REVIEW

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Comparative outcomes of indwelling pleural catheter versus chemical pleurodesis in malignant pleural effusion management: a systematic review and meta-analysis

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ABSTRACT

Introduction: Patients with advanced cancers frequently get malignant pleural effusions (MPEs). Chemical pleurodesis (CP) and the placement of an indwelling pleural catheter (IPC) are the two main therapy approaches. IPC installation in the outpatient context has grown in popularity. There is ongoing discussion over their relative efficacy. This study aimed to evaluate the comparison of outcomes of indwelling pleural catheter versus chemical pleurodesis in malignant pleural effusion management.

Methods: A thorough literature search was carried out using the databases of the Cochrane Library, PubMed, Google Scholar, Medline, Embase, and BMJ. Among these were six controlled trials. Random and fixed effects model is used with Review Manager. Continuous outcomes were measured using mean & SD differences, whereas dichotomous outcomes were measured using odds ratios (OR) with 95% CI.

Results: Significantly the IPC group has fewer further pleural procedures than CP group with OR 0.25 (95% CI: 0.15-0.43; p≤0.00001), despite its higher event of pleural infection OR 2.47 (95% CI: 1.07-5.67; p=0.03). The improvement in dyspnea score -0.65 (95% CI: -10.54-9.24; p=0.9), quality of life 1.35 (95% CI: -0.03–2.73 p=0.05), and number of hospital stay 0.23 (95% CI: -1.67-2.13; p=0.81) showed no significant differences between groups.

Conclusion: This study along with previous others, concerning other variable outcomes, may still highlights for personalized treatment considering patient preferences and clinician considerations in managing malignant pleural effusions. This study also showed that IPC may reduce repeat pleural procedures despite its tolerable pleural infection related problems.

Keywords: Indwelling pleural catheter, malignant pleural effusion, meta-analysis, pleurodesis.
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INTRODUCTION

Up to 50% of patients with advanced lung cancer will experience malignant pleural effusion (MPE), which can happen when non-pulmonary tumors cause metastatic pleural involvement.[1] Significant strides have been made in the management of MPE during the past ten years. Chemical pleurodesis has historically been the preferred method for preventing pleural fluid recurrence, with graded talc having the strongest evidence foundation.[2]

He pleural gap has been fused using a wide range of other substances, such as talc, povidone iodine, doxycycline, dextrose, and other sclerosants.[3] By causing a widespread inflammatory reaction and the deposition of fibrin between the visceral and parietal pleura, the chemical sclerosant closes the pleural gap and stops fluid from reaccumulating. The implantation of a chest drain and full fluid draining usually require an inpatient hospital stay, with around 70% of cases being successful.[2] A notable advantage of an indwelling pleural catheter (IPC) is the potential for spontaneous pleurodesis or auto-pleurodesis. IPCs are meant to remain permanently in the pleural cavity. According to studies, IPC is a safe treatment; 87.5% of patients (range: 54.5–100%) report no side effects.[1]

Chemical pleurodesis (CP) and the application of an IPC are the two main methods of treating malignant pleural effusions. Due to comparable benefits in dyspnoea and quality of life, as well as a lower cost of hospitalisation as compared to CP, IPC deployment in the outpatient setting is becoming a preferred strategy. The management aims to maximise time spent outside of the hospital and alleviate symptoms with the least amount of intervention.[4] Both strategies seek to reduce symptoms and enhance quality of life, but there is ongoing discussion on how beneficial they are in comparison. The results of IPC and chemical pleurodesis as

primary strategy treatment for MPE are evaluated and compared, with a focus on patient-centered outcomes, such as the relief of dyspnoea symptoms, improvement of quality of life (QoL), hospital length of stay (LoS), the need for repeat pleural procedures or reinterventions, and focused complications, such as pleural infection. This study aims to supplement data, despite the publication of a few similar meta-analyses in 2018 and 2020. Therefore, this study aimed to evaluate the comparison of outcomes of indwelling pleural catheter versus chemical pleurodesis in malignant pleural effusion management.

METHODS

Search strategy

Prior to 2022, on July 2024, relevant research was gathered from the Cochrane Library, PubMed, Google Scholar, Medline, Embase, and BMJ databases. We looked for "pleurodesis," "meta-analysis," "malignant pleural effusion," and "indwelling pleural catheter." No limitations on language were imposed. Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) criteria were used to write the sampling. In the PROSPERO International Prospective Register of Systematic Reviews, the review was not registered.

Selection criteria

This study included comparatives studies about IPC and chemical pleurodesis in managing malignant pleural effusion. The search included all age groups, genders and races undergoing pleural intervention, but was limited to unrandomized and randomized control trials (RCTs) study. Any study reporting pleurodesis via any kind of methods were included. When institution published duplicate studies, only the most complete one was used for quantitative assessment. The selection of original studies was according to the process of reviewing titles, abstracts, and full texts in accordance with predefined selection criteria. Sample size were 646 patients from 6 studies. For all included studies, the reviewers extracted data directly from article texts, tables, and/or figures. Study population characteristics, chemical pleurodesis instillation strategies, and five outcomes data included in this study were extracted. Discrepancies between the reviewers were resolved by discussion.

Statistical analysis

We conducted a meta-analysis using Review Manager (version 5.4). Using odds ratios (ORs) and 95% confidence intervals (CIs), the chance of a pleural infection and the reintervention of the pleural operation were examined as dichotomous variables. Using standardised mean differences (SMD) with 95% confidence intervals, QoL was investigated. The dyspnea score and LoS, on the other hand, were analyzed using the mean difference. Heterogeneity was assessed using the I2 statistic and the $\chi 2$ test. We used a random-effects

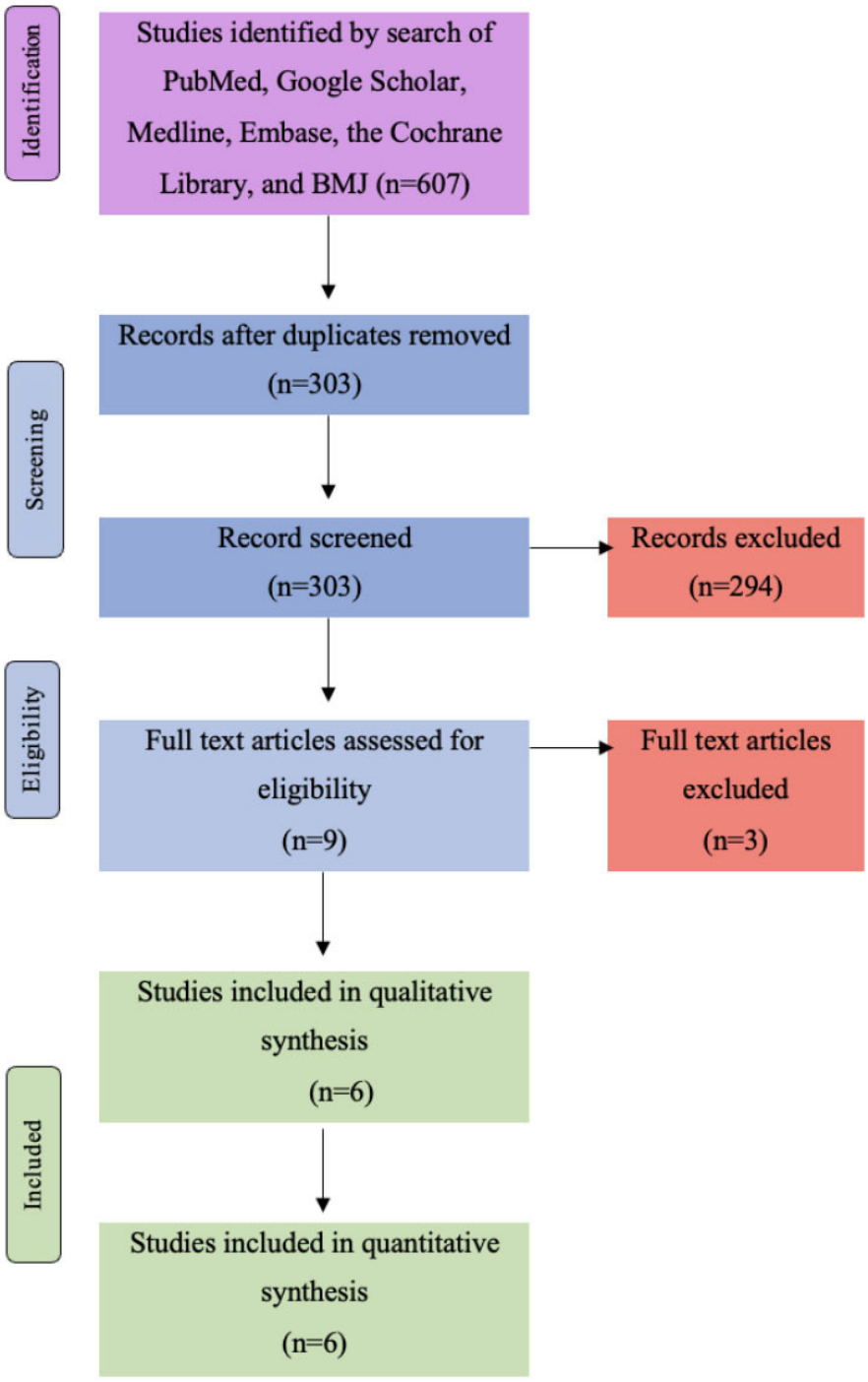

Figure 1. PRISMA schematic of search strategy. PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analyses.

Table 1. Characteristics of studies included in the meta-analysis

No	Author & Year	Country	Design	Sample size		Cancer Type	Pleurodesis
				IPC	CP		
1	Boshuizen et al 2017	Netherlands	RCT	46	48	Breast, 21% Lung, 33% other, 46% mesothelioma not specified	Talc via chest tube (size 15-20 Ch)
2	Thomas et al 2017	Multinational (Australia & Asia)	RCT	73	71	Breast, 12% Lung, 335 Mesithelionma, 26% Other, 29%	Talc via Thoracostomy (size 12-18 F)
3	Mehta et al 2017	India	RCT	50	50	Not specified	Talc or betadine
4	Davies et al 2012	UK	Unblinded RCT	52	54	Breast, 26% Lung, 24% Mesothelioma, 10% Other, 40%	4 g of sterile high grade talc (novatech) via chest tube (12F)
5	Fysh et al 2012	Australia	Non randomized CT	34	31	Mesothelioma vs adenocarcinoma vs others	Graded talc (Novatech)
6	Putnam et al 2000	U.S.A	RCT	40	68	Breast, 27% Lung, 40% Other, 33% Mesothelioma not specified	Doxycycline

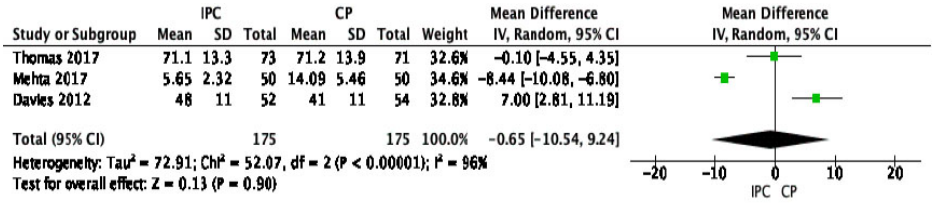

Figure 2. Forest plot of comparison IPC vs CP in terms of Dyspnea score.

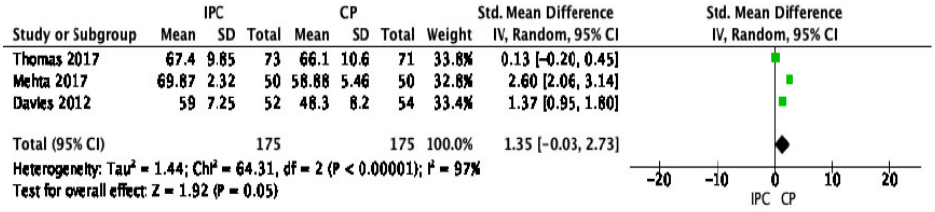

Figure 3. Forest plot of comparison IPC vs CP in terms of quality of life.

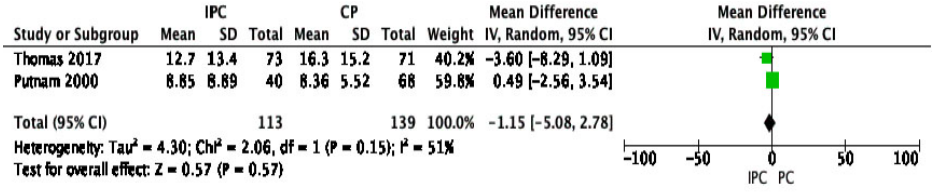

Figure 4. Forest plot of comparison IPC vs CP in terms of length of stay.

model when I2> 50%, indicating clear heterogeneity. Otherwise, we used a fixed-effects model. A p-value of less than 0.05 was regarded as statistically significant.

RESULTS

Figure 1 shows a PRISMA flow diagram of the overall search method, and Table 1 provides a thorough summary of the papers that were used for analysis.

Dyspnea score

We assessed the VAS dyspnea score of patients in both therapy groups. One trial used a 12-point Modified Borg Scale (MBS), one trial used a 100-point VAS (0 = highest possible dyspnea and 100 = no dyspnea), and two trials used a 100-point VAS (0 = no dyspnea and 100 = maximum possible dyspnea) to gauge the severity of dyspnea. Two of the six studies were excluded from the analysis due to the dichotomous nature of the data supplied. A 100-point rating system was created using the results of the three included trials, with 0 denoting no dyspnoea and 100 denoting the most severe possible case. The pooled mean difference in the increase of dyspnea score in this study analysis after 6 months follow up was 0.65 (95% CI: -10.54 - 9.24 p= 0.90). IPC was not significantly better compared to CP regarding dyspnea score for malignant pleural effusion.

Quality of life

Two of the included studies reported the mean and SD of QoL scores using the VAS measurement. VAS uses a 100-mm line that is anchored at 100 mm for "best quality of life" and 0 mm for "worst quality of life." Another mean and SD of QoL ratings, expressed as a percentage (a larger number indicates greater quality of life, limited clinically relevant improvement), was reported by Davies et al. using the EORTC QLQ-30 for evaluation. Breathlessness scores showed a similar trend to quality of life variables measured by VAS and EORTC QLQ-30. Therefore, we used SMD to perform a quantitative synthesis of QoL,

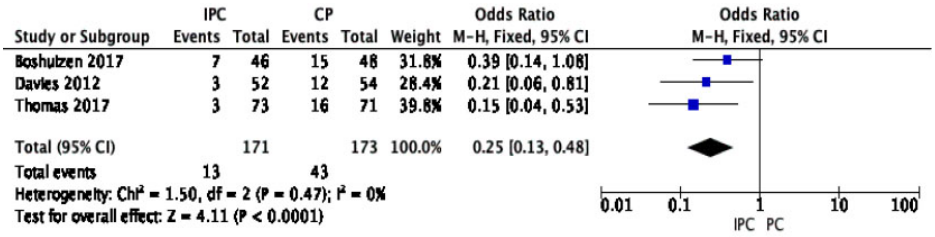

Figure 5. Forest plot of comparison IPC vs CP in terms of reintervention.

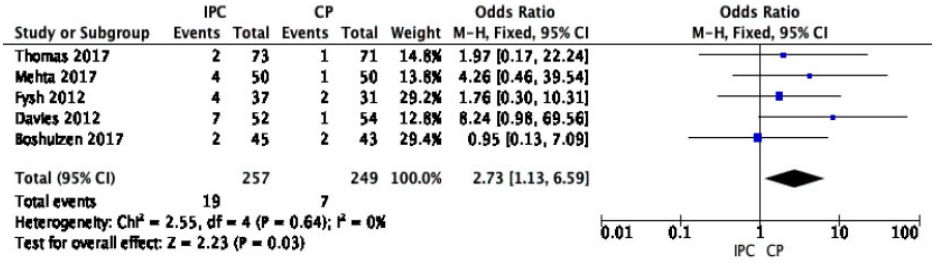

Figure 6. Forest plot of comparison IPC vs CP in terms of pleural infection.

and collected no significant difference in IPC and CP patients quality of life, 1.35 (95% CI: -0.03 – 2.73 p=0.05).

Length of stay

The number of length of stay (LoS) or total hospitalization time in our study was recorded in 2 studies. One of the 6 studies, Boshuizen et al. was excluded from the analysis due to the absence of the standard deviation. We also excluded 3 studies due to only median type data provided. Our study showed that there was no significant difference between IPC and chemical pleurodesis in term of overall hospital length of stay -1.15 (95% CI: -5.08-2.78; p=0.57).

Reintervention

Our results revealed that the IPC group had fewer further pleural procedures 0.25 times than the CP group, indicating better pleural fluid control of MPE (95% CI: 0.13-0.48; p ≤ 0.0001).

Pleural infection

The complications or adverse event of both groups were compared, focused on pleural infection event. Pooled data from studies included in our analysis significantly showed that chemical pleurodesis group has fewer pleural infection event compared to indwelling pleural catether group with OR 2.73 (95% CI 1.13-6.59; p=.03).

DISCUSSION

Although there was no discernible difference between the groups, our study, like Thomas et al.'s, showed a considerable improvement in dyspnea symptoms for MPE.[5] In comparison to CP, the IPC group had better symptoms following a 6-month follow-up, according to Davies et al. and Mehta et al.[6,7] Several studies that compare pleurodesis with IPC have shown conflicting findings. The IPC group had a clinically and statistically significant decrease in dyspnoea of −14.0 mm (p=0.01), but after six months, there was no significant difference in dyspnoea between the groups, according to Davies et al. But according to 6-month follow-up data, patients in the IPC group had better symptom reduction than those having pleurodesis. This difference was statistically significant.[6] Thomas et al's analysis, which was similar to this study, showed that although there was no statistical difference between the two groups, both IPC and pleurodesis significantly reduced dyspnoea. These results could help patients and doctors make decisions about MPE care.[5]

Although there were notable improvements from each baseline, the Thomas et al. study did not find any significant differences in the amount of QoL improvement brought about by pleurodesis or indwelling pleural catheter treatment. Davies et al. also observed no discernible change in the two groups' quality of life at any point in time, which is similar to these two investigations. The findings from the Mehta et al. investigation were different. The CP group's baseline quality of life (QoL) score was 43.21, whereas the IPC group's was 41.18. At 6-month follow-up, patients in the CP group scored 58.88 on the Quality of Life scale, compared to 69.87 for those in the IPC group. It was shown to be statistically significant (p <0.05). Based on their QoL score at 6-month follow-up, the results showed that patients in the IPC group had a higher quality of life than those in the CP group.[5–7]

Putnam et al and our investigation did not find any discernible differences in LoS. Different findings were found in the Mehta et al. investigation. Baseline quality of life (QoL) scores were 43.21 for the CP group and 41.18 for the IPC group. The 6-month follow-up QoL score for patients in the CP group was 58.88, but the IPC group's score was 69.87. The results showed that it was statistically significant. According to Liou et al., the length of stay following chemical pleurodesis was greater than that following IPC, but generally, the duration of stay was equivalent. Most frequently, the requirement to continuously inject talc or other sclerosing agents for high-chest tube output results in an extended period of stay. When these occurrences are eliminated, the two groups' LOS is equal.[4,5]

IPC insertion significantly decreased the need for reinterventions for recurring ipsilateral effusions. Our findings and all other studies showed that IPC had less needless pleural procedures, indicating better pleural fluid control of MPE, and that IPC placement would be more suitable than pleurodesis for palliation. The lower reintervention rate linked to IPC is a crucial consideration when deciding how best to treat patients with malignant pleural effusions.[4,5]

Davies et al.'s unblinded RCT found that the IPC group required 6% fewer further pleural treatments than the CP group (p=0.03). Only 4% of IPC-treated patients needed additional pleural drainages, according to Thomas et al.'s findings, while 22% of CP patients did (p = 0.001). It was also shown in the Boshuizen et al. study that CP patients

needed a reintervention more often than IPC patients (11% vs. 0.53). Chemical pleurodesis was more likely than IPC to require follow-up treatment for non-resolving MPE (15.7% vs. 6.3%, P=0.04), according to the Liou et al trial. Adding more talc at the patient's bedside was the most popular intervention. Hunt et al. found that indwelling pleural catheter led to fewer ipsilateral reinterventions than VATS talc, which is consistent with all of these other trials. According to these data, IPC installation would be a better palliative option than pleurodesis for patients with a poor prognosis and a short anticipated lifespan. When choosing how best to treat patients with malignant pleural effusions, the decreased reintervention rate associated with IPC is a significant factor.[8]

Consistent with our research, the potential benefits of IPCs are linked to a higher rate of observed adverse events with OR (4.7) in the Davies et al. study when compared to pleurodesis. This includes one patient without a major pleural infection and five patients (9.6%) with a serious pleural infection. All of these severe pleural infections happened after the fact. Like any indwelling device, they do have the potential to become infected; according to a research by Hunt et al., 2% of patients develop empyema using IPC.[6,8,9]

The Fysh et al. experiment, however, did not appear to have a major issue with the common concerns of infections linked to IPC. Therefore, IPC removal was not necessary because the likelihood of infection did not differ significantly and the empyema linked with IPC responded swiftly to medicines without generating any serious long-term negative effects. The 2017 study by Boshuizen et al. found that the pleural infection rate was modest and did not differ among treatment groups, with two out of forty-five IPC patients and two out of forty-three CP patients having a p-value of 1. From Thomas et al, two pleural infections have been linked to indwelling pleural catheter treatment. It's similar to chemical pleurodesis. The Mehta et al. study found that pleural infections happened in 1 patient (2%) in the CP group and 4 patients (8%) in the IPC group (p=0.362), which is again not significant.[10]

Analyzing side effects is crucial for evaluating how well the two medications work for MPE patients.[11] Even while the reported pleural infection outcome was more common in our IPC group than in CP, the number of occurrences in each group was comparable. for patients with malignant pleural effusions, so that both IPC and CP indicate the same impact.[11]

Furthermore, as was the case with other long-term studies, the data showed that issues with indwelling pleural catheters (such empyema) were not severe and did not raise the median number of inpatient days.[5] All IPC-related empyema's were effectively treated with antibiotics and catheter drainage. None of them needed the catheter to be removed early. Once the infection had cleared up, the catheters were removed from two patients who had spontaneously pleuroded.[10] Due to the asymptomatic nature of both individuals, some reported non-serious pleural infections might have been catheter colonization rather than infection.[6] One (4.3%) instance had a major IPC complication, empyema, which was successfully treated with antibiotics and IPC removal without resultant serious repercussions.[1] It was necessary to remove the catheter in every case of empyema; in two cases, this was done through open drainage, and in four cases, it was replaced with pigtail or chest tubes.[13] Infections usually do not require the removal of IPCs. Anti-biotherapy will be used to treat superficial and deep-seated pleural space infections. For deep-seated pleural infections, continuous drainage will be used, and in certain situations, such as when drainage is insufficient, fibrinolytics and DNase will be injected via catheter before IPC removal is considered. A good preventive measure is probably to teach patients and their families how to properly access the IPC.[12]

There are a number of other limitations to this meta-analysis. Due to a number of factors, our meta-analysis showed significant heterogeneity. These included the fact that different studies used different data types, which had an impact on calculations and results; that the different studies used different measurement tools for the dyspnoea score and quality of life; and that some studies measured different types of hospitalization and not all of them mentioned all causes of hospitalization. The reintervention into the pleural space of each group was not sufficiently explained. Lastly, infectious adverse events must be more closely monitored.

CONCLUSION

This study concludes that IPC may reduce futher pleural procedures for malignant pleural effusion patients despite its pleural infection event. Indwelling pleural catheter also appeared with its tolerable infection related problems. Taking notice into chemical pleurodesis, despite its fewer pleural infection event the needs for repeat pleural intervention are aware to be quite a lot of events. Admittedly, resemblant results in this study along with others concerning other outcomes still highlight the need for personalized treatment considering patient preferences and clinician considerations in managing malignant pleural effusions. Further even researches to minimize bias by exerting equal data type, synchronizing measurements tools or the use of several tools in one study, and also larger population are needed to constantly confirm all the previous studies and meta-analysis findings and so onwards guide to the best clinical decisions. As a consideration, next expected studies regarding MPE and its management may include new protocols followed by multiple multicenter studies, despite recent results from all past available meta-analysis, to improve entire patient's outcomes.

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DISCLOSURES

Ethical Considerations

None.

Conflict of Interest

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AUTHOR CONTRIBUTION

From researching topics, gathering material, conducting factual investigations, and revising the paper, each author makes a comparable contribution to the thought process until the publication of the paper details the consideration.

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