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Is thoracoscopy superior to thoracotomy in the treatment of congenital lung malformations? An updated meta-analysis

Junhua Xie*, Yuhao Wu* and Chun Wu

Abstract

Background: A meta-analysis was performed for a comparison of outcomes between video-assisted thoracoscopic surgery (VATS) and thoracotomy for congenital lung malformations (CLM).

Methods: Electronic databases, including PubMed, Scopus, Embase, and the Cochrane Library were searched systematically for literature aimed mainly at reporting the therapeutic effects for CLM administrated by VATS and thoracotomy.

Results: A total of 40 studies meeting the inclusion criteria were included, involving 2896 subjects. VATS was associated with fewer complications [odds ratio (OR) 0.54; 95% confidence interval (CI), 0.42–0.69], less use of epidural anesthesia (OR, 0.08; 95% CI, 0.03–0.23), shorter length of hospital stay [standard mean difference (SMD) −0.98; 95% CI, −1.4 to −0.55] and chest drainage (SMD, −0.43; 95% CI, −0.7 to −0.17), as compared with thoracotomy. However, thoracotomy showed superiority in reduced operative time (SMD, 0.44; 95% CI, 0.04–0.84). Pearson analysis (Pearson $r=0.85$, 95% CI, 0.28 to 0.98, $p=0.01$) and linear regression (R square 0.73) confirmed a positive correlation between percentage of symptomatic cases and conversion in patients using VATS.

Conclusion: VATS is associated with fewer complications, less use of epidural anesthesia, shorter length of stay and length of chest drainage, but longer operative time, as compared with thoracotomy. Symptomatic patients with CLM using VATS may be prone to conversion to thoracotomy.

The reviews of this paper are available via the supplemental material section.

Keywords: children, congenital lung malformation, thoracoscopy, thoracotomy

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Correspondence to:
Chun Wu
Yuhao Wu
Department of Cardiothoracic Surgery, Children's Hospital of Chongqing Medical University, No. 136 Zhongshan Second Road, Yuzhong District, Chongqing, 400014, China

Ministry of Education Key Laboratory of Child Development and Disorders, China

International Science and Technology Cooperation Base of Child Development and Critical Disorders, National Clinical Research Center for Child Health and Disorders, Chongqing Key Laboratory of Pediatrics, Chongqing, 400014, China

wuyuhao91@icloud.com
250734291@qq.com

Junhua Xie
Division of Pediatric Surgery, Department of General surgery, Fengdu People's Hospital, Chongqing, China

*These authors contributed equally.

Introduction

Congenital lung malformations (CLM) is a rare congenital disorder that accounts for 5–18% of all congenital diseases.[1] There is a wide spectrum of congenital pulmonary abnormalities,[2] including congenital pulmonary airway malformations (CPAM, formerly known as congenital cystic adenomatoid malformations), pulmonary sequestration (PS), congenital lobar emphysema (CLE), and bronchogenic cyst (BC). In recent years, prenatal ultrasonography and magnetic resonance imaging (MRI) have contributed significantly to the early diagnosis of CLM.

The presentations of CLM vary widely, from respiratory distress to entirely asymptomatic lesions. It is unquestionable that symptomatic CLM cases can benefit from surgical resection. A meta-analysis also further indicated the advantages of elective surgery in the management of asymptomatic conditions, preventing the risks of chest infection and malignancy later in life.[3] Thoracotomy is a traditional and well-known surgical approach for CLM. However, long-term complications, such as breast deformity, rib fusion, winged scapula, and scoliosis have been reported to occur in up to 30% of children with the use of thoracotomy.[4] Video-assisted thoracoscopic surgery (VATS) – a minimally invasive procedure – has been introduced for the management of CLM in experienced pediatric surgery centers in the last two decades.[5] However, the use of VATS also raises concerns regarding prolonged general anesthesia, hypercapnia, and difficulty with single-lung ventilation.

Two published meta-analyses compared VATS *versus* open surgery for patients with CLM[6,7]; however, there were some significant drawbacks in each study. The Nasr and Bass study involved a study adopting cervical incision or laparotomy for CLM, which was against their inclusive criteria.[6] The risk of bias in their included studies was not evaluated. Although this was the first meta-analysis in this field, their results were less conclusive since heterogeneity across studies was not evaluated. Adams *et al.* published a meta-analysis involving both single- and two-arm studies.[7] Unfortunately, they did not take into account publication bias in their meta-analysis; therefore, selection bias due to incomplete retrieval of literature might exist. Though their aim was to evaluate only asymptomatic patients, several included studies were found to have symptomatic cases. Therefore, our study aims to perform an updated meta-analysis comparing the outcomes of VATS and thoracotomy for patients with CLM, and to address the limitations of the two previous meta-analyses.

Methods

Literature search

Our methods were in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.[8] The protocol of this study was registered on PROSPERO (CRD42020171061, https://www.crd.york.ac.uk/prospero). A systematic search of the PubMed, EMbase, Scopus, and Cochrane Library CENTRAL for the relevant published studies comparing the outcomes of VATS *versus* thoracotomy for CLM cases was conducted in February 2020. VATS was not used commonly for CLM until the late 1990s; therefore, to avoid potential selection bias, year of publication was restricted from January 2000 to February 2020. The strategy used for searching was (congenital cystic adenomatous malformation OR congenital pulmonary airways malformation OR bronchogenic cyst OR pulmonary sequestration OR congenital lobar emphysema OR congenital lung lesions OR congenital lung diseases) AND [(thoracoscopy OR thoracoscopic surgery OR video-assisted thoracic surgery OR minimally invasive surgery) OR (open surgery OR conventional surgery OR thoracotomy)]. References from all included studies and other relevant literature were also reviewed manually to identify additional eligible studies. This search was restricted to articles that were published in English. We contacted the authors to obtain extra information *via* e-mail as necessary.

Study selection

A study was included in this systematic review when the following criteria were met: (1) single-arm case series, observational studies (cohort or case-controlled studies) or randomized controlled trials (RCTs) that presented outcomes of VATS and thoracotomy for CLM; (2) the procedure of each surgical approach was described. Briefly, thoracotomy should be performed through a conventional posterolateral thoracotomy. VATS was performed through several port incisions and under the observation of thoracoscopy.

A study was excluded in this systematic review when the following criteria were met: (1) multiple studies were based on the same data; (2) sample size of single-arm studies was less than 10 cases; (3) studies involved patients over 16 years of age. Reviews, letters, conference abstract, case reports, and animal experiments were also excluded. When several studies were based on the same sample (same database and time period), only the study with most complete set of data was included.

Data extraction and definition of variables

Data was extracted by both reviewers (X.J.H. and W.Y.H.) independently, any disagreement was resolved by consensus with the help of a third reviewer (W.C.). A standardized extraction form in an Excel spreadsheet was used. The following information was extracted: (1) baseline characteristics of included studies: first author, publication year, study area, types of study design, types of CLM, surgical approach, sample size, operative age, recommended age for elective surgery, percentage of symptomatic cases, conversion, and follow-up time; (2) outcomes of VATS and thoracotomy approaches: causes of conversion, operative time, length of hospital stay (LOS) and chest drainage time, use of epidural anesthesia, and complications after surgery.

Symptomatic patients with CLM were defined as patients who presented with respiratory symptoms or chest infection before surgery. Complications after surgery referred to wound infection, pneumonia, pleural effusion, air leaks, etc. Operative time was defined as time duration of each operation. LOS was defined as the time period from admission to discharge. Chest drainage time was defined as the time period from insertion to removal of the chest tube. Conversion was considered when thoracoscopic surgery was converted to thoracotomy due to unsatisfied exposure, bleeding, adhesion, or other reasons.

Quality assessment and risk of bias

Quality assessment and risk of bias were performed by two reviewers (W.Y.H. and X.J.H.) independently, and any disagreements on the assessed quality were resolved with a third reviewer (W.C.) by consensus. The risk of bias of non-RCTs (NRCTs) was evaluated with the ROBINS-I tool.[9] The risk of bias of single-arm case series was evaluated using the methodological index for non-randomized studies (MINORS) guidelines.

Statistical analysis

All statistical analyses were conducted using RevMan software (version 5.3; The Nordic Cochrane Centre, Copenhagen, Denmark). Odds ratio (OR) and standard mean difference (SMD) were employed for dichotomous and continuous data, respectively. The χ^2-Q statistics and I^2 statistics were used to assess heterogeneity, with $I^2 > 50\%$ indicating heterogeneity. If the I^2 statistic was $>50\%$, a random-effect model was adopted. Subgroup analysis and sensitivity analysis were used to explore the sources of heterogeneity; otherwise, a fixed-effect model of analysis was used. Sensitivity analysis was performed using the leave-one-out method. Subgroup analysis was conducted in terms of types of CLM, operative age, conversion to thoracotomy and percentage of symptomatic cases. If only the median value and range were available in our included studies, the formulas provided by Hozo *et al.* were used to estimate the mean value and standard difference.[10] Publication bias was evaluated with funnel plot, Begg's and Egger's tests (Stata 12.0, Stata Corp, College Station, TX, USA). Pearson analysis and linear regression were performed using Graphpad (V7.0, GraphPad Software Inc., La Jolla, CA, USA). A p value <0.05 was considered statistically significant for all analyses in our study.

Results

Characteristics of included studies

A total of 3747 studies were obtained initially from the electronic databases and seven papers were further identified manually on reference lists of the retained studies. After screening for duplicates and relevance in titles and abstracts, only 109 studies were available for the full-text evaluation for eligibility; 69 studies were excluded after full-text evaluation. Eventually, this review was based on 40 NRCTs,[11–50] which encompassed 23 two-arm case-controlled studies,[11–33] and 17 single-arm case series.[34–50] A flowchart depicting the search strategy is shown in Figure 1.

All 40 studies were retrospective NRCTs (Table 1) published between 2004 and 2020. A total of 2896 patients were involved, of which 1372 patients were in the VATS group and 1524 patients in the thoracotomy group. Over half of our included studies reported 'hybrid' types of CLM, and 15 studies focused on each specific type. CPAM was the main reported type of CLM. Lobectomy was the approach used most frequently for lung resection (Supplemental Table S1). Only five studies were based completely on asymptomatic cases. Rate of conversion ranged from 0% to 40.9%. The leading causes of conversion were hemorrhage, poor visualization, and intolerance to single-lung ventilation. The most frequently recommended timing for elective surgery in the management of CLM was 6–12 months of age. A total of four studies reported post-operative death in 11 patients.

Complications

A total of 22 studies compared the complications after surgery of both procedures.[11–31,33] Air leaks and chest infection were the most common complications after surgery. Pectus excavutum and scoliosis, which were the long-term complications with the use of thoracotomy, were reported in only one study.[15] This meta-analysis result indicated that VATS was associated with fewer complications after surgery, as compared with thoracotomy [OR, 0.52; 95% confidence interval (CI), 0.40 to 0.67; $P < 0.00001$; $I^2 = 29\%$, Figure 2A]. Infectious complications, which included wound infections and respiratory infections, and bleeding were more common using thoracotomy, as shown in Supplemental Table S2.

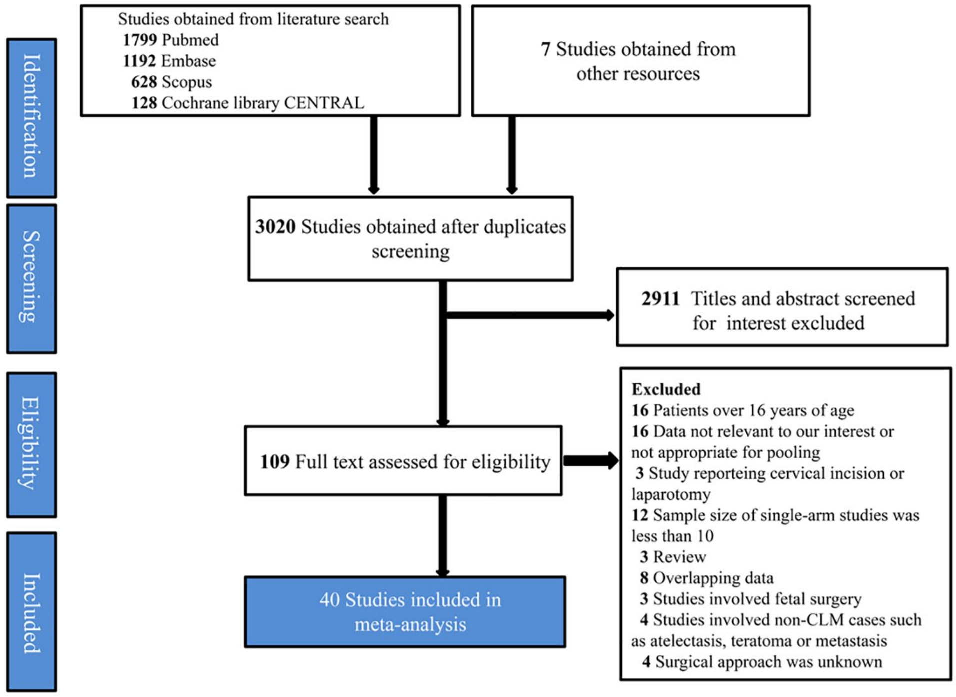

Figure 1. Flowchart of process for literature screening for this meta-analysis according to PRISMA guidelines. CLM, congenital lung malformations; PRISMA, preferred reporting items for systematic reviews and meta-analyses.

A total of 10 and 7 single-arm studies reported complications from thoracotomy and VATS, respectively. Among 10 single-arm studies that reported complications of thoracotomy, the pooled estimate of complications of thoracotomy was 22% (95% CI 12–32%, $I^2 = 87.3\%$). Among seven single-arm studies that reported complications from VATS, the pooled estimate of complications was 7.1% (95% CI 0.8% to 13.3%, $I^2 = 53.3\%$) using VATS.

Use of epidural anesthesia

Four studies compared the use of epidural anesthesia after surgery.[11,13,14,16] This meta-analysis indicated that VATS was associated with less use of epidural anesthesia after surgery than with thoracotomy (OR, 0.08; 95% CI, 0.03–0.23; $p < 0.00001$; $I^2 = 0\%$, Figure 2B).

Operative time

A total of 17 studies compared the operative time of both surgical approaches.[11,12,15,17,19,20,22–27,29–33] However, in one study, Laje *et al.* incorrectly reported the operative time data.[24] Therefore, this meta-analysis included the remaining 16 studies. This meta-analysis indicated that VATS was associated with longer operative times than with thoracotomy (SMD, 0.44; 95% CI, 0.04–0.84; $p = 0.03$; $I^2 = 88\%$, Figure 3A). Due to significant heterogeneity, sensitivity analysis with the use of the leave-one-out method was adopted. I^2 reduced to 72% when we removed the studies of Zhang *et al.* and Lima *et al.* in turn.[31,32] This did not appreciably change the direction and magnitude of the pooled estimates (SMD, 0.65; 95% CI, 0.32–0.98; $p = 0.0001$).

Length of hospital stay

A total of 17 studies compared the LOS.[11,12,14,17,19,21–24,26,27,29,31–33] This meta-analysis indicated that VATS was associated with shorter LOS when compared with thoracotomy (SMD, −0.98; 95% CI, −1.4 to −0.55; $p < 0.00001$; $I^2 = 91\%$, Figure 3B). Sensitivity analysis was performed due to significant heterogeneity. I^2 was reduced to 72% when we removed Mahida *et al.*, Lau *et al.* and Mattioli *et al.* studies in turn.[20,26,27] The direction and magnitude of the pooled estimates did not change (SMD, −0.48; 95% CI, −0.74 to −0.21; $p = 0.0004$).

Table 1. Baseline characteristics of included studies.

First author, year, and study area	Study design	Surgical approach	Male/female (gender)	Types of CLM	Operative age[b]	Recommended age for elective surgery in asymptomatic cases[b]	Follow-up time[b]
Bonnard 2004[11]	Single-center	VATS	2/1	3PS	7.3 ± 1.7 months	NA	1.2 ± 0.2 months
France	Retrospective	Thoracotomy	3/1	4PS	3.5 ± 1.1 months		2.7 ± 2.5 months
Tolg 2004[12]	Single-center	VATS	4	BC[a]	7.8 years	4–6 months	5.9 (3–13 years)
France	Retrospective	Thoracotomy	4		3.3 years		
Sundararajan 2007[13]	Single-center	VATS	16	CPAM, PS, BC, FD[a]	16–168 months	16–18 months	12 (1–38 months)
UK	Retrospective	Thoracotomy	23		0.1–164 months		24 (6–60 months)
Diamond 2008[14]	Single-center	VATS	6/6	9CPAM, 3PS	7.2 (0.3–19.8 months)	NA	3 (1–5 months)
Canada	Retrospective	Thoracotomy	13/11	18CPAM, 2PS, 2BC, 1CLE	7.6 (0.1–21.4 months)		3 (2–7 months)
Vu 2008[15]	Single-center	VATS	7/5	CPAM[a]	6.7 (0.1–131.8 months)	Early resection before chest infection	1.5 months (2–8.6 years)
US	Retrospective	Thoracotomy	10/14		3.7 (4.2–17.8 months)		
Rahman 2008[16]	Single-center	VATS	6/8	8CPAM, 2PS, 4CLE	10 months	NA	NA
UK	Retrospective	Thoracotomy	5/9	10CPAM, 2PS, 2CLE	7 months		
Cho 2012[17]	Multi-center	VATS	7	32PS, 2CPAM	21.0 ± 19.1 months	<1 year	8.3 ± 6.2 months
Korea	Retrospective	Thoracotomy	27		100.0 ± 12.6 months		51.5 ± 16.0 months
Fievet 2012[18]	Single-center	VATS	9	BC[a]	23.7 months	6–12 months	NA
France	Retrospective	Thoracotomy	2		84.5 months		
Fascetti-Leon 2013[19]	Single-center	VATS	26	23CPAM, 17Hybrid, 10PS, 1BC, 3	8.6 months (0.5 months–14 years)	6 months	NA
Italy	Retrospective	Thoracotomy	28	Others			
Lau 2013[20]	Single-center	VATS	19/20	25CPAM, 13PS, 1CLE	10.4 ± 2.3 months	>5 kg	NA
China	Retrospective	Thoracotomy	23/5	22CPAM, 3PS, 1CLE, 2BC	11.7 ± 4.3 months		
Bagrodia 2014[21]	Single-center	VATS	19	17CPAM, 2CLE	0–180 months	Diameters of lesion >2 cm	0–97 months
US	Retrospective	Thoracotomy	26	17CPAM, 9CLE			

(Continued)

Table 1. (Continued)

First author, year, and study area	Study design	Surgical approach	Male/female (gender)	Types of CLM	Operative age[b]	Recommended age for elective surgery in asymptomatic cases[b]	Follow-up time[b]
Kunisaki 2014[22]	Single-center	VATS	28/21	33CPAM, 10PS, 2CLE, 4Hybrid	1.5 ± 2.5 years	6 months	NA
US	Retrospective	Thoracotomy	8/5	9CPAM, 1PS, 1CLE, 2Hybrid	0.9 ± 0.4 years		
Kulaylat 2015[23]	Multi-centers	VATS	66/46	68CPAM, 30PS, 4CLE, 10Other	1.3 ± 2.5 years	NA	NA
US	Retrospective	Thoracotomy	89/57	80CPAM, 26PS, 20CLE, 20Other	1.5 ± 3.2 years		
Laje 2015[24]	Single-center	VATS	54/46	53CPAM, 8PS, 19Hybrid, 19Other	1.8 (0.5–4 months)	4 months	1 year
US	Retrospective	Thoracotomy	91/97	94CPAM, 14PS, 52Hybrid, 2CLE, 26Other	2 (0.5–4 months)		
ChunHong 2015[25]	Single-center	VATS	3/0	3PS	2.7 ± 2.5 months	NA	2–3 months
China	Retrospective	Thoracotomy	5/3	8PS	4.5 ± 5.5 months		2–3 months
Mahida 2015[26]	Multi-centers	VATS	40/16	CLM[a]	6 (4–10 months)	<10 kg	NA
US	Retrospective	Thoracotomy	39/24		5 (2–9 months)		
Mattioli 2016[27]	Single-center	VATS	13	11CPAM, 2PS	1 (0.6–4.1 years)	NA	NA
Italy	Retrospective	Thoracotomy	18	12CPAM, 5PS, 1Other	1.5 (0.6–4 years)		
Polites 2016[28]	Multi-centers	VATS	210/154	237CPAM+BC, 118PS	1.2 ± 3.2 years	NA	NA
US	Retrospective	Thoracotomy	153/117	180CPAM+BC, 74PS, 16Hybrid	1.8 ± 4.3 years		
Ito 2016[29]	Single-center	VATS	2/2	CPAM[a]	36 (21–68 months)	>1 year	NA
Japan	Retrospective	Thoracotomy	4/5		14 (12–44 months)		
Khen-Dunlop 2018[30]	Single-center	VATS	36	PS[a]	17 months (8 months–15.2 years)	NA	26.5 months[b]
France	Retrospective	Thoracotomy	23		10 months (5 months–12.6 years)		26.5 months

(Continued)

Table 1. (Continued)

First author, year, and study area	Study design	Surgical approach	Male/female (gender)	Types of CLM	Operative age[b]	Recommended age for elective surgery in asymptomatic cases[b]	Follow-up time[b]
Lima 2019[31]	Single-center	VATS	67	76CPAM, 6Hybrid, 41PS, 3BC, 41Other	33.98 ± 58.3 months	6–12 months	25 ± 20 months
Italy	Retrospective	Thoracotomy	100		15.45 ± 32.9 months		35.7 ± 35.9 months
Zhang 2019[32]	Single-center	VATS	139	PS[a]	19.70 ± 48.82 months	6–12 months	NA
China	Retrospective	Thoracotomy	65				
Bawazir 2020[33]	Single-center	VATS	6/3	CLE[a]	3.4 (1–6 months)	NA	18 months–9 years
Saudi Arabia	Retrospective	Thoracotomy	24/1		3.9 (1–7 months)		
Aziz 2003[34]	Single-center	Thoracotomy	12/18	30CPAM	2 months–15 years	NA	3 years
Canada	Retrospective						
Kumar 2008[35]	Single-center	Thoracotomy	18/7	14CPAM, 5CLE, 3PS, 3BC	1 day–11 years	NA	1.8 (1–5) months
India	Retrospective						
Mullassery 2008[36]	Single-center	Thoracotomy	28/13	21CPAM, 14CLE, 4PS, 1BC	4.7 months	NA	39 (2–88 months)
UK	Retrospective						
Tsai 2008[37]	Single-center	Thoracotomy	49/56	64CPAM, 26Hybrid, 8CLE, 6PS, 1Other	2.5 ± 2.4 months	NA	NA
US	Retrospective						
Wong 2009[38]	Single-center	Thoracotomy	23/12	35CPAM	0–13 years	NA	NA
Australia	Retrospective						
Nazem 2010[39]	Single-center	Thoracotomy	26	26CLE	NA	NA	NA
Iran	Retrospective						
Paramalingam 2010[40]	Single-center	Thoracotomy	10	10CLE	1 (0.4–5.2 years)	NA	6 (2–60 months)
UK	Retrospective						
Rothenberg 2011[41]	Multi-center	VATS	75	52CPAM, 20PS, 3CLE	2 day–11 months	<5 Kg is feasible	48 months
US	Retrospective						

(Continued)

Table 1. (Continued)

First author, year, and study area	Study design	Surgical approach	Male/female (gender)	Types of CLM	Operative age[b]	Recommended age for elective surgery in asymptomatic cases[b]	Follow-up time[b]
Muller 2012[42]	Single-center	VATS	9/3	12CPAM	12 (2–24 months)	Early resection before symptoms	7.5 (2–28 months)
France	Retrospective						
Seong 2013[43]	Single-center	VATS	27/23	30CPAM, 12PS, 2BC, 6Other	3.2 (0.3–16 years)	NA	NA
Korea	Retrospective						
Tanaka 2013[44]	Single-center	VATS	9/3	4CPAM, 3PS, 4CLE, 1Other	65.6 ± 29.7 months	<10 kg is feasible	NA
Japan	Retrospective						
Furukawa 2015[45]	Single-center	Thoracotomy	27	16CPAM, 5CLE, 3PS, 3BC	NA	<6 months	8.1 months (4 months–17.8 years)
Japan	Retrospective						
Raman 2015[46]	Single-center	Thoracotomy	29/11	19CPAM, 11CLE, 5BC, 5PS	25 months	NA	36 months
India	Retrospective						
Tainaka 2016[47]	Single-center	VATS	17/21	34CPAM, 3PS, 1CLE	0–12 months	NA	1.6–95 months
Japan	Retrospective						
Mohamed 2018[48]	Single-center	Thoracotomy	39/14	53CLE	3 (0.8–15 months)	NA	1 year
Egypt	Retrospective						
Macchini 2019[49]	Single-center	VATS	10/10	3CPAM, 13PS, 3BC, 1CLE	6.4 ± 1.5 months	NA	NA
Italy	Retrospective						
Murakami 2020[50]	Single-center	VATS	22/30	44CPAM, 8PS	0.03–8.9 years	NA	0.9–10.9 years
Japan	Retrospective						

[a]Numbers or categorizations of cases in each group are not reported.
[b]Data was expressed as mean value and standard error, median value and range or mean value.
BC, bronchogenic cyst; CLE, congenital lobar emphysema; CLM, congenital lung malformations; CPAM, congenital pulmonary airway malformations; FD, foregut duplication; NA, not available; PS, pulmonary sequestration; VATS, video-assisted thoracoscopic surgery; UK, United Kingdom; US, United States.

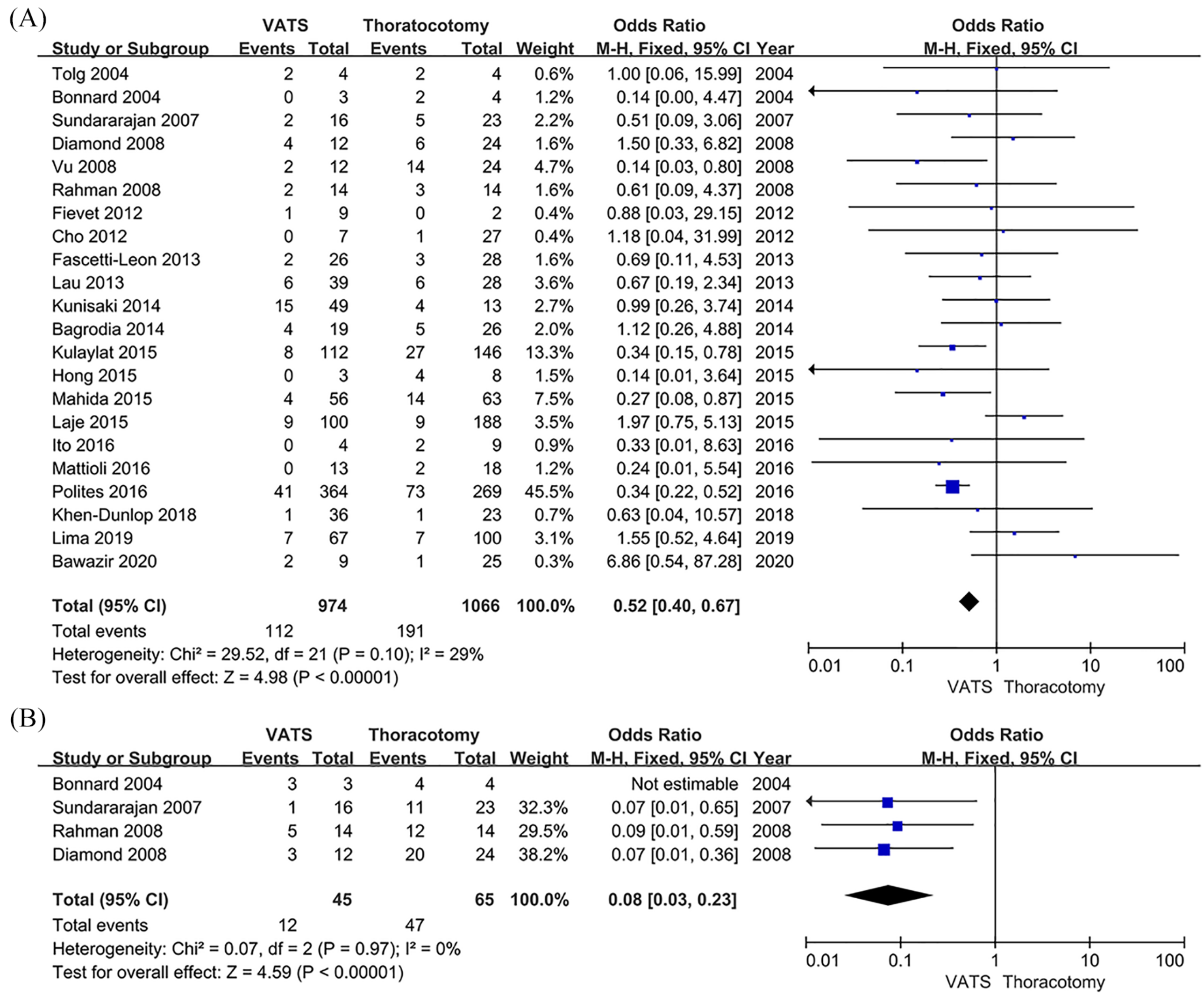

Figure 2. Forest plots of complications and use of epidural anesthesia. Forest plot of OR of (A) post-operative complications and (B) use of epidural anesthesia.
CI, confidence interval; M–H, Mantel–Haenszel; OR, odds ratio; VATS, video-assisted thoracoscopic surgery.

Length of chest drainage

A total of 13 studies compared the length of chest drainage (Figure 4A).[11,12,14,17,19,21–24,26,27,29,31–33] This meta-analysis indicated that VATS was associated with shorter length of chest drainage than with thoracotomy (SMD, −0.43; 95% CI, −0.7 to −0.17; $p = 0.001$; $I^2 = 65\%$). Sensitivity analysis was also performed to explore the origin of heterogeneity. I^2 reduced to 44% when we removed Laje *et al.* and Kunisaki *et al.* studies in turn.[22,24] The direction and magnitude of the pooled estimates did not change (SMD, −0.58; 95% CI, −0.83 to −0.33; $P < 0.00001$).

Subgroup analysis

In the subgroup analysis of operative time, when studies were stratified by the mean operative age, thoracotomy was associated with a shorter operative time in 0–6 months and 6–12 months groups. Similarly, thoracotomy was associated with shorter operative times in groups with no conversion (Supplemental Table S3). In the subgroup analysis of LOS, shorter LOS was observed in PS group using VATS. In the subgroup analysis of complications, when studies were stratified by the types of CLM, fewer complications were observed in CPAM and mixed type groups using VATS. Fewer complications were also observed in the group

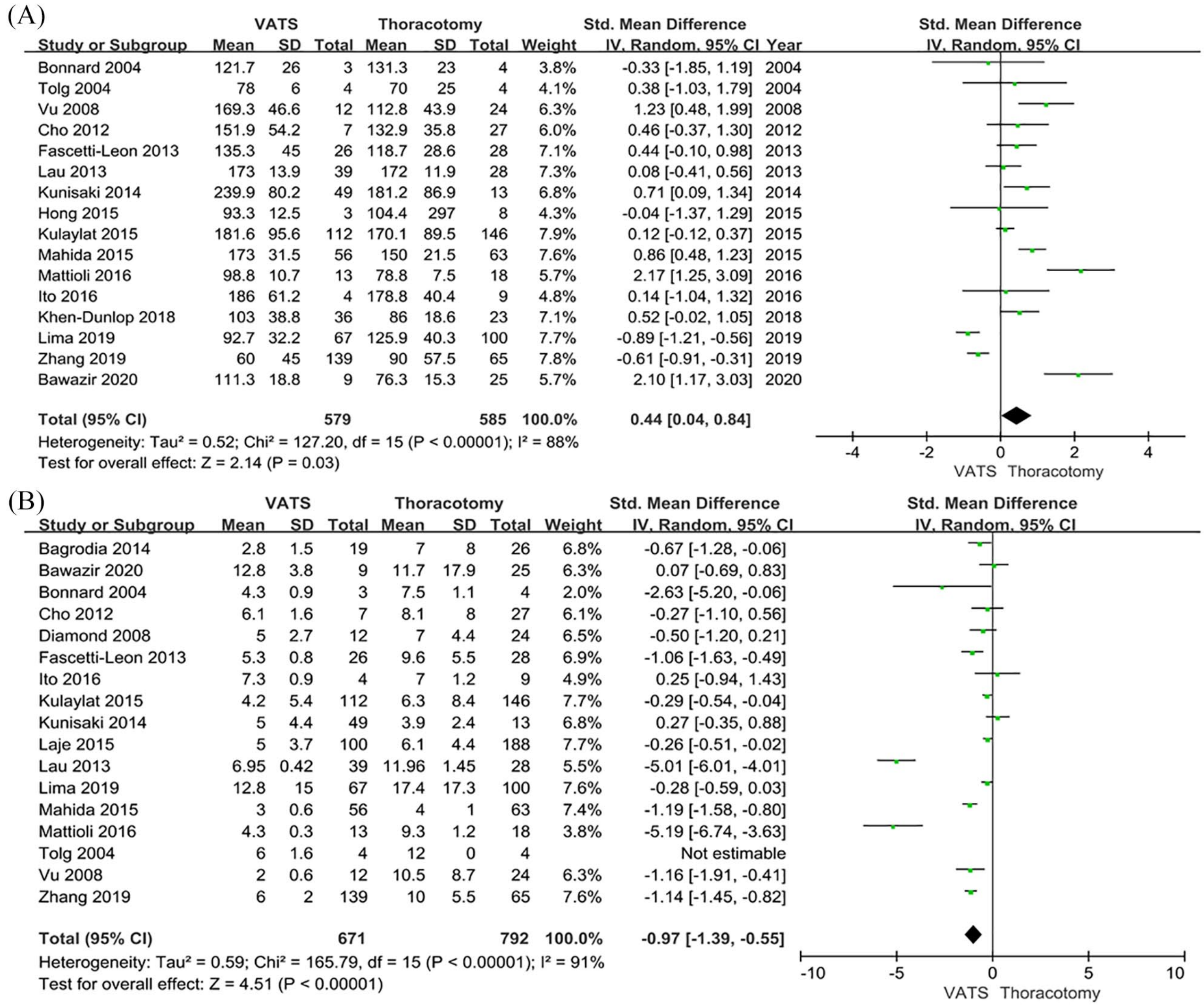

Figure 3. Forest plot of operative time (min) and LOS (days). (A) Forest plot of SMD of operative time; (B) forest plot of SMD of LOS.
CI, confidence interval; LOS, length of stay; OR, odds ratio; SD, standard deviation; SMD, standard mean difference; VATS, video-assisted thoracoscopic surgery.

where patients were over 1 year of age. Similar results were found in studies without conversion and with low percentage of symptomatic cases. In the subgroup analysis of length of chest drainage, VATS was superior in PS and mixed type groups. It also showed superiority in patients over 6 months of age. VATS entailed shorter length of chest drainage in studies without conversion and with low percentage of symptomatic cases.

Risk of bias

To evaluate the publication bias, we conducted the funnel plot of complications (Figure 4B); no significant publication bias was found (Begg's test $p=0.96$, Egger's test $p=0.17$). ROBINS-I toll was used for bias assessment of comparatives studies; 14 studies were found to be at moderate risk of bias (Supplemental Table S4), and 9 studies were deemed to be at serious risk of bias. MINORS scores of nine single-arm studies were higher than 10 points and with high qualities.[34–36,40,42,45,46,48,50]

Correlation between symptomatic percentage and conversion using VATS

A total of 11 studies were involved for Pearson analysis, which was used to evaluate the correlation between percentage of symptomatic cases and conversion in patients who underwent VATS.

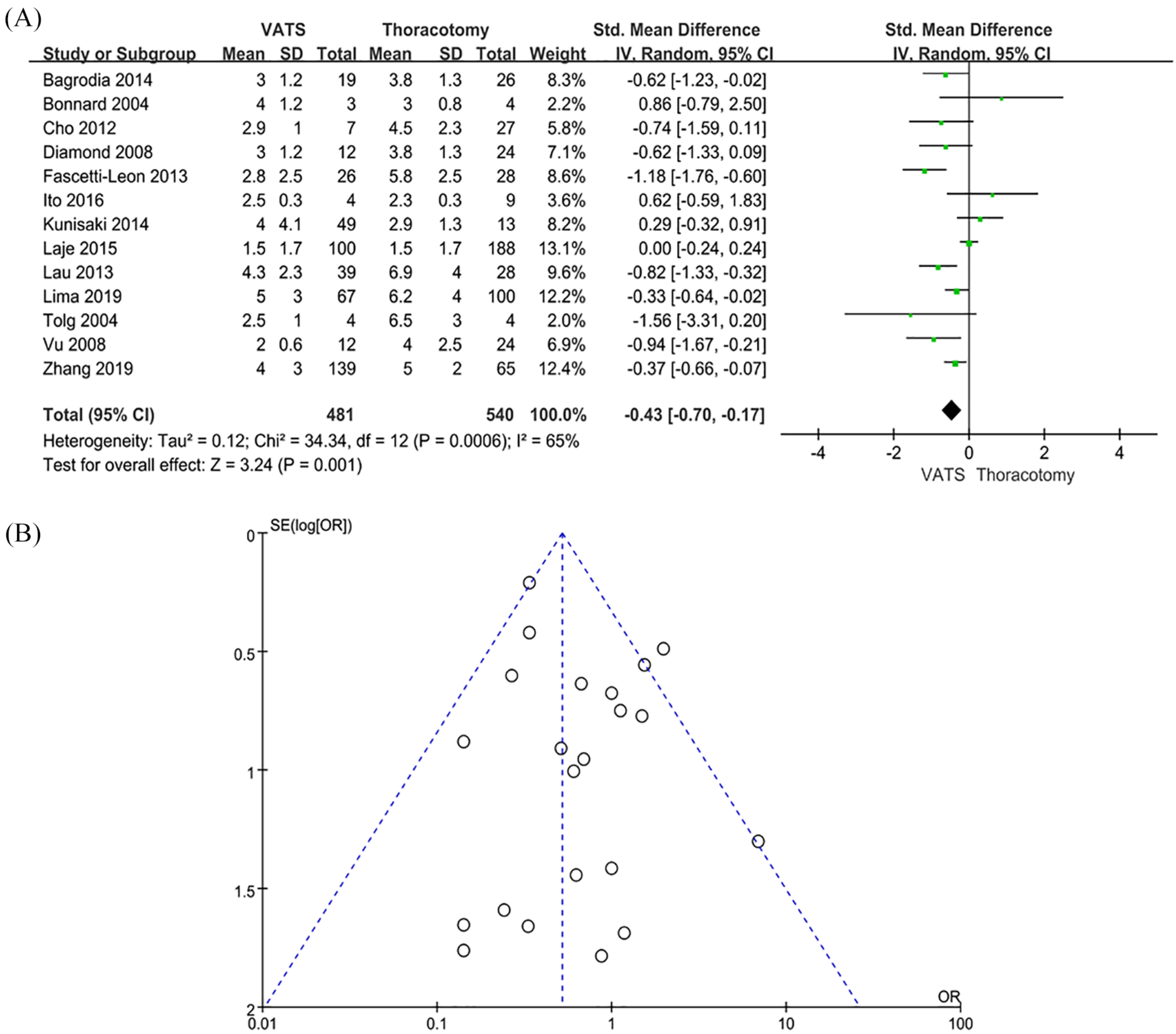

Figure 4. Forest plot of length of chest drainage (days) and publication bias analysis by funnel plot. (A) Forest plot of SMD of length of chest drainage; (B) publication bias analysis by funnel plot.
CI, confidence interval; OR, odds ratio; SD, standard deviation; SE, standard error; SMD, standard mean difference; VATS, video-assisted thoracoscopic surgery.

It turned out that the Pearson correlation coefficient was 0.92 (95% CI, 0.71–0.98, $P < 0.0001$) and R square was 0.84 (Figure 5A).

Correlation between percentage of symptomatic cases and lobectomy

A total of 15 studies were used to evaluate the correlation between percentage of symptomatic cases and lobectomy. Pearson correlation coefficient was 0.24 (95% CI, −0.32 to 0.67, $p = 0.39$) and R square was 0.24 (Figure 5B).

Discussion

VATS has emerged as the standard procedure for many conditions in pediatric patients.[51] So far, no definitive consensus that thoracoscopic resection yields better outcomes in the treatment of CLM has been established though two meta-analyses,[6,7] which compared VATS with thoracotomy for CLM. Nasr and Bass found no differences between thoracotomy *versus* VATS for CLM with respect to complications and operative time.[6] Adams *et al.* further confirmed the superiority of VATS when comparing for complications.[7] Since

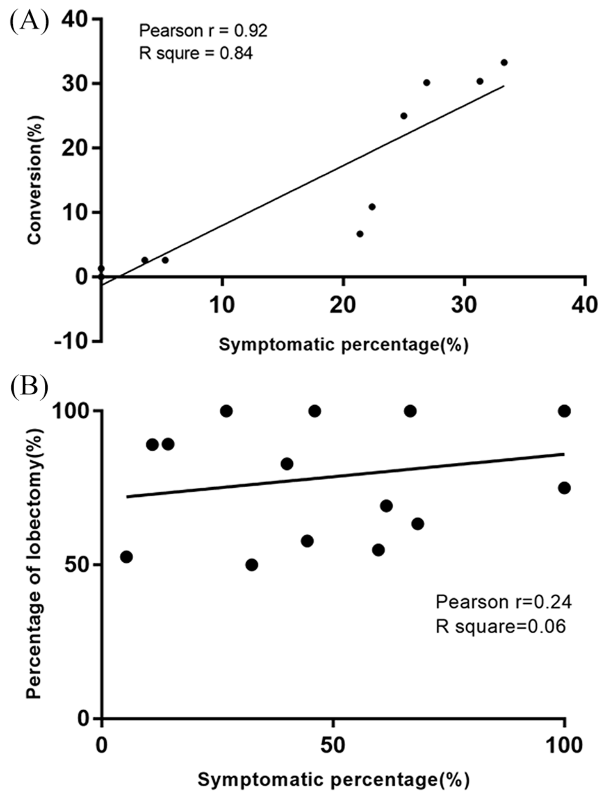

Figure 5. Pearson analysis and linear regression. (A) Correlation between percentage of symptomatic cases and conversion using the VATS; (B) correlation between percentage of symptomatic cases and lobectomy.
VATS, video-assisted thoracoscopic surgery.

these two reports, there have been a large number of high-volume case-controlled studies. Therefore, we updated this study to further explore the comparison between use of VATS and thoracotomy. Our meta-analyses indicated that VATS was associated with fewer complications, less use of epidural anesthesia, and shorter LOS and length of chest drainage when compared with thoracotomy. However, thoracotomy showed superiority in reduced operative time. Pearson analysis and linear regression confirmed a positive correlation between percentage of symptomatic cases and conversion in patients using VATS. However, the correlation between percentage of symptomatic cases and lobectomy was not significant ($p = 0.39$). Therefore, we concluded that VATS prompts a faster recovery with less pain and trauma in children with CLM. Use of VATS in symptomatic patients was more prone to be converted to thoracotomy. This was due to adhesion and difficulty in dissection in patients with previous chest infections.

According to the results of our study, we recommend the use of VATS in asymptomatic patients to reduce complications, LOS, use of epidural anesthesia, and length of chest drainage. The magnification provided by thoracoscopy improves discrimination between normal and diseased lung tissue and offers better visualization of fissures and vascular structures.[1] However, in symptomatic cases, surgeons should evaluate each individual cautiously to determine whether VATS is feasible, since it is more prone to conversion due to adhesion. In experienced centers, VATS is feasible in neonates or young infants, although thoracoscopic technique and single-lung ventilation can be challenging. Surgeons must be cautious regarding CO_2 insufflation on the operative side, and prolonged general anesthesia can lead to hypoxia, hypercapnia, and hemodynamic changes, especially in young infants, which potentially influences the selection of operative approach.

Sensitivity analyses were used to explore the sources of heterogeneity in our study. The sensitivity analysis of operative times suggested a significant reduction in heterogeneity when we removed the studies of Zhang *et al.* and Lima *et al.* in turn,[31,32] and the pooled estimate remained statistically significant, which indicated a confirmed and robust result. In these two studies, the operative time for VATS was significantly shorter than that of thoracotomy. Their low rate of conversion and advanced thoracoscopic technique may have contributed to these differences. In the sensitivity analysis of LOS, heterogeneity was significantly reduced when we removed the studies of Mahida *et al.*, Lau *et al.* and Mattioli *et al.*[20,26,27] In their studies,[20,26,27] higher symptomatic percentages and more severe complications (i.e., re-intubation and hemorrhage) in patients who underwent thoracotomy yielded much slower recovery. However, the heterogeneity was still significant ($I^2 = 72\%$) when we performed leave-one-out sensitivity analyses; therefore, the results with regard to operative times and LOS should be interpreted cautiously. In the sensitivity analysis of length of chest drainage, heterogeneity was also reduced when we removed the studies of Laje *et al.* and Kunisaki *et al.*[22,24] Heterogeneity was attributed to prolonged air leaks and hemorrhage in these two studies, which contributed to much longer length of chest drainage in the thoracotomy group.

Subgroup analysis was also performed in our current study. In the subgroup analysis of operative times, we observed that, compared with VATS, thoracotomy was associated with shorter operative times in patients younger than 1 year of age. Therefore, to reduce anesthetic and surgical times, thoracotomy might be considered in patients with very young age and critical illness. Besides, in patients with pulmonary sequestration, VATS was found to reduce the LOS in the subgroup analysis. Furthermore, in cohorts with low percentage of symptomatic cases, shorter LOS was also observed using VATS. In patients with CPAM, in patients over 1 year of age, in patients who underwent VATS without conversion, and in patients with low percentage of symptomatic cases, VATS was associated with fewer complications after surgery.

Limitations

Some limitations of our study are acknowledged here. First, all included studies were retrospective and observational; hence our meta-analysis is of low quality. Second, only nine studies had follow-up data in excess of 1 year, so long-term complications remain unknown. Last, since most of our included studies reported different types of CLM and lung resection, heterogeneity across all 23 comparative studies was significant. Therefore, conclusions from this study may not be appropriate to apply to all CLM conditions.

Conclusion

In conclusion, as compared with thoracotomy, VATS is associated with fewer complications, less use of epidural anesthesia, shorter LOS and length of chest drainage, but longer operative times. Symptomatic patients with CLM using VATS may be more prone to conversion to open surgery. However, our study is based on retrospective studies, and our results may not be applied conclusively to all CLM conditions. Larger sample size RCTs should be designed to explore the differences in clinical outcomes between VATS and thoracotomy.

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Author contributions

The literature search was conducted by authors X.J.H. and W.Y.H.; variable selection was performed by X.J.H. and W.Y.H.; data extraction was conducted by X.J.H. and W.Y.H.; various phases of study conceptualization, data analysis, and results interpretation were led by X.J.H., W.Y.H., and W.C. All authors contributed to the preparation, review, and final approval of the manuscript for publication.

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Research involving human participants and/or animals

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ORCID iD

Chun Wu https://orcid.org/0000-0001-9263-7938

Supplemental material

The reviews of this paper are available via the supplemental material section.

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