Original Article

Incidence and risk factors for recurrent primary spontaneous pneumothorax after video-assisted thoracoscopic surgery: a systematic review and meta-analysis

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Background: The incidence and risk factors for recurrent primary spontaneous pneumothorax (PSP) after video-assisted thoracoscopic surgery (VATS) remain controversial. A systematic review and meta-analysis were conducted to determine the incidence and risk factors for recurrence of PSP after VATS.

Methods: A systematic search of PubMed, Web of Science, Embase, and Cochrane Library databases was conducted to identify studies that reported the rate and risk factors for recurrence of PSP after VATS published up to December 2023. The pooled recurrence rate and odds ratio (OR) with 95% confidence interval (CI) were calculated using a random-effects model. In addition, risk factors were similarly included in the meta-analysis, and sources of heterogeneity were explored using meta-regression analysis.

Results: A total of 72 studies involving 23,531 patients were included in the meta-analysis of recurrence. The pooled recurrence rate of PSP after VATS was 10% (95% CI: 8–12%). Male sex (OR: 0.61; 95% CI: 0.41–0.92; P=0.02), younger age [mean difference (MD): −2.01; 95% CI: −2.57 to −1.45; P<0.001), lower weight (MD: −1.57; 95% CI: −3.03 to −0.11; P=0.04), lower body mass index (BMI) (MD: −0.73; 95% CI: −1.08 to 0.37; P<0.001), and history of contralateral pneumothorax (OR: 2.46; 95% CI: 1.56–3.87; P<0.001) were associated with recurrent PSP, whereas height, smoking history, affected side, stapling line reinforcement, and pleurodesis were not associated with recurrent PSP after VATS.

Conclusions: The recurrence rate of PSP after VATS remains high. Healthcare professionals should focus on factors, including sex, age, weight, BMI, and history of contralateral pneumothorax, that may influence recurrence.

Keywords: Primary spontaneous pneumothorax (PSP); video-assisted thoracoscopic surgery (VATS); recurrence; risk factors; meta-analysis

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Introduction

Primary spontaneous pneumothorax (PSP) is a type of spontaneous pneumothorax which occurs in the absence of any trauma or underlying lung disease (1,2). Previous study reported an annual incidence of PSP of 7.4 and 1.2 cases per 100,000 men and women, respectively (3). Due to its high recurrence rate, which ranges between 20% and 60% with conservative treatment, PSP remains a significant clinical concern (4-9).

Recently, with the development of thoracic surgical techniques, the use of video-assisted thoracoscopic surgery (VATS) has been widely promoted. Owing to its advantages (i.e., smaller incision and more rapid recovery), it has replaced thoracotomy as the primary surgical treatment for PSP (2,10). Several studies reported a higher risk of recurrence for PSP after VATS ranging from 3% to 17%, while thoracotomy ranged from 3% to 12% (11-13). However, the specific incidence rate of recurrence is currently unknown. Several studies demonstrated the advantage of VATS in reducing the complications (14-16). Existing studies have reported that the young age, low body mass, smoking history, contralateral bulla neogenesis and intense follow-up are associated with risk for recurrent PSP after VATS (15,17-21). Studies performed thus far have not comprehensively and systematically analyzed the recurrence and risk factors of PSP in patients who underwent VATS.

The aim of this systematic review and meta-analysis was to determine the pooled estimates for the recurrence rate of PSP after VATS based on a thorough investigation of the available evidence. In addition, risk factors identified in studies with sufficient sample size were also evaluated in the meta-analysis. This systematic review and meta-analysis focused on two questions: (I) what is the recurrence rate of PSP after VATS; and (II) which risk factors increase the rate of recurrence. We present this article in accordance with the PRISMA reporting checklist (available at https://jtd.amegroups.com/article/view/10.21037/jtd-24-175/rc).

Highlight box

Key findings

- The incidence of primary spontaneous pneumothorax (PSP) in patients after video-assisted thoracoscopic surgery (VATS) is about 11%. Sex, age, weight, body mass index, and contralateral pneumothorax are risk factors of recurrent PSP.

What is known and what is new?

- Incidence for recurrence of PSP after VATS reported in the existing literature is inconsistent.
- In this study, we conducted a quantitative meta-analysis of recurrent PSP after VATS based on a review of the existing clinical studies.

What is the implication, and what should change now?

- This study quantitatively analyzed the pooled rate of recurrence and risk factors, and provide guidance for the clinical management of people at high risk of recurrence.

Methods

Search strategy

The research protocol for this systematic review has been registered with PROSPERO (registration number: CRD42023491211). Four electronic databases were comprehensively searched, namely PubMed, Web of Science, Embase, and Cochrane Library. A search strategy combining Medical Subject Headings (MESH) terms and free words was used to search for available publications in these four databases from their inception date to December 31, 2023. The following MESH terms and free words were used: "Primary spontaneous pneumothorax" was combined with "Spontaneous pneumothorax" to define the population. To define the types of surgical treatment, "Video-assisted thoracic surgery" was combined with "Thoracoscopy". Recurrence and risk were determined by using the terms "recurrence" and "risk factor", respectively. Further details regarding the search strategy are provided in the appendix available at https://cdn.amegroups.cn/static/public/jtd-24-175-1.docx.

Study selection

Two reviewers (N.H. and S.H.) independently screened the titles and abstracts of all articles for inclusion in the study after removing duplicate studies. When at least one reviewer considered that the article met the criteria of inclusion after reading the title and abstract, the full article was included in the next step of the review. In case of disagreement between the two reviewers during the screening stage, the results were compared and discussed to reach a consensus. Disagreements that could not be resolved by the two reviewers were adjudicated by a third reviewer.

The criteria for inclusion of a study in the systematic review were: (I) patients with PSP, including first occurrence and recurrence; (II) patients who underwent VATS; and (III) recurrences of pneumothorax were confirmed by chest radiography. The exclusion criteria were: (I) studies with incomplete data; (II) studies conducted in languages other than Chinese or English; (III) animal or cell studies; and (IV) reviews, meta-analyses, comments, meeting summaries, letters, case reports, and duplicate literature.

Data extraction

Two reviewers (N.H. and S.H.) independently extracted data from the studies and input them into Microsoft Excel (Microsoft Corporation, Redmond, WA, USA) for analysis. The following information was recorded: first author's name, year of publication, study design, region, country, sample size, patient characteristics, overall recurrence rate of PSP after VATS, and associated risk factors.

Quality appraisal

Two reviewers (N.H. and S.H.) independently evaluated the quality of the included studies using the Newcastle-Ottawa scale (22). Two different versions of this scale were used to respectively assess the quality of cohort studies and case-control studies by evaluating three aspects of the study, namely selection, comparability, and exposure (outcome). Any disagreement during the evaluation of quality was resolved by discussion between the two reviewers; in case the disagreement could not be resolved by discussion, a third reviewer (J.H.) was consulted to reach a consensus.

Statistical analysis

The metaprop package (23) in R Statistical Software (v4.3.2; R Core Team 2023) was used to perform the meta-analysis of recurrence rate, while the meta package (24), metafor package (25), and dmetar package (26) were utilized to conduct the meta-analysis of risk factors. Inverse variance models with inverse sine transformation were used for the estimation of pooled recurrence and 95% confidence intervals (CIs). The Cochrane's Q statistic was tested using the heterogeneity among studies. The degree of heterogeneity was determined using the calculated value of I^2, with a P value <0.1 indicating significant heterogeneity among studies. All available data were extracted from the studies for meta-analysis of risk factors. Odds ratios (ORs) and 95% CIs were extracted for categorical variables, while means and standard deviations (SDs) were extracted for continuous variables. Meta-analysis of both recurrence and risk factors was based on the calculation of Q to determine the most appropriate model to be used (i.e., random-effects model or fixed-effects model). In case of heterogeneity, the source of heterogeneity was explored by subgroup analysis. Both funnel plot and Begg test were performed to identify potential publication bias; P values <0.01 indicated statistically significant differences. In addition, assessment of publication bias was also performed with regard to the risk factors; this assessment included more than ten studies.

Results

Study selection

The initial search yielded 1,982 articles. After excluding 566 duplicates, 1,416 articles were included in the next stage of title and abstract review. Next, 120 articles were included in the stage of full-article review. Thirty studies were excluded owing to the lack of defined diagnosis of PSP. Fourteen investigations were excluded because they used non-objective indicators of definite postoperative recurrence of pneumothorax, while two were excluded due to the unavailability of the full text. A total of 72 studies were utilized for the meta-analysis of recurrence, including 45 retrospective cohort studies, seven prospective cohort studies, fourteen case-control studies, and six randomized controlled trials (*Figure 1*). The year of publication ranged from 1994 to 2023. Finally, seventeen studies (two retrospective cohort studies, one prospective cohort study, and fourteen case-control studies) were included in the meta-analysis of risk factors (*Table 1*).

Quality appraisal

The mean quality score for the seventeen studies included in the risk factor analysis was 7.07±0.48. Further details on the quality score are shown in the appendix available at https://cdn.amegroups.cn/static/public/jtd-24-175-1.docx.

Prevalence

The 72 studies included in this meta-analysis involved >23,000 patients, with a median sample size of 163 (range, 15–6,654). Of those patients, 3,371 experienced postoperative recurrence, with a median recurrence rate of 9.5% (range, 0–52%) and a mean follow-up period ranged from 321.5 days to 8.5 years. Basic information on the 72 studies is shown in the appendix available at https://cdn.amegroups.cn/static/public/jtd-24-175-1.docx.

Based on a random-effects model-based meta-

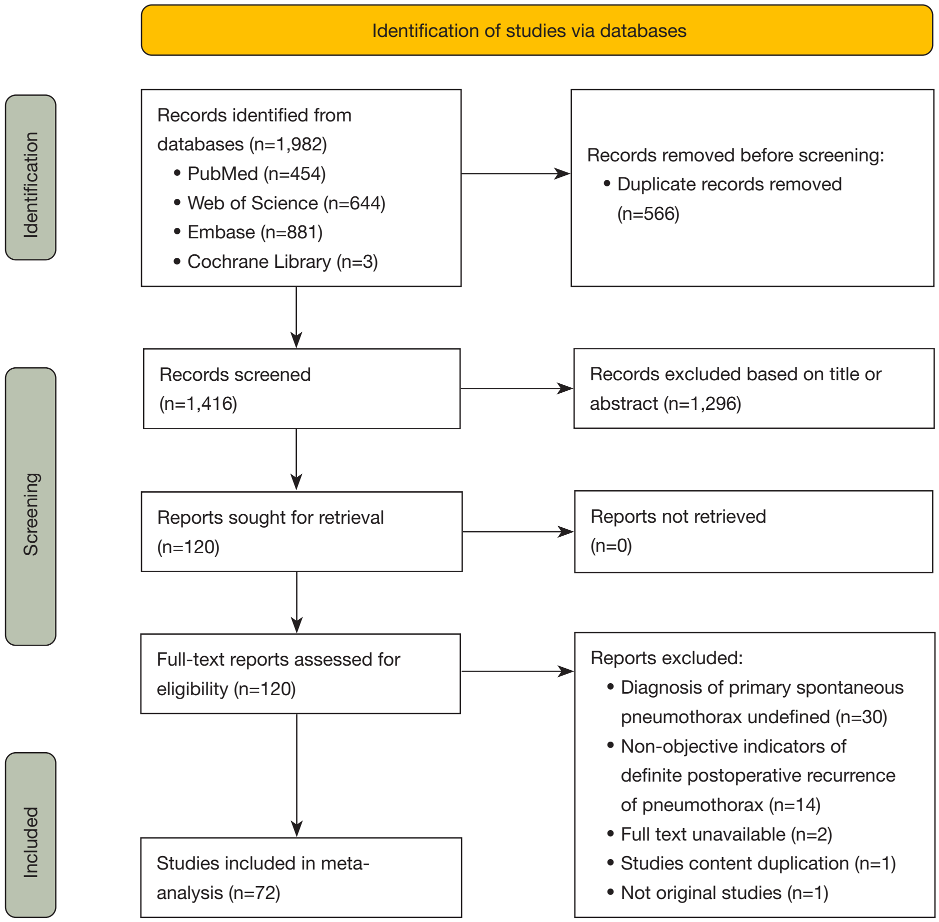

Figure 1 The flow diagram for screening studies according to PRISMA criteria.

analysis for the data after inverse sine transformation, the estimated pooled recurrence rate was 10% (95% CI: 8–12%) (*Figure 2*). Testing for heterogeneity revealed significant heterogeneity among the included studies that reported recurrence of PSP after VATS (I^2=96%; P<0.001). Therefore, we investigated the sources of heterogeneity through subgroup analysis. The visual result of the funnel plot was asymmetrical, suggesting the possibility of missing some negative results (*Figure 3*). The Egger test (P=0.002) confirmed the asymmetry of the funnel plot and the potential publication bias (*Figure 4*). The trim-and-fill method was used to adjust for publication bias. After filling up with 24 missing studies, the adjusted pooled incidence rate of recurrence was 16% (95% CI: 13–19%) (*Figure 5*).

According to the subgroup analysis of 72 studies for recurrence, the incidence rate of recurrence reported in Asia, Europe, Middle East, and Americas was 11.9% (95% CI: 9.5–14.7%; I^2=96.1%), 8.0% (95% CI: 4.4–12.7%; I^2=91.1%), 3.8% (95% CI: 0.2–11.4%), and 18.7% (95% CI: 5.3–37.9%; I^2=76.7%), respectively. Regarding the type of study, the incidence rate of recurrence reported in retrospective studies, prospective studies, case-control studies, and randomized controlled trials was 12.2% (95% CI: 8.6–14.1%; I^2=97.1%), 27.4% (95% CI: 1.3–11.2%; I^2=74.0%), 12.2% (95% CI: 8.6–14.1%; I^2=74.0%), and 11.3% (95% CI: 4.9–20.2%; I^2=89.3%), respectively. The incidence rate in studies published from 1994 to 2019 and from 2020 to 2023 was 10.8% (95% CI: 8.3–13.6%; I^2=95.1%) and 10.5% (95% CI: 7.1–14.6%; I^2=96.6%), respectively. Concerning the sample size, the incidence rate in studies with a sample size ≤100 and >100 was 14.6% (95% CI: 10.5–19.3%; I^2=89.4%) and 9.2% (95% CI: 7–11.7%; I^2=97.4%), respectively. Regarding the follow-up, the incidence rate of recurrence reported in less than 24 months, more than 24 months, and not stated was 5.8% (95% CI: 0.021–0.111; I^2=88.5%), 9.8% (95% CI:

Table 1 Study characteristics

First author [year], country	Study type	Sample size, n (M/F)	ORR (%)	Side of recurrence, n (L/R)	Age, years	Height, m	Weight, kg	BMI, kg/m^2	Smoking history (yes/no)	NOS score	Follow-up, months	Risk factors
Huang [2007], China (27)	Case-control	231 (215/16)	14.30	NA						7	22.94†	Age, height, weight, BMI, laterality blebs/bullae
RG					20.18±3.66	1.75±6.14	55.87±7.46	18.13±2.02	18/15			
NRG					22.36±5.63	1.74±7.91	59.57±7.91	19.72±2.16	98/100			
Haraguchi [2008], Japan (28)	Case-control	62 (54/8)	16.10			NA	NA	NA		7	64†	Age, sex, smoking history, pathological findings, laterality (left/right), first or second episode
RG				6/4	21.6±5.4				2/8			
NRG				25/27	24.0±7.0				22/30			
Chang [2015], China (29)	Case-control	149 (141/8)	11.40			NA	NA			7	11.2†	Age, sex, BMI, smoking history, laterality (left/right), pleurodesis, postoperative air leakage, chest tube days, follow-up period
RG				11/6	20.7±3.7			18.7±2.0	1/16			
NRG				64/68	18.2±2.4			19.4±1.9	31/101			
Huang [2015], China (30)	Case-control	248 (226/22)	4.80							7	NA	Age, height, weight, BMI, laterality (left/right), history of contralateral PSP, pleurodesis, duration of air leakage (days), duration of chest tube drainage (days), bulla or bleb resection, follow-up period
RG				7/5	17 [14–21]	1.71±0.05	52.46±6.49	17.67±1.78	1/11			
NRG				108/128	19 [14–38]	1.73±0.05	55.42±7.19	18.5±1.82	28/208			
Ciriaco [2016], Italy (31)	Case-control	58 (48/10)	13		16.6±1.6	NA	NA	NA	NA	7	95†	Age, sex, laterality, postoperative chest tube (days), pleurodesis
RG				6/1								
NRG				42/9								
Cardillo [2016], Italy (32)	Cohort study	1,415 (1,078/337)	1.90		25.3 [21.0–29.4]	NA	NA	NA		7	102†	Age, sex, current smoking status, pleurodesis, laterality
RG				12/14					24/2			
NRG				554/826					551/803			
Chiu [2017], China (33)	Case-control	89 (77/12)	51.70	NA	21.0±5.2	1.723±0.73	56.3±9.0	18.9±2.2		9	NA	Age, sex, height, weight, BMI, smoking history, side involved
RG									6/40			
NRG									11/32			
Choi [2018], Korea (34)	Case-control	85 (75/10)	24.71						NA	7	24.9†	Age, sex, height, weight, BMI, use of reinforcing material, new bullae in the staple/non-staple line, lung resection volume, laterality (left/right)
RG				13/8	17.1±1.2	1.75±0.06	56.2±6.7	18.2±1.6				
NRG				39/25	18.6±3.6	1.74±0.08	56.6±8.4	18.6±2.1				
Choi [2018], Korea (35)	Case-control	360 (269/91)	11.11						NA	7	44.5†	Age, sex, height, weight, BMI, laterality (left/right), use of reinforcing material, lung resection volume, follow-up period
RG				26/14	17.6±2.4	1.75±0.07	57.1±7.8	18.6±1.9				
NRG				173/147	19.3±3.6	1.74±0.08	57.4±9.0	18.9±2.3				
Asano [2019], Japan (36)	Case-control	192 (164/28)	7.30	NA	NA	NA	NA	NA		7	NA	Age, sex, BMI, smoking history, history of pneumothorax, use of reinforcing material, identification of bullae on CT
RG									4/10			
NRG									79/99			
Tsuboshima [2019], Japan (37)	Case-control	91 (83/8)	8.80		20 [14–86]	NA	NA	NA		8	22.6†	Age, sex, BMI, smoking history, laterality, bullae, the use of reinforcing material, pleurodesis, follow-up period
RG				2/6					2/6			
NRG				50/33					50/33			

Table 1 (*continued*)

Table 1 (*continued*)

First author [year], country	Study type	Sample size, n (M/F)	ORR (%)	Side of recurrence, n (L/R)	Age, years	Height, m	Weight, kg	BMI, kg/m^2	Smoking history (yes/no)	NOS score	Follow-up, months	Risk factors
Onuki [2019], Japan (38)	Cohort study	66 (60/6)	13.64						NA	8	31.3†	Age, sex, height, weight, BMI, laterality (left/right), history of contralateral PSP
RG				6/3	17±1.6	1.742±0.64	56.7±7.0	18.6±2.3				
NRG				32/25	17±1.3	1.714±0.65	56.0±7.3	19.1±1.8				
Liu [2020], China (39)	Case-control	335 (294/41)	14.33	NA	NA	NA	NA	NA		6	75‡	Age, sex, BMI, smoking history
RG									7/41			
NRG									65/222			
Jeon [2020], Korea (40)	Case-control	154 (144/10)	13	NA	19 [15–39]	NA	NA	NA		7	NA	Age, sex, height, weight, BMI, smoking history, postoperative air leakage
RG									0/20			
NRG									36/98			
Jeon [2020], Korea (41)	Case-control	276 (261/15)	8.33	NA	19 [13–36]	NA	NA	NA		8	50‡	Age, sex, height, weight, BMI, smoking history, postoperative air leakage, resection volume
RG									0/23			
NRG									54/199			
Iwazawa [2021], Japan (42)	Case-control	357 (322/35)	14		20.9±3.8	NA	NA	NA	NA	7	50†	Age, sex, laterality, history of pneumothorax, pleural coverage
RG				29/21								
NRG				154/203								
Shigenobu [2023], Japan (43)	Case-control	207 (185/22)	13		NA	NA	NA	NA		7	31.3‡	Age, sex, smoking history, laterality, history of pneumothorax, stapling line reinforcement
RG				17/10					4/23			
NRG				104/76					46/134			

Data are presented as numbers, the mean ± SD, or median [range]. †, mean; ‡, median. M/F, male/female; ORR, overall recurrence rate; L/R, left/right; BMI, body mass index; NOS, Newcastle-Ottawa scale; NA, not available; RG, recurrence group; NRG, non-recurrence group; CT, computed tomography; PSP, primary spontaneous pneumothorax; SD, standard deviation.

Study	Events	Total	Weight	IV, Random, 95% CI
Waller 1994	2	15	0.8%	0.13 [0.02; 0.40]
Yim 1995	3	100	1.4%	0.03 [0.01; 0.09]
Cardillo 2000	16	432	1.5%	0.04 [0.02; 0.06]
Ayed 2000	4	72	1.3%	0.06 [0.02; 0.14]
Cardillo 2001	23	597	1.5%	0.04 [0.02; 0.06]
Ayed 2003	2	100	1.4%	0.02 [0.00; 0.07]
Ayed 2006	3	94	1.4%	0.03 [0.01; 0.09]
Chen 2006	10	202	1.5%	0.05 [0.02; 0.09]
Huang 2007	7	102	1.4%	0.07 [0.03; 0.14]
Huang 2007	33	231	1.5%	0.14 [0.10; 0.19]
Bialas 2008	9	32	1.1%	0.28 [0.14; 0.47]
Cho 2008	11	227	1.5%	0.05 [0.02; 0.09]
Haraguchi 2008	33	231	1.5%	0.14 [0.10; 0.19]
Nakanishi 2009	12	48	1.2%	0.25 [0.14; 0.40]
Ryu 2009	12	158	1.4%	0.08 [0.04; 0.13]
Choi 2013	19	281	1.5%	0.07 [0.04; 0.10]
Chiu 2014	18	84	1.3%	0.21 [0.13; 0.32]
Li 2014	3	180	1.4%	0.02 [0.00; 0.05]
Chou 2014	11	239	1.5%	0.05 [0.02; 0.08]
Min 2014	17	289	1.5%	0.06 [0.03; 0.09]
Lee 2014	192	1414	1.5%	0.14 [0.12; 0.15]
Son 2015	1	104	1.4%	0.01 [0.00; 0.05]
Yamazaki 2015	4	141	1.4%	0.03 [0.01; 0.07]
Pompili 2015	13	136	1.4%	0.10 [0.05; 0.16]
Chang 2015	17	149	1.4%	0.11 [0.07; 0.18]
Huang 2015	12	248	1.5%	0.05 [0.03; 0.08]
Noh 2015	51	285	1.5%	0.18 [0.14; 0.23]
Primavesi 2016	4	33	1.1%	0.12 [0.03; 0.28]
Ciriaco 2016	7	58	1.3%	0.12 [0.05; 0.23]
Herrmann 2016	4	185	1.4%	0.02 [0.01; 0.05]
Chen 2016	191	553	1.5%	0.35 [0.31; 0.39]
Cardillo 2016	26	1380	1.5%	0.02 [0.01; 0.03]
Cho 2017	11	25	1.0%	0.44 [0.24; 0.65]
Chiu 2017	46	89	1.3%	0.52 [0.41; 0.62]
Nakayama 2017	16	167	1.4%	0.10 [0.06; 0.15]
Dagnegard 2017	31	234	1.5%	0.13 [0.09; 0.18]
Zhang 2017	10	345	1.5%	0.03 [0.01; 0.05]
Cho 2018	2	76	1.3%	0.03 [0.00; 0.09]
Choi 2018	40	360	1.5%	0.11 [0.08; 0.15]
Olesen 2018	25	88	1.3%	0.28 [0.19; 0.39]
Kutluk 2018	7	135	1.4%	0.05 [0.02; 0.10]
Choi 2018	21	85	1.3%	0.25 [0.16; 0.35]
Onuki 2019	9	66	1.3%	0.14 [0.06; 0.24]
Asano 2019	14	192	1.5%	0.07 [0.04; 0.12]
Yamanaka 2019	17	66	1.3%	0.26 [0.16; 0.38]
Tsuboshima 2019	8	91	1.4%	0.09 [0.04; 0.17]
Tsuboshima 2019	44	252	1.5%	0.17 [0.13; 0.23]
Mithiran 2019	15	202	1.5%	0.07 [0.04; 0.12]
Tsuboshima 2019	30	92	1.4%	0.33 [0.23; 0.43]
Kim 2020	3	59	1.3%	0.05 [0.01; 0.14]
Liu 2020	48	335	1.5%	0.14 [0.11; 0.19]
Jeon 2020	23	276	1.5%	0.08 [0.05; 0.12]
Fujiwara 2020	16	117	1.4%	0.14 [0.08; 0.21]
Jeon 2020	20	154	1.4%	0.13 [0.08; 0.19]
Tsuboshima 2020	57	627	1.5%	0.09 [0.07; 0.12]
Cattoni 2020	79	843	1.5%	0.09 [0.07; 0.12]
Fung 2022	6	62	1.3%	0.10 [0.04; 0.20]
Zhu 2021	1	20	0.9%	0.05 [0.00; 0.25]
Adachi 2021	3	25	1.0%	0.12 [0.03; 0.31]
Kao 2021	32	132	1.4%	0.24 [0.17; 0.32]
Jung 2021	0	175	1.4%	0.00 [0.00; 0.02]
Hsu 2021	19	204	1.5%	0.09 [0.06; 0.14]
Brophy 2021	28	222	1.5%	0.13 [0.09; 0.18]
Iwazawa 2021	50	357	1.5%	0.14 [0.11; 0.18]
Woo 2021	77	841	1.5%	0.09 [0.07; 0.11]
Hung 2021	1648	6654	1.6%	0.25 [0.24; 0.26]
Fung 2021	7	58	1.3%	0.12 [0.05; 0.23]
Shigefuku 2022	16	143	1.4%	0.11 [0.07; 0.18]
Oda 2022	44	373	1.5%	0.12 [0.09; 0.16]
Campisi 2022	38	505	1.5%	0.08 [0.05; 0.10]
Aprile 2023	13	177	1.4%	0.07 [0.04; 0.12]
Shigenobu 2023	27	207	1.5%	0.13 [0.09; 0.18]
Total (95% CI)		**23531**	**100.0%**	**0.10 [0.08; 0.12]**

Heterogeneity: $Tau^2 = 0.0179$; $Chi^2 = 1918.08$, df = 71 (P = 0); $I^2 = 96\%$

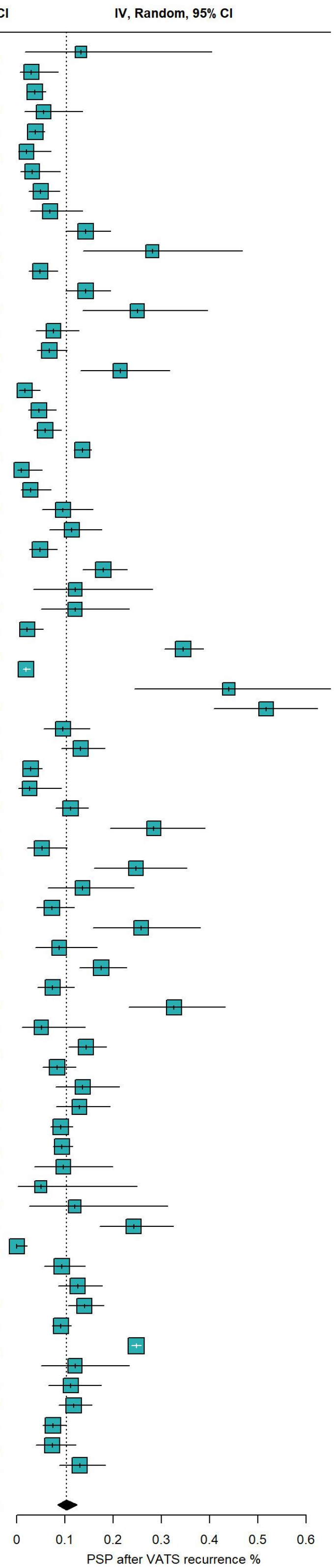

Figure 2 Forest plot of recurrence of PSP after VATS. IV, inverse variance; CI, confidence interval; PSP, primary spontaneous pneumothorax; VATS, video-assisted thoracoscopic surgery.

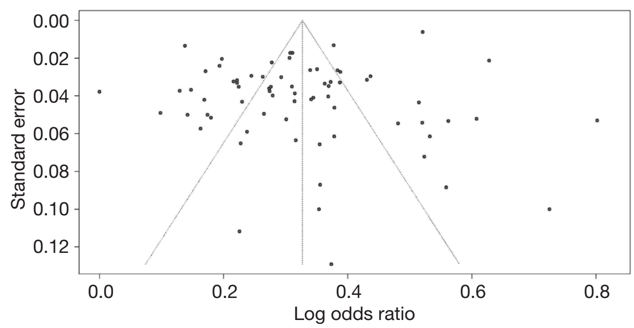

Figure 3 Funnel plot of recurrence of PSP after VATS. PSP, primary spontaneous pneumothorax; VATS, video-assisted thoracoscopic surgery.

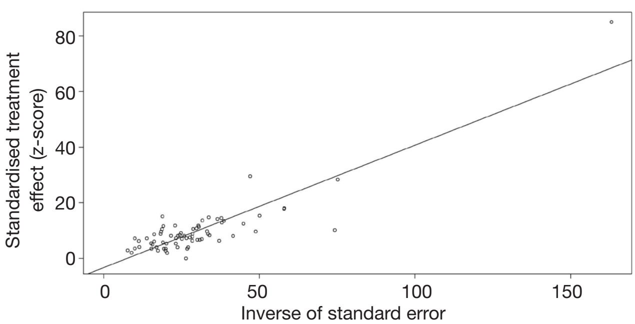

Figure 4 Egger plot of recurrence of PSP after VATS. PSP, primary spontaneous pneumothorax; VATS, video-assisted thoracoscopic surgery.

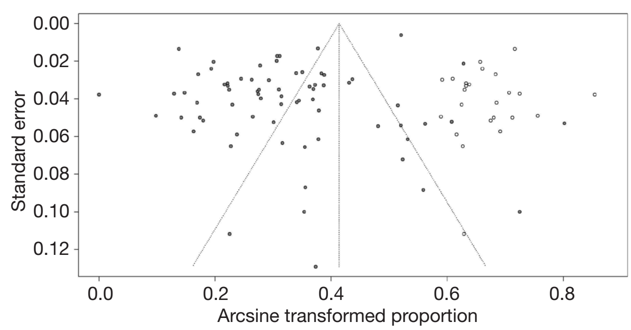

Figure 5 Funnel plot recurrence of PSP after the trim-and-fill method. PSP, primary spontaneous pneumothorax.

0.071–0.129; I^2=97.6%), and 13.6% (95% CI: 0.102–0.174; I^2=94.2%), respectively (*Table 2*).

The meta-regression results indicated that the region, year of publication, study design, and sample size were not sources of heterogeneity (P>0.05), while the follow-up was significantly associated with heterogeneity (P<0.05) (*Table 3*).

Table 2 Subgroup analysis of risk factors of recurrence

Subgroup	Heterogeneity test		ES% (95% CI)
	I^2 (%)	P	
Region			
Asia (n=51)	96.1	<0.001	12.3 (0.098, 0.151)
Europe (n=15)	91.1	<0.001	8.1 (0.044, 0.127)
Middle East (n=4)	–	–	3.8 (0.002, 0.114)
Americas (n=2)	76.7	<0.001	18.7 (0.053, 0.379)
Study design			
Retrospective (n=45)	97.1	<0.001	12.2 (0.082, 0.146)
Prospective (n=6)	74.0	<0.001	27.4 (0.023, 0.079)
Case-control (n=15)	80.7	<0.001	13.1 (0.107, 0.301)
RCT (n=6)	89.3	<0.001	11.3 (0.057, 0.184)
Public year			
1994–2019 (n=49)	95.2	0.76	11.3 (0.084, 0.145)
2020–2023 (n=23)	96.6	0.76	10.6 (0.080, 0.135)
Sample size			
≤100 (n=24)	89.8	0.02	15.4 (0.105, 0.211)
>100 (n=48)	97.4	0.02	9.2 (0.072, 0.115)
Follow-up (months)			
≤24 (n=9)	88.5	<0.001	5.8 (0.021, 0.111)
>24 (n=34)	97.6	<0.001	9.8 (0.071, 0.129)
Not stated (n=29)	94.2	<0.001	13.6 (0.102, 0.174)

ES, effect size; CI, confidence interval; RCT, randomized controlled trial.

Risk factors

In total, seventeen studies (27-43) examined the risk factors of recurrence, including fourteen case-control studies, one retrospective study, and two prospective studies. The majority of patients in these studies underwent thoracoscopic bullectomy in combination with mechanical or chemical pleurodesis (*Table 1*). The duration of follow-up ranged from 11.2 to 102 months, and the interval between relapse ranged from 0.7 to 72 months.

Fifteen studies (27-30,32-39,41-43) reported the sex of patients; of a total of 4,128 patients (female: n=601; male:

Table 3 Results of the meta-regression analysis of recurrence

Variable	β	SE	t	P value	95% CI
Region	−0.032	0.023	−1.366	0.17	−0.077, 0.014
Year of publication	0.004	0.003	1.290	0.20	−0.002, 0.009
Study design	−0.008	0.020	−0.395	0.69	−0.047, 0.031
Sample size	0.000	0.000	0.547	0.59	0.000, 0.000
Follow-up	0.0652	0.0257	2.5352	0.01	0.015, 0.116

SE, standard error; CI, confidence interval.

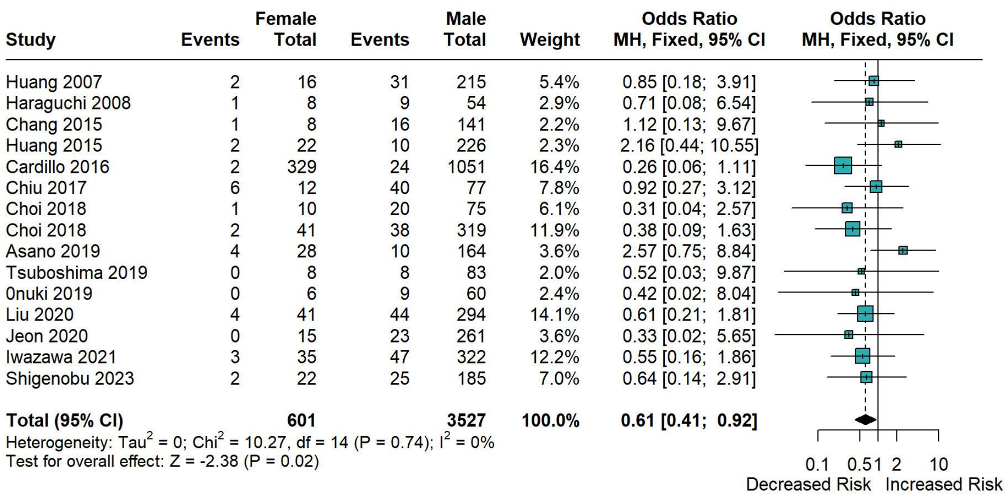

Figure 6 Forest map for the risk factors of sex. MH, Mantel-Haenszel; CI, confidence interval.

n=3,527), 384 experienced recurrence. The forest plot for sex revealed a significant OR of 0.61 (95% CI: 0.41–0.92; P=0.02) with non-significant heterogeneity (I^2=0%; P=0.74) (*Figure 6*) and an asymmetrical funnel plot in the appendix available at https://cdn.amegroups.cn/static/public/jtd-24-175-1.docx.

Six studies (27-30,34,35) examined the association between the age of patients and recurrence, with five (27,29,30,34,35) reporting statistically significant differences. Five studies (27-29,34,35) were included in the meta-analysis. The pooled mean difference (MD) was −2.01 (95% CI: −2.57 to −1.45; P<0.001) indicating the potential role of age as a protective factor. The results showed non-significant heterogeneity (I^2=0%; P=0.91). In addition, in all studies, a higher mean age was recorded in the non-recurrence group *vs.* the recurrence group (*Figure 7*).

A total of five studies (27,30,33-35) examined the association between weight and recurrence, with two showing a significant association. All studies were comparable because they reported the same unit of weight; therefore, they were included in the meta-analysis. The studies had a pooled MD of −1.57 (95% CI: −3.03 to −0.11; P=0.04) and non-significant heterogeneity (I^2=19%; P=0.30) (*Figure 8*). The results show that weight may be a protective factor.

Six studies (27,29,30,34,35,38) compared the mean body mass index (BMI) between the recurrence and control groups. Five studies did not show statistically significant differences; however, one study (27) showed that being underweight (BMI <18.5 kg/m^2) was a significant independent risk factor for recurrence (OR: 5.327; 95% CI: 2.23–12.71). All six studies were included in the analysis because they reported the same unit, and the pooled MD was −0.73 (95% CI: −1.08 to −0.37; P<0.001), indicating the potential role of BMI as a protective factor. There were no significant differences in heterogeneity among the studies (I^2=33%; P=0.19) (*Figure 9*).

Four studies (involving 878 patients) (30,38,42,43) reported the history of contralateral pneumothorax of

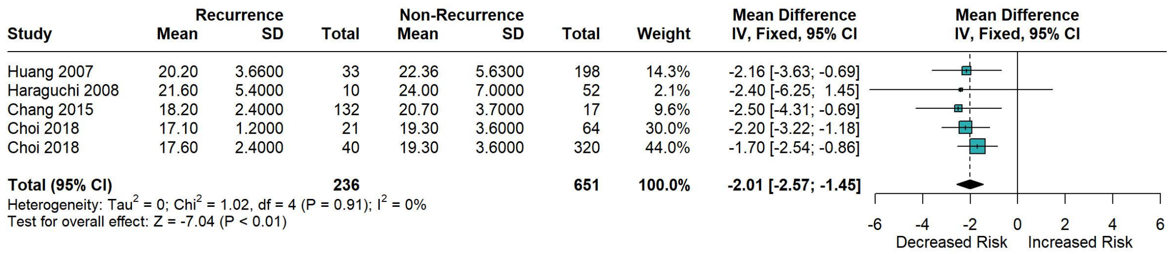

Figure 7 Forest map for the risk factors of age. SD, standard deviation; IV, inverse variance; CI, confidence interval.

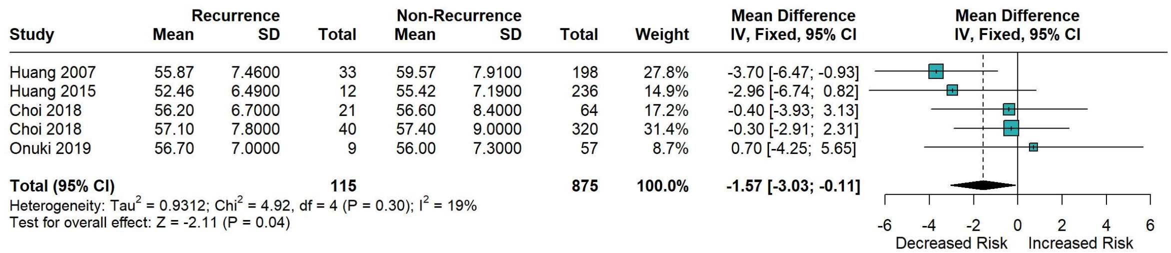

Figure 8 Forest map for the risk factors of weight. SD, standard deviation; IV, inverse variance; CI, confidence interval.

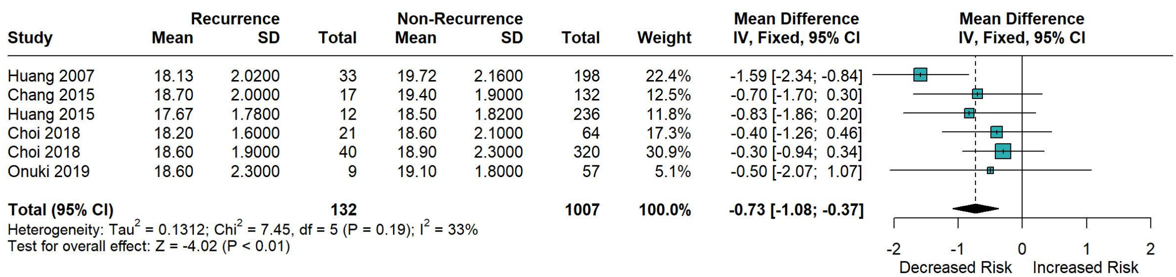

Figure 9 Forest map for the risk factors of BMI. SD, standard deviation; IV, inverse variance; CI, confidence interval; BMI, body mass index.

PSP; of those, 98 patients had a history of contralateral pneumothorax. The pooled OR was 2.46 (95% CI: 1.56–3.87; P<0.001) with non-significant heterogeneity (I^2=36%; P=0.20) (*Figure 10*).

Discussion

This was the first systematic review of all available evidence on the recurrence and risk factors for PSP after VATS. The analysis involved 72 studies with 23,531 participants, yielding an estimated pooled recurrence rate of 10%. Sex, age, weight, and BMI were considered protective factors against recurrence. Regardless of the administration of conservative treatment or surgical treatment, PSP is associated with a risk of recurrence. The pooled rate of recurrence is similar to the recurrence rates reported in previous studies (14-16,32), highlighting that VATS offers a favorable advantage over other treatment options in terms of reducing the recurrence rate of PSP.

A recent meta-analysis showed that female patients are linked to a higher risk of PSP recurrence compared with male patients (6). However, whether sex is the original risk factor for the recurrence of spontaneous pneumothorax after thoracoscopic surgery remains unknown. The present meta-analysis, which included fifteen studies, found significant differences between male and female patients

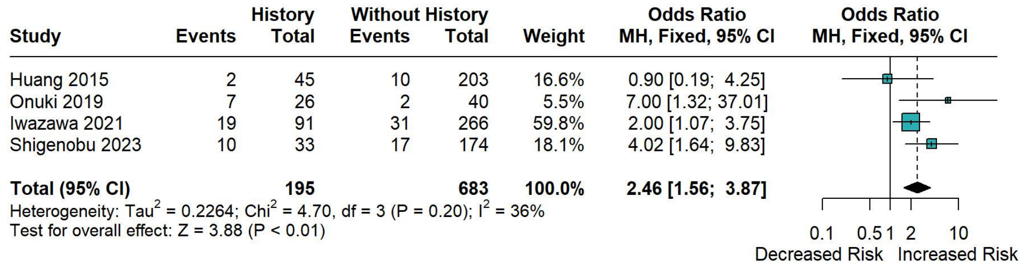

Figure 10 Forest map for the risk factors of history of contralateral pneumothorax. MH, Mantel-Haenszel; CI, confidence interval.

who underwent VATS; the risk of recurrence was higher for males *vs.* females. This result may be related to the exclusion of all potential sex-related diseases, including menstrual pneumothorax, from the analysis. In addition, the higher prevalence of smoking among males may also be an important factor promoting the increased risk of recurrence (44).

According to the results of the present meta-analysis, younger patients experienced more frequently PSP recurrence compared with older patients. This is consistent with the results of a recent retrospective study that also found a decreased rate of pneumothorax recurrence in older patients (P=0.01; 95% CI: 0.93–0.99) (5).

Similarly, several recent studies also demonstrated that an age <20 or <30 years is strongly associated with recurrence of PSP, including in patients who underwent VATS (15,43,45,46). These findings emphasize the importance of age in reducing the recurrence rate of PSP. Younger age seems to has greater tension of staple line and the higher risk of postoperative bullae, ultimately leading to increased recurrence (34). Morphometric analysis of variation in the ribs has indicated that the length of the rib reaches the first peak after the age of 20 years (47), which may give the lungs sufficient space for reducing vertical pressure. These results are consistent with those of the above studies (9,48). These observations may offer an explanation for the significant decrease in recurrence rate noted after 20 years of age in the above studies.

In this analysis, patients in the recurrence group had a lower weight compared with those in the non-recurrence group. The specific risk associated with body weight has not been confirmed due to the lack of direct evidence; however, as a factor strongly associated with the BMI, weight has been associated with recurrence in several studies. Guo *et al.* (49) found that spontaneous pneumothorax patients with lower weight are more likely to experience recurrence *vs.* those with higher weight. Weight is further identified as a significant predictor of PSP recurrence in a retrospective study (18). As another important component of the BMI, the role of height was also analyzed in this review; nevertheless, the results did not reveal a significant difference. As one of the key indicators of patient's body, height is associated with the development and progression of pneumothorax, particularly in adolescents. Previous studies showed that the rapid growth in height observed during adolescence is accompanied by a rapid growth in the upper chest and increases in upper chest width (50,51). This phenomenon may be the result of uneven chest pressure, accelerating the development of pneumothorax. Patients with PSP often have both abnormal height and weight. A study showed an association between height and recurrent PSP, which patients had higher height, lower weight, and lower BMI compared with non-recurrence patients (18). Although often occurred together, height or weight alone can only reflect a part of the nutritional and developmental status (52). This may also explain the non-significant result of meta-analysis for height. Additional high-quality prospective studies are warranted to further determine the importance of height or weight alone as risk factors.

In studies, the BMI (as a ratio of height to weight) appears to be a better indicator of the recurrence risk of an individual than heigh or weight alone. It is established that a lower BMI is a risk factor and a better predictive factor for recurrence compared with height or weight alone. Lower BMI has been confirmed by several studies as a risk factor for the recurrence of PSP after treatment and may be a clinically useful predictor of recurrence (5,18,27). Previous systematic review found a higher risk of recurrence in patients with lower *vs.* higher BMI (6). This study also showed that patients in the recurrence group had lower BMI than those in the non-recurrence group, indicating that recurrence after VATS was similarly influenced by the

BMI of an individual. An initial explanation provided in a previous study suggests that a lower BMI is often associated with abnormal growth of the chest and malnutrition, which may increase chest negative pressure and cause recurrence (18,53).

The present meta-analysis is the first to identify the history of pneumothorax as a risk factor for recurrent PSP after VATS. This finding indicates the higher risk of recurrence in patients with history of contralateral pneumothorax. Based on the higher incidence of bilaterally symmetrical bulla on computed tomography images of patients with PSP, the history of contralateral or ipsilateral pneumothorax has been reported as a risk factor for recurrence after VATS in clinical experience, and it warrants further validation with more prospective studies in the future (21).

In addition, in this meta-analysis, there was no statistically significant difference between recurrence and smoking history; of note, significant differences were observed in only two studies (32,40). Smoking exerts adverse effects on the lungs and bronchi, and eventually leads to adverse respiratory health outcomes (54). Nonetheless, the rate of smoking among young males remains high. Although, there is no direct pathological evidence confirming the effect of smoking on the recurrence of pneumothorax, some evidence indicated a potential association. According to a previous study in young adults smoking cannabis, marijuana smoking appears to be strongly associated with lung emphysema in imaging results (55). Furthermore, another study of imageology revealed a significant difference in the areas of low-attenuation between smokers and non-smokers (0.7% *vs.* 0.1%, respectively, P=0.03) (56). Several studies also found that the recurrence of PSP is associated with the smoking history of the patient (including electronic cigarettes) (6,27,57-59). A single-center retrospective study of 567 patients with PSP also indicated that smoking (P=0.02) is an independent risk factor for contralateral pneumothorax after VATS. Another study further revealed pathologic findings of respiratory bronchiolitis in all smokers compared with non-smokers after VATS (100% *vs.* 49%, respectively, P<0.001). Importantly, those pathologic findings were associated with a higher rate of recurrence (P<0.001). As with the study conducted by Walker *et al.* (6), this study is limited by the fact that the smoking history was determined only by simple consultation and a "yes" or "no" response, which does not inquire further on the detailed frequency of smoking. This approach may have increased the heterogeneity, potentially obscuring the association of smoking with recurrence. Therefore, it is necessary to further assess the effects of smoking history in future studies.

This systematic review has several limitations. Firstly, although all included studies considered the imaging-based objective result as the base of diagnosis, the diagnostic criteria of studies varied. Consequently, an attempt to unify the diagnostic criteria for risk stratification regarding the recurrence of PSP in the future is necessary. Secondly, subgroup analysis was performed to explore the sources of heterogeneity; nevertheless, a high level of unexplained heterogeneity remained. Thirdly, retrospective studies were the major component of this systematic review, potentially increasing the risk of bias. Hence, additional high-quality studies should be included in future analyses. Furthermore the surgical details differed across studies, which introduced unavoidable heterogeneity. Finally, some non-first-episode patients were included in this study; thus, the heterogeneity of the population should have been resolved.

Conclusions

This systematic review provides a pooled analysis of the latest studies on the recurrence and risk factors for PSP in patients who underwent VATS. The pooled recurrence rate obtained from this analysis was 10%. Male sex, younger age, lower weight, lower BMI, and history of contralateral pneumothorax were associated with a higher risk of recurrent PSP after VATS. Close attention should be paid to the management of factors that may influence PSP recurrence. This study mainly included retrospective cohort studies, which are characterized by a potentially increased risk of selection bias. Therefore, high-quality randomized controlled trials should be conducted in the future.

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Footnote

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Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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