

# Effect of intraoperative fluid volume on postoperative pulmonary complications in thoracic surgeries: A systematic review and meta-analysis

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## ABSTRACT

**Background and Aims:** There is a lack of clear recommendations on fluid strategies in patients undergoing thoracic surgeries. The primary objective of this study was to compare the amount of intraoperative intravenous fluid (IVF) infused between those who developed postoperative pulmonary complications (PPCs) and those who did not. **Methods:** All studies comparing PPCs in intraoperative restrictive versus liberal fluid therapies were included. Those studies where the average fluid infused was compared between PPC and the 'no PPC' groups were also included. The pooled mean difference in IVF between patients with and without PPC and the pooled risk ratio of PPC in restricted versus liberal fluid arms were calculated. **Results:** Articles from PubMed ( $n = 157$ ), EMBASE ( $n = 724$ ) and citation searching ( $n = 4$ ) were included. After excluding duplicates, title–abstract screening for 759 articles and full-text screening for 24 articles were done. The mean fluid infused in the 11 included articles was significantly higher in those with PPC (mean difference: 1.51 ml/kg/h,  $P = 0.001$ ). The pooled proportion of PPC in liberal fluid arms was higher than in restricted fluid arms [risk ratio = 0.58 (95% confidence interval: 0.33, 1.02),  $P = 0.06$ ]. There was high heterogeneity in both the meta-analyses. **Conclusion:** The meta-analysis showed that increased intraoperative IVF is associated with higher PPCs, and a restricted fluid strategy might be safer to reduce PPCs. However, since most studies were observational with a high risk of bias and high heterogeneity, well-conducted randomised controlled trials are needed to derive recommendations.

**Keywords:** Acute respiratory distress syndrome, fluid therapy, lung injury, pneumonia, postoperative complications, pulmonary atelectasis, thoracic surgery

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## INTRODUCTION

Postoperative pulmonary complications (PPCs), such as respiratory failure, acute respiratory distress syndrome (ARDS), acute lung injury (ALI), prolonged air leak, pneumonia, pleural effusion, etc., have been described in 12%–40% of the patients after lung surgeries in literature, with a mortality of more than 50%.<sup>[1-3]</sup> The mortality rates increase proportionally with the number of PPCs per patient.<sup>[4]</sup> The strategies to reduce their incidence have been explored, especially in thoracic surgeries. One of the leading strategies is to reduce the fluid administered intraoperatively,

thereby decreasing the hydrostatic pressure in pulmonary capillaries, which in turn can reduce postoperative complications. In addition, overzealous

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fluid administration may flood the lungs and stress the myocardium. In one of the earlier studies on the risk factors for pulmonary oedema in 10 cases undergoing pneumonectomy, a large perioperative fluid load was an important contributor.<sup>[5]</sup>

There is a lack of clear recommendations on intraoperative fluid management strategies in patients undergoing thoracic surgeries. While some studies favour a restricted fluid strategy, others do not. Therefore, this study aimed to systematically collect and analyse the available literature to study the impact of fluid strategies/volume on PPCs in patients undergoing thoracic surgeries. The primary objective of this systematic review and meta-analysis (SRMA) was to evaluate whether the infused intraoperative fluids were significantly different in those with PPCs compared to those without PPCs among patients undergoing thoracic surgery under general anaesthesia. The secondary objective was to see whether the incidence of PPC in patients undergoing thoracic surgery was significantly different in those receiving restrictive fluids compared to those receiving liberal fluids.

## METHODS

We conducted this SRMA according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.<sup>[6]</sup> Before initiating the systematic review, the protocol was registered with the International Prospective Register of Systematic Reviews (PROSPERO) (ID: CRD42023468574, dated 13.10.2023).

Research questions following the PICO (Population, Intervention or Exposure, Comparison, Outcome) framework were as follows:<sup>[7]</sup>

- a) In patients undergoing thoracic surgery (P), is the amount of intravenous fluid (O) significantly different between those who developed PPC (I) and those who did not (C)?
- b) In patients undergoing thoracic surgery (P), does restricted fluid administration (I), compared to liberal fluid administration (C), reduce postoperative pulmonary complication (O)?

In studies comparing the mean fluid infused between PPC and no PPC, PPC was treated as the primary outcome, with fluid infusion serving as the exposure.

Conversely, in studies evaluating the incidence of PPC between restricted and liberal fluid strategies, the liberal fluid approach was considered the exposure and PPC was regarded as the secondary outcome.

The primary outcome measure was the amount of intraoperative fluids infused, and the secondary outcome was postoperative complications in adult patients undergoing thoracic surgery under general anaesthesia.

*Eligibility criteria:* In patients undergoing thoracic surgery, studies comparing PPCs in restrictive versus liberal fluid therapy or the studies comparing average intravenous fluid infused in those who developed PPCs versus those who did not were included. Those studies where mean [standard deviation (SD)] or median (interquartile range) were not provided and restrictive/liberal strategies were not defined clearly were excluded. Case studies, case series, conference abstracts and letters to the editor were excluded.

*Information sources:* All articles published till 31.08.2024 in PubMed and Excerpta Medica Database (EMBASE) were screened. Articles published in all languages were included. All comparative studies were included.

*Search strategy:* The following search string was used: ('thoracic surgery' OR 'lung transplant' OR thoracotomy OR pneumonectomy OR VATS OR thoracoscopy OR lobectomy OR 'lung resection') AND (perioperative OR intraoperative) AND (fluid\*) AND ('post-operative pulmonary complication' OR 'pulmonary oedema' OR 'pulmonary oedema' OR ARDS OR 'acute respiratory distress syndrome' OR 'lung injury' OR pneumonia OR 'pleural effusion') [Supplementary Table 1]. Further studies were selected by manually researching the references identified from the original studies.

*Selection process:* Duplication removal was done using the Rayyan software (<http://rayyan.qcri.org>). One of the authors reviewed the possible duplicates flagged by the software through the title and abstract. After duplicate removal, the studies were selected in two phases: title–abstract and full-text screening. SDA and NG independently performed the two phases of screening. RG resolved disagreements. Both SDA and NG independently extracted data from the final selected articles. An Excel sheet was used to record the extracted data.

*Data items:* The following variables were collected: author details, type of study, total number of patients, definition of restricted and liberal fluid strategies, number of patients with postoperative complications in restrictive and liberal strategies, and mean fluid infused in those who developed complications and those who did not.

*Study of risk of bias assessment:* The Joanna Briggs Institute checklist for analytical cross-sectional studies was used to assess the quality of included studies.<sup>[8]</sup> Publication bias was addressed with funnel plots.

*Synthesis methods:* For those studies where mean fluid infused was compared between PPC and no PPC, PPC was considered the primary outcome, with fluid infused considered as the exposure. For those studies where the incidence of PPC was measured between restricted and liberal fluid, the liberal fluid strategy was considered the exposure, with PPC considered as the secondary outcome.

Wherever more than two groups of fluid strategies were present, the lowest volume was taken as restrictive, and the remaining groups were compiled into one group of liberal strategies. The total fluid intake used for defining the strategy and the mean/standard deviation (SD) of total fluid infused was expressed in ml/kg/h. Whenever the value was unavailable, the study population's mean operating time and average weight were converted into the desired unit. The pooled mean difference (MD) in intraoperative fluid infused between those who developed PPC and those who did not was calculated using a random-effect model (inverse variance method). The pooled proportion of PPC in restricted and liberal intraoperative fluid arms was compared using a random-effects model (Mantel-Haenszel method) to calculate the pooled risk ratio (RR).

*Certainty assessment:* The results were represented by a point estimate with a 95% confidence interval (CI). The heterogeneity across studies for all the outcomes was tested using Tau<sup>2</sup>, Chi<sup>2</sup> and I<sup>2</sup> tests. An I<sup>2</sup> of more than 60% was taken as significant heterogeneity. Review Manager (version 5.3; Cochrane Nordic, Copenhagen, Denmark) was used for the meta-analysis.

*Trial sequential analysis (TSA):* TSA was conducted for the primary outcomes to evaluate the cumulative evidence and adequacy of the recruited sample size using the TSA program version 0.9.5.10 Beta.<sup>[9]</sup> The

cumulative, sequential Z score curve was constructed by calculating Z statistics from each study. The meta-analysis monitoring boundaries for definitive benefit and harm and the required sample size were calculated based on an overall type I error of 5%, a power of 80% and the pooled effect size derived from the actual meta-analysis.

## RESULTS

*Study selection:* This review included 157 articles from PubMed and 724 articles from EMBASE [Figure 1]. A total of 24 articles were included for full-text screening. Of these, 13 articles were excluded (incomplete data on outcomes- eight, wrong article type- three, incomplete data on intervention- one, full-text not available- one), and 11 articles were finally included for quantitative synthesis.

*Study characteristics:* Three of the 11 studies were prospective observational studies, whereas the remaining were retrospective cohort studies. Of the 11 studies in SRMA, the most common indication for surgery was lung malignancy, followed by idiopathic pulmonary fibrosis [Table 1]. Lobectomy [open or video-assisted thoracic surgery (VATS)] was the most common surgery performed. Neoadjuvant therapy varied from 4% to 22% in the studies. Thoracic epidural anaesthesia was given in 25%–100% of the patients in various studies. In various studies, the American Society of Anesthesiologists (ASA) physical status of > 3 was seen in 7%–93% of the patients. The most common types of PPCs were pneumonia (range: 4.2%–41.2%), ALI/ARDS (0.67%–7.8%), atelectasis (1.4%–37%) and respiratory failure requiring pressure support (1%–18%) [Table 2].

*Risk of bias in studies:* Inclusion criteria were mentioned in all studies except three. Study subjects and settings were clearly described in all but one study [Supplementary Table 2]. Exposure was measured validly and reliably in only six studies. Objective and standard criteria for measurement of the condition were mentioned in all the studies. Confounding factors were identified in all studies, but three studies did not clearly define strategies to deal with confounding. Except for one study, outcomes were measured clearly. Appropriate statistical analysis was used in all studies [Supplementary Table 2].

*Results of individual studies:* Six of the 11 articles had data comparing mean intraoperative fluid

between those who developed PPC and those who did not [Table 3]. Most of the studies ( $n = 5$ ) were reported after 2010. All the included studies were observational. The incidence of PPC ranged from 2.8% to 54.7%. The mean fluid infused in those with PPC ranged from 6.58 to 11.1 ml/kg/h, while it was 4.61 to 11.2 ml/kg/h for those without PPC. Five articles compared the incidence of PPC in those with restrictive fluid strategy and those with liberal fluid strategy [Table 4]. Most

of the studies were published after 2018 ( $n = 4$ ). The sample size of the studies ranged from 146 to 1426. The definition of restrictive fluid strategies ranged from less than 6 to less than 16.8 ml/kg/h. The definition of liberal fluid strategy ranged from more than or equal to 6 to more than 16.8 ml/kg/h. The proportion of PPC in patients who received restrictive fluid ranged from 6.1% to 43.9%, whereas it was 10% to 36.6% in those receiving liberal fluid strategy.

**Table 1: Baseline characteristics of the 11 studies included in the systematic review**

Author	Sample size	Indication for surgery	Type of surgery	Surgical modality	Neoadjuvant therapy	Thoracic epidural	ASA physical status $\geq 3$
Wu 2019 <sup>[10]</sup>	446	Mx (95%)	Lobectomy (100%)	VATS (100%)	NA	NA	NA
Kim 2020 <sup>[11]</sup>	1031	Mx (100%)	Lobectomy (94%)	Open (100%)	22%	41%	7%
Parquin 1996 <sup>[12]</sup>	146	Mx (93%)	Pneumonectomy	NA	10%	NA	NA
Jing 2018 <sup>[13]</sup>	451	Mx (100%)	Lobectomy (73%)	VATS (86%)	NA	25%	41%
Baar 2022 <sup>[4]</sup>	1426	Mx (100%)	Lobectomy (70%)	Open (100%)	Radiotx (13%) Chemotx (10%)	58%	93%
Licker 2003 <sup>[14]</sup>	868	Mx (100%)	Lobectomy (51%)	Open (100%)	NA	84%	27%
Blank 2011b <sup>[15]</sup>	129	Mx (89%)	Pneumonectomy (100%)	NA	NA	95%	86%
Mizuno 2012 <sup>[16]</sup>	52	IPF (100%)	Lobectomy (84.6%)	Open (100%)	NA	100%	NA
Arslantas 2015 <sup>[17]</sup>	139	Mx (89.2%)	Lobectomy (50%)	Open (100%)	NA	52%	NA
Kim 2019 <sup>[18]</sup>	287	Mx (100%)	Lobectomy (100%)	VATS (66%)	NA	NA	7%
Kaufmann 2019 <sup>[19]</sup>	376	Mx (100%)	Lobectomy (69%)	VATS (100%)	4%	27%	73%

ASA=American Society of Anesthesiologists, Chemotx=chemotherapy, IPF=idiopathic pulmonary fibrosis, Mx=lung malignancy, Open=open surgery, Radiotx=radiotherapy, SN=serial number, VATS=video-assisted thoracic surgery, NA=Not applicable

**Table 2: Frequency of major postoperative pulmonary complications reported in each study**

Author	Sample size	Pneumonia (%)	ALI/ARDS (%)	Atelectasis (%)	Bronchopleural fistula (%)	Respiratory failure (%)	Pulmonary oedema (%)	Exacerbation of IPF (%)
Wu 2019 <sup>[10]</sup>	446	35.9	0.67	2.5	2	-	-	-
Kim 2020 <sup>[11]</sup>	1031	5.5	5.2	1.4	8	-	-	-
Parquin 1996 <sup>[12]</sup>	146	-	-	-	-	-	100	-
Jing 2018 <sup>[13]</sup>	451	41.2	7.8	31.4	-	1	-	-
Baar 2022 <sup>[4]</sup>	1426	34	-	-	36	18	-	-
Licker 2003 <sup>[14]</sup>	868	4.2	4.2	7.1	1.8	-	-	-
Blank 2011 <sup>[15]</sup>	129	13	7	12	4	13	-	-
Mizuno 2012 <sup>[16]</sup>	52	-	-	-	-	-	-	100
Arslantas 2015 <sup>[17]</sup>	139	16	3	37	12	6	-	-
Kim 2019 <sup>[18]</sup>	287	-	100	-	-	-	-	-
Kaufmann 2019 <sup>[19]</sup>	376	10	-	-	19	4	-	-

ALI=acute lung injury, ARDS=acute respiratory distress syndrome, IPF=idiopathic pulmonary fibrosis

**Table 3: Comparison of mean intravenous fluid between those who developed postoperative pulmonary complications and those who did not**

Author	Year of research	Sample size	PPC			No PPC		
			n	Mean fluid (ml/kg/h)	SD (ml/kg/h)	n	Mean fluid (ml/kg/h)	SD (ml/kg/h)
Licker 2003 <sup>[14]</sup>	1991–2002	868	37 (4.2%)	9.1	4.1	831 (95.8%)	7.2	4.2
Blank 2011a <sup>[15]</sup>	1997–2008	129	27 (20.9%)	8.3	4.3	102 (79.1%)	6.6	2.7
Mizuno 2012 <sup>[16]</sup>	2004–2011	52	7 (13.5%)	10.3	3.66	45 (86.5%)	7.71	3.11
Arslantas 2015 <sup>[17]</sup>	2012–2013	139	76 (54.7%)	6.58	3.64	63 (45.3%)	4.61	2.28
Kim 2019 <sup>[18]</sup>	2012–2015	287	8 (2.8%)	7.14	2.63	279 (97.2%)	5.06	2.98
Kaufmann 2019 <sup>[19]</sup>	2016–2017	376	114 (30.3%)	11.1	4.1	262 (69.7%)	11.2	5.7

IQR=interquartile range, n=number of patients, PPC=postoperative pulmonary complications, SD=standard deviation. \*Median and IQR were changed to mean and SD. For calculation, the average weight was assumed to be 60 kg. The mean and SD fluid infused were divided by the mean duration of surgery in hours and average weight. <sup>b</sup>Mean and SD fluid infused were divided by the mean duration of surgery. <sup>c</sup>Median and IQR were changed to mean and SD using the calculations suggested by Wan *et al.* (Wan X, Wang W, Liu J, Tong T. Estimating the sample mean and standard deviation from the sample size, median, range and/or interquartile range. BMC Med Res Methodol. 2014 Dec 19;14:135.)

**Results of syntheses:** The pooled mean difference (MD) in intraoperative fluid infused between those who developed PPC and those who did not was significantly different ( $P = 0.001$ ) [Figure 2]. The mean fluid infused was significantly higher in those with PPC (MD: 1.51 ml/kg/h). The heterogeneity measured in terms of  $I^2$  was 56%. The pooled proportion of PPC in liberal intraoperative fluid arms was higher than that in restricted fluid [RR: 0.58 (95% CI: 0.33, 1.02)] [Figure 3]. The  $P$  value was, however, not significant ( $P = 0.06$ ). The

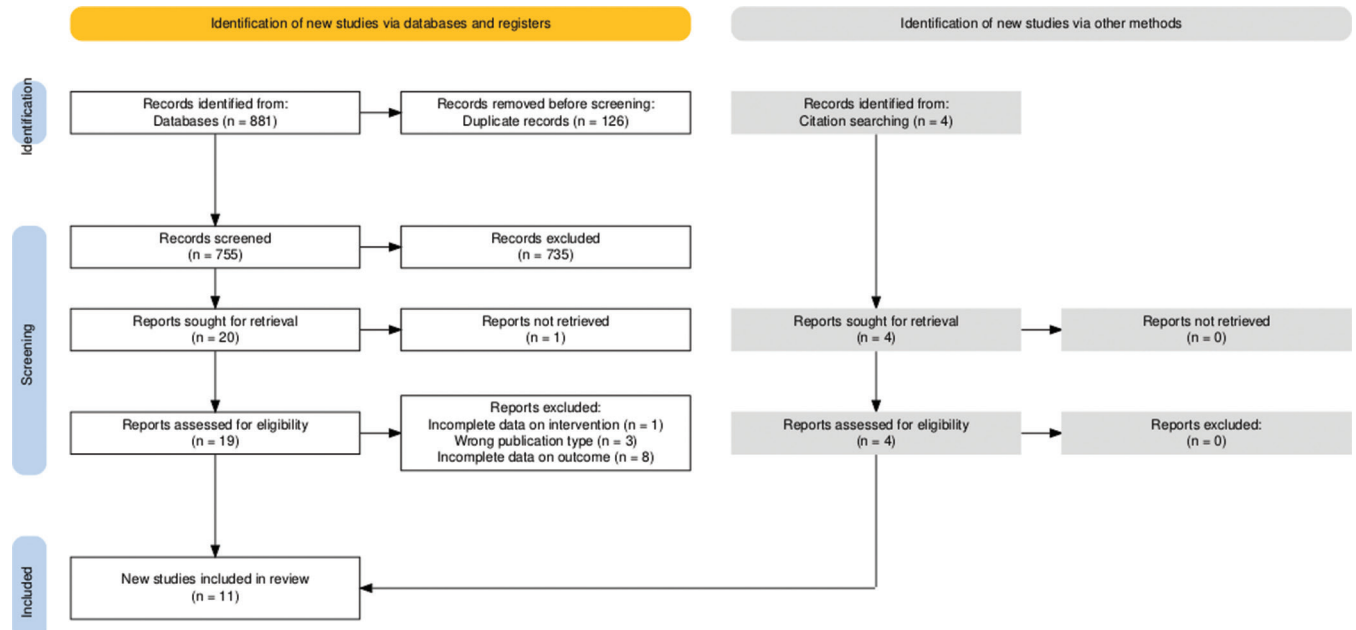
heterogeneity measured in terms of  $I^2$  was 91%. When the analysis was restricted to those studies where the cut-off for differentiating liberal versus restrictive fluid strategies was between 6 and 10 ml/kg/h, the results did not change significantly [RR: 0.76 (95% CI: 0.47, 1.24),  $P = 0.27$ ,  $I^2 = 87%$ ] [Supplementary Figure 1].

**TSA:** The cumulative Z scores line crossed the line to reach the required sample size and benefit line for both analyses [Supplementary Figure 2a and b].

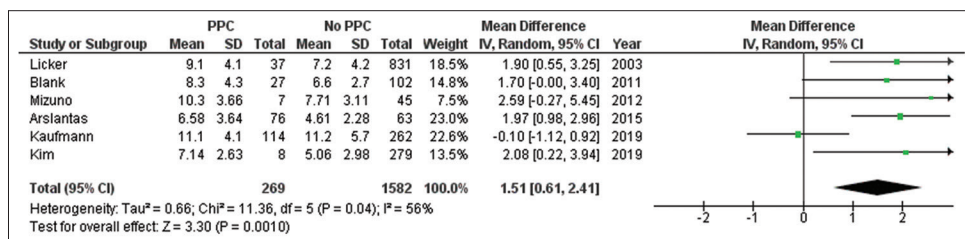
**Table 4: Comparison of incidence of PPCs in liberal versus restricted fluid strategies**

Author	Year of research	Sample size	Restrictive fluid			Liberal fluid		
			Defn (ml/kg/h)	n	PPC	Defn (ml/kg/h)	n	PPC
Wu 2019 <sup>[10]</sup>	2016–2017	446	<9.4	116	51 (43.9%)	>9.4	330	121 (36.6%)
Kim 2020 <sup>[11]</sup>	NA	1031	<6	851	87 (10.2%)	>6	180	18 (10%)
Parquin 1996 <sup>a[12]</sup>	1992	146	<7.75	111	12 (10.8%)	>8.3	35	10 (28.6%)
Jing 2018 <sup>b[13]</sup>	2010–2014	451	<16.8	165	10 (6.1%)	>16.8	288	92 (31.9%)
Baar 2022 <sup>[4]</sup>	2016–2020	1426	<6	344	75 (21.8%)	>6	1082	397 (36.75%)

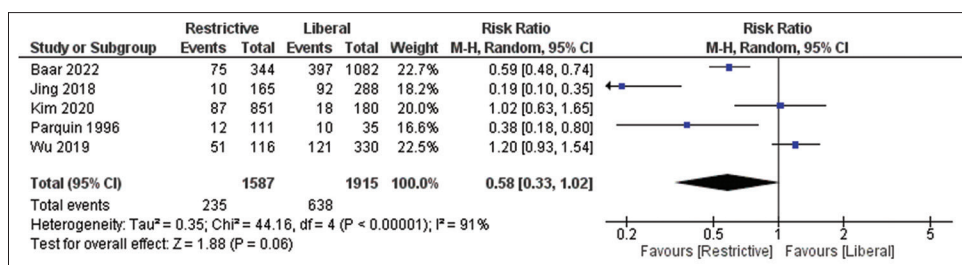
Defn=definition, n=number of patients. PPC=postoperative pulmonary complication, SN=serial number. <sup>a</sup>The average weight was assumed to be 60 kg for calculation. The total fluids were divided by average weight and average duration of surgery in hours to get the average fluids in ml/kg/h. <sup>b</sup>The average weight in the study was 63.8 kg. The total fluids were divided by average weight and average duration of surgery in hours to get the average fluids in ml/kg/h



**Figure 1:** PRISMA flow chart showing inclusion and exclusion of studies. PRISMA = Preferred Reporting Items for Systematic Reviews and Meta-Analyses



**Figure 2:** Forest plot showing that patients with PPCs had higher mean fluid transfused when compared to those who did not have PPC. CI = confidence interval, IV = inverse variance, PPC = postoperative pulmonary complication, SD = standard deviation



**Figure 3:** Forest plot showing the proportion of postoperative complications in liberal versus restrictive fluid strategies. CI = confidence interval, M-H = Mantel–Haenszel

*Reporting biases:* The funnel plots did not clearly show publication bias [Supplementary Figure 3]. However, there were far too few studies to interpret the graphs.

## DISCUSSION

This SRMA included 11 observational studies, primarily published after 2010. There were 1142 (21.33%) PPCs in 5353 patients included in 11 studies. The prevalence of PPCs varied across the studies, likely due to baseline differences in the inclusion. Smoking, physical status, neoadjuvant therapy, diabetes and pre-existent respiratory diseases had an impact on PPC incidence.<sup>[4,11,15,17]</sup> ASA's physical status varied across the studies. Poor preoperative status would likely lead to higher PPCs. Pulmonary infection within 4 weeks before surgery showed worse outcomes in one of the studies.<sup>[4]</sup> One study identified ischaemic heart disease and interstitial lung disease as risk factors.<sup>[18]</sup>

In a study by Kaufmann *et al.*<sup>[19]</sup>, the PPC group had more elderly and undernourished patients. The study by Parquin *et al.*<sup>[12]</sup> revealed that preoperative radiotherapy, or chemotherapy, also affected the incidence of PPCs. The indication for thoracic surgery varied in different studies. While malignancy was the most common indication, some studies focussed exclusively on idiopathic pulmonary fibrosis [Table 1]. Blank *et al.*<sup>[15]</sup> noted that PPCs were higher in surgeries for malignant than benign conditions. The surgical technique varied from open to VATS across the studies. In the study by Kim *et al.*<sup>[18]</sup>, PPCs were lower in VATS than in the open thoracotomy technique. The elective versus emergency nature of surgery also affected PPCs in that study.<sup>[18]</sup> Pneumonectomy, extended resections and the duration of surgery were associated with an increased risk of lung injury, according to a study by Licker *et al.*<sup>[14]</sup> Some studies focussed on lobectomy<sup>[10,11,13,14,16–19]</sup>, while others focussed on pneumonectomy [Table 1].<sup>[12,15]</sup> ALI occurred more frequently after pneumonectomy

than lobectomy or lesser resections. In one study, the duration of the surgery had a bearing on PPCs as well.<sup>[14]</sup> Neoadjuvant chemo/radiotherapy rates varied across the studies [Table 1]. The most common type of PPC varied across the studies. Some studies, such as the one by Parquin *et al.*<sup>[12]</sup>, reported only post-pneumonectomy pulmonary oedema and Mizuno *et al.*<sup>[16]</sup> reported the postoperative acute exacerbation of idiopathic pulmonary fibrosis.

In our SRMA, we could not account for the baseline differences but were able to show that increased infusion of intravenous fluid was associated with higher PPC. The studies in both analyses were too few to perform any subgroup analysis or create a funnel plot (to look for publication bias). The fluid administered varied significantly between the studies, as shown in Tables 1 and 2. In the study by Blank *et al.*,<sup>[15]</sup> increased intraoperative fluid infused was related to more PPC in univariate analysis but not in multivariable analysis. In a study, the optimal intraoperative fluid for the lowest PPC was less than 4–5 ml/kg/h.<sup>[11]</sup> It must be noted that most studies included in this systematic review used fluids above this range. In the study by Alam *et al.*,<sup>[20]</sup> the odds of primary lung injury increased by a factor of 1.2 for each additional 500 ml of perioperative fluid administered. Most studies either favoured using a restrictive strategy or showed no difference between the two strategies. In the study by Wu *et al.*,<sup>[10]</sup> although the risk of postoperative pneumonia increased with restrictive practices, it must be noted that this was a retrospective study, and the difference was not significant.

This SRMA had several limitations. All the studies were observational and had biases inherent to the study design. There was high methodological and statistical heterogeneity. Most studies did not uniformly record fluid strategies, and the definitions of restrictive and liberal strategies varied across the studies.

Despite these limitations, this SRMA has several strengths. To our knowledge, this is the first SRMA to address this question systematically. Although an SRMA by Han *et al.*<sup>[21]</sup> has been published on postoperative complications in patients undergoing thoracic surgery, the article had a different research question than ours (goal-directed therapy vs. conventional therapy). We reviewed three databases comprehensively to screen the published literature to date. Along with a critical appraisal of the included studies, we performed two different meta-analyses to pool all the relevant data. To address heterogeneity, we performed relevant subgroup analyses. We also performed TSA to demonstrate the completeness of the current SRMA.

## CONCLUSION

The mean intraoperative fluid in those who developed PPC was significantly higher. A trend was noted towards higher PPC in those who received liberal intraoperative fluids compared to the restrictive strategy. Although there was significant methodological and statistical heterogeneity, the results did not change after including a subgroup with somewhat uniform definitions of restrictive versus liberal fluid. TSA showed that the cumulative Z score crossed both the required sample size and the line of benefit, indicating that no further studies are required to be added to the meta-analyses. In conclusion, a restrictive fluid strategy might be beneficial in preventing PPCs. However, owing to the high heterogeneity and absence of quality data, a randomised controlled trial comparing these strategies is needed to provide definite recommendations.

## Data availability

The data for this systematic review and/or meta-analysis may be requested with reasonable justification from the authors (email to the corresponding author) and shall be shared upon request.

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## Conflicts of interest

There are no conflicts of interest.

## Disclosure

The Editor-in-Chief, being an co-author of this manuscript was not involved in decision making for this manuscript and was independently handled by other Editor of the journal.

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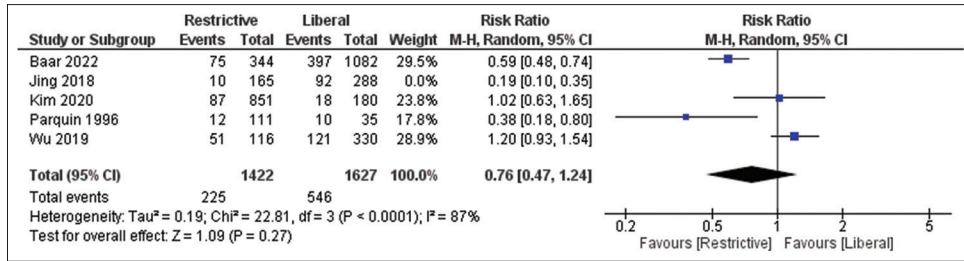
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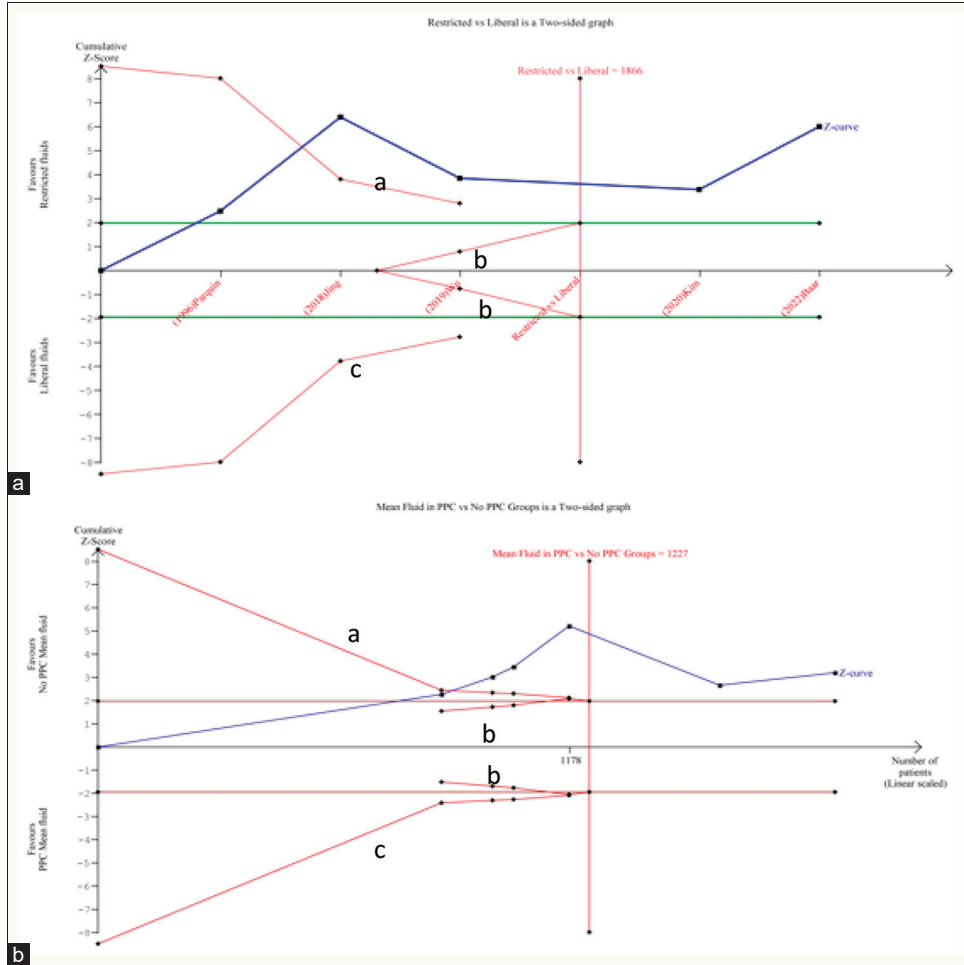
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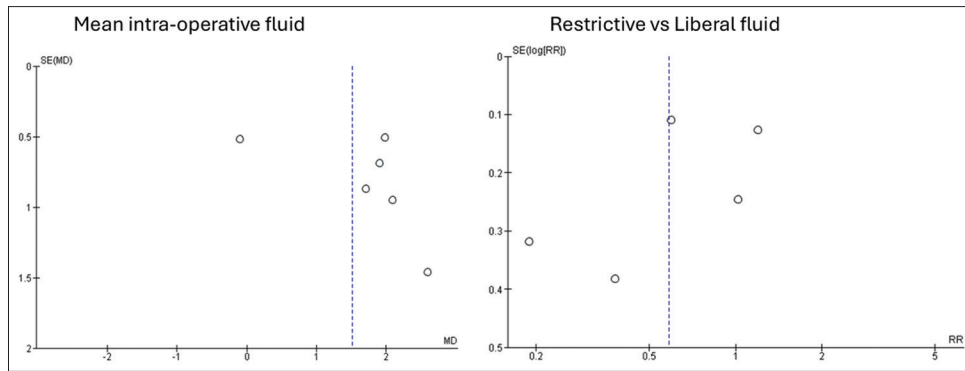




**Supplementary Figure 1:** Subgroup analysis showing the proportion of postoperative pulmonary complications in liberal versus restrictive fluid strategies after restricting to studies with the cut-off for differentiating liberal versus restrictive fluid strategies between 6 and 10 ml/kg/h. CI = confidence interval, M-H = Mantel-Haenszel



**Supplementary Figure 2:** (a and b) TSA of the two meta-analyses. PPC = postoperative pulmonary complication, TSA = trial sequential analysis. Z curve = measure of treatment effect in the meta-analysis, a = superiority boundary, b = futility boundary, c = inferiority boundary



**Supplementary Figure 3:** Funnel plot for the studies included in the systematic review and meta-analysis

**Supplementary Table 1: Search string used for retrieving articles**

Database	Search string
PubMed	(‘thoracic surgery’[All Fields] OR ‘lung transplant’[All Fields] OR (‘thoracotomy’[MeSH Terms] OR ‘thoracotomy’[All Fields] OR ‘thoracotomies’[All Fields]) OR (‘pneumonectomy’[MeSH Terms] OR ‘pneumonectomy’[All Fields] OR ‘pneumonectomies’[All Fields]) OR (‘thoracic surgery, video assisted’[MeSH Terms] OR (‘thoracic’[All Fields] AND ‘surgery’[All Fields] AND ‘video assisted’[All Fields]) OR ‘video-assisted thoracic surgery’[All Fields] OR ‘vats’[All Fields]) OR (‘thoracoscopy’[MeSH Terms] OR ‘thoracoscopy’[All Fields] OR ‘thoracoscopies’[All Fields]) OR (‘lobectomies’[All Fields] OR ‘lobectomy’[All Fields] OR ‘lung resection’[All Fields]) AND (‘fluid’[All Fields] OR ‘fluid s’[All Fields] OR ‘fluids’[All Fields]) AND (‘perioperative’[All Fields] OR ‘perioperatively’[All Fields] OR (‘intraop’[All Fields] OR ‘intraoperative’[All Fields] OR ‘intraoperatively’[All Fields])) AND (‘post operative pulmonary complication’[All Fields] OR ‘pulmonary oedema’[All Fields] OR ‘pulmonary edema’[All Fields] OR ‘ARDS’[All Fields] OR ‘Acute respiratory distress syndrome’[All Fields] OR ‘lung injury’[All Fields] OR (‘pneumonia’[MeSH Terms] OR ‘pneumonia’[All Fields] OR ‘pneumonias’[All Fields] OR ‘pneumoniae’[All Fields] OR ‘pneumoniae s’[All Fields]) OR ‘pleural effusion’[All Fields])
EMBASE	(‘thoracic surgery’ OR ‘lung transplant’ OR thoracotomy OR pneumonectomy OR VATS OR thoracoscopy OR lobectomy OR ‘lung resection’) AND (perioperative OR intraoperative) AND (fluid*) AND (‘post-operative pulmonary complication’ OR ‘pulmonary oedema’ OR ‘pulmonary oedema’ OR ARDS OR ‘Acute respiratory distress syndrome’ OR ‘lung injury’ OR pneumonia OR ‘pleural effusion’)

**Supplementary Table 2: The JBI checklist for critical appraisal of included studies**

Criteria	Licker 2003 <sup>[14]</sup>	Blank 2011 <sup>[15]</sup>	Mizuno 2012 <sup>[16]</sup>	Arslantas 2015 <sup>[17]</sup>	Kim 2019 <sup>[18]</sup>	Kaufmann 2019 <sup>[19]</sup>	Wu 2019 <sup>[10]</sup>	Kim 2020 <sup>[11]</sup>	Parquin 1996 <sup>[12]</sup>	Jing 2018 <sup>[13]</sup>	Baar 2022 <sup>[4]</sup>
Inclusion criteria defined	Yes	Yes	Unclear	Yes	Yes	Yes	No	No	Yes	Yes	Yes
Study subjects and setting described	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Unclear	Yes	Yes	Yes
Exposure measured	Unclear	Unclear	Yes	Yes	No	Yes	Yes	Yes	Unclear	Unclear	Yes
Criteria for measurement of condition	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Confounding identified	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Confounding dealt with	Yes	Yes	Yes	Unclear	Unclear	Yes	Yes	Yes	Yes	Yes	Unclear
Outcomes measured	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes
Statistical analysis	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes

JBI=Joanna Briggs Institute