC in place. Despite a longer IPC duration in BPE, the estimated average rate of all complications was 17.2%, which is similar to the overall complication rate in MPE.[44] There was only one death related to IPC use in the study by Herlihy et al,[27] which also showed a significantly higher complication rate compared with other studies performed in patients with CHF. A possible explanation for the lower complication rate in subsequent studies and our analysis could be better patient selection and the fact that the studies were conducted in centers experienced in the management of patients with chronic IPC.[8,10,11,13,20,25,34] Two cases of renal failure with IPC use were reported by Bhatnagar et al.[8] Both these patients had IPC drainage of more than 3 L per week while receiving oral diuretic agents and experiencing concomitant diarrhea. Thus, it is unclear whether the renal failure could be solely attributed to IPC. Although none of the other studies reported any significant electrolyte abnormalities with IPC use for BPE, it would be prudent to monitor electrolyte and serum protein levels in these patients.

The major limitation of our study is that none of the included studies is a high-quality randomized controlled trial, as none have been published on this topic. There is a significant heterogeneity among the studies included in clinical outcomes ($I^2 = 87.2\%$) and complications ($I^2 = 74.7\%$). Heterogeneity was related to differences in underlying cause, patient selection, follow-up period, and handling of outcome measures. We used a random-effects model to minimize the effect of heterogeneity. Another significant limitation is the effect of missing data on the results. For example, from 38 IPCs that were removed secondary to complications, detailed information about the complications was reported in only five cases. We assumed that the missing information was at random but do acknowledge that a significant number of minor complications could have been severe enough to have led to catheter removal.

Conclusions

We conclude that IPC is an acceptable therapeutic option for the management of refractory pleural effusion secondary to benign conditions. The overall complication rate of IPC is comparable to the complication rate in MPE but with a longer IPC placement period. Studies of higher quality are required further to evaluate the use of IPC in the treatment of BPE.

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