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REVIEW ARTICLE

Thoracoscopy vs. thoracotomy for the repair of esophageal atresia and tracheoesophageal fistula: a systematic review and meta-analysis

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Abstract

Esophageal atresia (EA) and tracheoesophageal fistula (TEF) require emergency surgery in the neonatal period to prevent aspiration and respiratory compromise. Surgery was once exclusively performed via thoracotomy; however, there has been a push to correct this anomaly thoracoscopically. In this study, we compare intra- and post-operative outcomes of both techniques. A systematic review and meta-analyses was performed. A search strategy was developed in consultation with a librarian which was executed in CENTRAL, MEDLINE, and EMBASE from inception until January 2017. Two independent researchers screened eligible articles at title and abstract level. Full texts of potentially relevant articles were then screened again. Relevant data were extracted and analyzed. 48 articles were included. A meta-analysis found no statistically significant difference between thoracoscopy and thoracotomy in our primary outcome of total complication rate (OR 0.98, [0.29, 3.24], $p=0.97$). Likewise, there were no statistically significant differences in anastomotic leak rates (OR 1.55, [0.72, 3.34], $p=0.26$), formation of esophageal strictures following anastomoses that required one or more dilations (OR 1.92, [0.93, 3.98], $p=0.08$), need for fundoplication following EA repair (OR 1.22, [0.39, 3.75], $p=0.73$)—with the exception of operative time (MD 30.68, [4.35, 57.01], $p=0.02$). Considering results from thoracoscopy alone, overall mortality in patients was low at 3.2% and in most cases was due to an associated anomaly rather than EA repair. Repair of EA/TEF is safe, with no statistically significant differences in morbidity when compared with an open approach.

Level of evidence 3a systematic review of case–control studies.

Keywords Thoracoscopy · Esophageal atresia · Tracheoesophageal fistula · Minimally invasive surgery · Systematic review · Meta-analyses

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Abbreviations

EA	Esophageal atresia
TEF	Tracheoesophageal fistula
MA	Meta-analyses
RCTs	Randomized controlled trials
MD	Mean differences
OR	Odds ratios
CI	Confidence intervals
SRs	Systematic reviews

Introduction

Esophageal atresia (EA) and tracheoesophageal fistula (TEF) are relatively common congenital anatomical anomalies, occurring in 1 in 3000–4500 live births [1]. Of neonates who present with signs of esophageal compromise, 80–85% have EA with a distal esophageal pouch and a proximal TEF, while the other 15–20% have various other esophageal malformations [1]. Surgery is considered urgent to prevent aspiration and respiratory compromise and is generally performed on day 1 or 2 of life.

Surgery for congenital EA with or without TEF is debatably one of the most difficult operations to perform [2]. The two main techniques utilized are the classic thoracotomy and the modern minimally invasive technique of thoracoscopy. Currently, the international "gold standard" is thoracotomy, however, many tertiary centers are moving towards the minimally invasive approach.

Thoracoscopic technique carries theoretical advantages over open surgery due to its minimally invasive nature, including superior cosmetic result; minimization of growth deformities of the thorax, shoulder and spine that have been observed after thoracotomy [2–5]; and shorter hospital stay and faster recovery [6, 7]. Still, thoracoscopy has a steep learning curve [8–10], as neonatal anatomy presents limitations with regard to port placement and instrument mobility. It is, therefore, unclear whether thoracoscopy can be performed with comparably low post-operative complication rates to that of the well-established thoracotomy technique while offering all the aforementioned benefits of a minimally invasive approach. As such, we conducted a systematic review (SR) and meta-analysis (MA) to compare these two techniques by synthesizing and summarizing the existing literature.

Methods

Selection of study topic

We used a Delphi-like method [11] to identify issues of greatest concern to pediatric surgeons regarding the surgical management of EA and TEF.

First round

We distributed an online survey to experts in this area, identified primarily via a literature search. This survey was conducted using a REDCap online data capture form [12] and consisted of the open-ended question: "In your practice with the surgical management of congenital anomalies of the esophagus, what issues do you find to be controversial and in need of further research and/or consensus?".

Second round

We developed a questionnaire listing the expert responses from the first round. We sent this questionnaire to the respondents of the first round, asking them to vote on topics based on their importance. The issue that received the highest number of votes has been addressed in a previous SR [13]. The second most controversial issue is the focus of this SR.

Literature search

We conducted electronic searches of the Cochrane Central Register of Controlled Trials (CENTRAL), MEDLINE and EMBASE from inception to January 2017. We used the following search terms: "esophageal atresia" OR "tracheoesophageal fistula" AND "thoracoscopy/VATS". We limited our search to studies in English, Spanish and French and excluded editorials and case studies. We also hand-searched the reference sections of included articles for additional relevant studies.

Study selection

We included all studies that either compared thoracoscopic (minimally invasive) repair to open repair, or discussed the safety or efficacy of thoracoscopic repair alone, for the surgical correction of EA with or without TEF, even if this was not the primary focus of the study. Our primary outcome of interest was total complications composed of pooled indices with countable events, which included rates of anastomotic leak, recurrent fistula, esophageal stricture, need for future antireflux surgery (fundoplication), peri-operative injury, wound infection, post-operative cosmesis/musculo-skeletal deformity, phrenic nerve paralysis, vocal cord paralysis, pulmonary complications (i.e., pneumothorax, pleural effusion, etc.) and mortality. Our secondary outcomes of interest comprised all the individual outcomes as noted for the primary outcome above with the addition of days to extubation, length of surgery, length of hospital stay, time to full oral feeds, length of narcotic use, blood loss and the rate of conversion from thoracoscopy to open procedure. Two reviewers screened articles in two stages—title and abstract and full-text—independently, followed by a consensus process. If they could not reach consensus at either stage of screening, they consulted a third reviewer.

Quality assessment

Systematic reviews

We used AMSTAR to assess the quality of SRs. AMSTAR contains 11 items, where a review scores one point for each 'yes' and zero points for each 'no' or 'can't answer', for a maximum score of 11. The version of AMSTAR that we used has additional notes to help clarify the items; these were established through discussions between the tool's creator and the Cochrane Effective Practice and Organisation of Care review group.

Randomized controlled trials

We used the Cochrane 'Risk of bias' tool to assess randomized controlled trials (RCTs) [14]. This tool assesses the risk of six types of bias that may be present in RCTs; it does not give an overall quality score, but the risk of each type of bias is judged as being high, low or unclear.

Non-randomized studies

We used MINORS to assess the quality of all relevant non-randomized studies (comparative or non-comparative; [15]. MINORS contains 8 items for non-comparative and 12 items for comparative studies, whereby a study scores zero points if the information is not reported, one point if the information is reported but inadequate, or two points if the information is reported and adequate, for a maximum possible score of either 16 or 24, respectively.

Two reviewers independently assessed each included study and compared the scores for each item on the applicable quality assessment tool to reach a consensus. If they could not reach a consensus, they consulted a third reviewer.

Data extraction, analysis and summarization

One reviewer extracted data from each of the included studies and a second reviewer checked the data for accuracy and completeness. We synthesized and summarized the results, with an emphasis on higher quality evidence; we considered SRs to be the highest quality evidence, followed by RCTs and non-randomized studies [16], taking the results of our quality assessment into consideration. We conducted MAs of comparative data in Review Manager 5.3 [17], using either the random-effects or fixed-effect model depending on the degree of heterogeneity in the data assessed using I^2 values (more than or less than 20%, respectively), to produce mean differences (MD) for categorical variables and odds ratios (OR) for continuous variables, along with 95% confidence intervals (CI). Only outcomes reported as counts (i.e., number of anastomotic leaks) or means with standard deviations (i.e., length of operation) could be used. We attempted to reach the authors to obtain useable data for outcomes where this was not the case but either did not receive a response or the data were not available. Had we included a sufficient number of studies, we would have created funnel plots to help assess the risk of reporting bias and other biases [18]. For outcomes with insufficient data to be pooled and analyzed, we describe it narratively.

Results

Literature search and screening

Our initial search strategy yielded 438 articles, with 3 additional articles found from hand-searching; de-duplication reduced this number to 275. Following title–abstract screening, 113 studies remained. We performed full-text screening on these articles and excluded 55 that did not meet our criteria [1, 2, 10, 19–70]. We considered an additional 10 articles to be companion pieces to included studies [71–80]. A total of 48 studies were eligible. The studies comprised 6 SRs, 1 RCT, 14 non-randomized comparative studies and 27 non-randomized non-comparative studies; we quality assessed and summarized these (Table 1). Two of the SRs received high scores of 6 [81] and 7 [82], and the remaining received low scores of 1 [83, 84] and 0 [85, 86] out of a possible 11. Two SRs [81, 82] included an RCT [87] as well as meta-analyses of surgical outcomes. Three SRs included several comparative studies [81–83], all of which were included in this present SR unless ineligible as per our inclusion criteria. The RCT [87] had a fairly low overall risk of bias with four items ranked as low, two as high and one as unclear. The quality scores for the non-randomized comparative studies ranged from 12 to 18 out of 24. We conducted an MA on several outcomes, pooling data from the comparative studies. The quality scores from the non-comparative studies ranged from 5 to 12 out of 16. The breakdown of our search and screening process can be seen in Fig. 1.

Treatment of type C EA with TEF: thoracoscopy vs. open approach

We pooled the data from 1 RCT [87] and 13 comparative studies to run meta-analyses [6, 7, 26, 87–97]. MAs were possible for our primary outcome and four secondary outcomes. In studies that reported timing of surgery, the majority of procedures were conducted within the first few days of life on neonates born between 37 and 40 weeks [7, 87, 89–91]. Eight studies included complications that could be counted toward the total complication rate [6, 7, 87–90, 93, 94]. There was no statistically significant difference between thoracoscopy and thoracotomy regarding total complications (OR 0.98, [0.29, 3.24], $p=0.97$; Fig. 2). Almost all of the comparative studies reported on anastomotic leak rates as a short-term post-operative complication [6, 7, 87–90, 92–95]. Anastomotic leaks were generally handled conservatively and there was no difference in leak rates between approaches (OR 1.55, [0.72, 3.34], $p=0.26$; Fig. 3). The other complication that

Table 1 Summary of study design, EA type, number of participants, pertinent findings, and quality rating for each included study

References	Study design	EA type	*N*	Associated anomalies	Findings	Quality
Systematic reviews						*AMSTAR*
Dingemann et al. [83]	SR	Type C	4 studies	NS	2 of the studies found no differences between outcomes of TR and OR, 1 study found longer OT with TR, and 1 study found TR to have lower stricture and leakage, while having a longer OT	1
Oomen [85]	SR	11 Type A, 332 Type C, 1 Type D	22 studies	38–65% (only 6 studies specified % of patients with anomalies)	No differences between OR and TR for mortality, anastomotic leakage, or stricture occurrence	0
Parolini (2014) [86]	SR	96 Type E	22 studies (81 CR, 6 TR, 9 OR)	NS	No significant differences between OR and TR for complications or mortality	0
Parolini et al. [84]	SR	NS	8 Studies	Cardiac anomalies specified: 2 TR, 23 OR	2 studies reported TR, with no differences observed in leaks, strictures, or mortality between left or right approaches	1
Wu et al. [82]	SR	Type C	10 studies	NS	OR had shorter OT, no significant differences in rate of leaks, strictures, or fundoplication between TR and OR	7
Yang et al. [81]	SR	Type C	9 studies	NS	OR had shorter OT, no significant differences in rate of leaks or strictures between TR and OR	6
Randomized control trials						*Risk of bias*
Bishay et al. [87]	RCT	NS	5 TRs, 5 ORs	Patients excluded if < 1.6 kg, > 40% O_2, major congenital heart defects, pulmonary HTN, or bilateral grade 4 intra-ventricular hemorrhage	1 TR was converted to OR for technical reasons. There were no significant differences in outcomes or mortality between TR and OR	4 low 2 high 1 unclear

Table 1 (continued)

References	Study design	EA type	*N*	Associated anomalies	Findings	Quality
Non-randomized studies—comparative						*MINORS*
Allal et al. [88]	Retrospective	Type C	14 TRs, 14 ORs	NS	The TR group had a longer OT. There were no significant differences short-term post-op complications such as leak, stricture, or need for antireflux surgery between OR and TR	15
Ceelie et al. [26]	Retrospective	NS	14 TRs, 28 ORs	NS	The TR group had a longer duration of surgery	18
Fonte et al. [122]	Retrospective	Type C	11 TRs, 7 treated with ATREA; 4 treated with classic approach	3 patients with VACTERL association	OT was shorter for anatomic thoracoscopic repair of esophageal atresia (Group A) compared to the classic thoracoscopic approach (Group B). There were no surgical complications in either group. Group B had 1 case of anastomotic leak	10
Kawahara et al. [89]	Retrospective	Type C	7 TRs, 10 ORs	5 TR, 7 OR	Anastomotic leakage and esophageal stricture rates were similar between TR and OR, and no significant difference in esophageal acid exposure or mean reflux time. 2 patients from each group required fundoplication post-op	18
Koga et al. [90]	Retrospective	Type C	25 TRs, 40 ORs	48 patients with associated anomalies	There were 3 anastomotic leaks in TR vs. 1 in OR, and OT was longer in TR	12
Lugo et al. [6]	Retrospective	Type C	8 TRs, 25 ORs	7 TR, 18 OR	There was a shorter OT in the OR group. The TR group had lower leak and stricture rates. There was no mortality related to the surgery in either group	14
Ma et al. [91]	Prospective	Type C	20 TRs, 13 ORs *18 TRs because 2 were converted and neglected from study	11 TR, 9 OR	The OR had a shorter OT and there was no mortality related to the surgery in either group	16

Table 1 (continued)

References	Study design	EA type	*N*	Associated anomalies	Findings	Quality
Miyano et al. [92]	Retrospective	Type C	13 TRs, 24 ORs	7 patients with associated anomalies Patients excluded if < 2 kg or had cardiac or chromosomal anomalies	There were no intra-operative complications or mortality in either approach. There were 2 cases of anastomotic leaks in TR and fundoplication was required in 1 OR and 3 TRs	
Nice et al. [96]	Retrospective	Type A: 7 Type B: 2 Type C: 102 Type D: 3 Type E: 7	23 TRs, 98 ORs	No differences between associated anomalies between approaches. Patients who died prior to discharge were excluded	Both thoracoscopic and staged open repair were associated with an increased risk of stricture formation. 3 cases required conversion to OR	
Szavay et al. [93]	Retrospective	Type C	25 TRs, 32 ORs	10 TR, 10 OR	The TR group had a significantly longer OT	15
Al Tokhais et al. [94]	Retrospective case-matched	Type C	23 TRs, 22 ORs	Only cardiac anomalies specified: 9 TR, 13 OR	The OT was slightly shorter in the TR group, and the anastomotic leak, stricture and mortality rates were similar between the groups. There were fewer early complications in the TR group	16
Woo et al. [95]	Retrospective	Type A: 5 Type C: 26	17 TRs, 14 ORs	No differences between associated anomalies between approaches	There were no differences in rates of anastomotic stricture or leak between approaches and 5 cases were converted to OR	
Yamoto (2014) [7]	Retrospective	NS	11 TRs, 15 ORs	6 TR, 7 OR	All outcomes, such as leakage, stricture, and fundoplication rates were statistically similar	18
Zani et al. [97]	Retrospective	Type C	25 TRs, 180 ORs	NS	Operative time was shorter in OR and 5 TRs required conversion to OR	18
Non-randomized studies—non-comparative						*MINORS*
Acher et al. [123]	Retrospective	NS	53 TRs	NS	17 cases of leaks	9
Al-Qahtani and Almaramhi [99]	Retrospective	NS	8 TRs	NS	The average OT was 132 m, and 2 procedures were converted to OR. Intra/post-op complications included 1 case of anastomotic leak	10

Table 1 (continued)

References	Study design	EA type	*N*	Associated anomalies	Findings	Quality
Allal et al. [100]	Retrospective	2 Type C, 1 Type D	3 TRs	NS	The mean operating time was 100 m and 1 child required fundoplication	10
Dingemann et al. [101]	Retrospective	1 Type A, 1 Type B, 19 Type C, 1 Type D,	22 TRs	15 anomalies in 9 patients	The mean OT was 142 m (75–220 m), and 8 were converted to OR for various reasons (exposure, ventilation, tension, bleeding). There were 2 leaks, 7 strictures requiring dilatation and no associated mortality	12
García et al. [102]	Retrospective	Type C	13 TRs	NS	1 patient had an anastomotic leak and 4 had esophageal stricture and secondary reflux leading to fundoplication	10
Hiradfar et al. [33]	Retrospective	Type C	24 TRs	NS	Rate of conversion to OR reduced following learning curve; 2 cases of anastomotic leaks; 1 mortality	9
Holcomb et al. [103]	Retrospective	Type C	104 TRs	83 anomalies (# of patients in which they were present not specified)	The average OT was 129.9 m, and there were 8 anastomotic leaks, 33 patients requiring at least one dilatation and 2 recurrent fistulas. 5 procedures were converted to OR and 25 patients required fundoplication; there was 1 death related to the procedure	10
Huang et al. [104]	Retrospective	Type C	33 TRs	10 with VACTERL type	The average OT was 146 m and 2 cases were converted to an open procedure. There were 3 minor leaks, 7 strictures, 1 recurrent fistula, 1 patient requiring fundoplication and 2 post-op deaths	10
Kanojia et al. [117]	Retrospective	NS	29 TRs	NS	There were 4 cases of leaks, 4 conversions to OR, and 6 mortalities	5

Table 1 (continued)

References	Study design	EA type	*N*	Associated anomalies	Findings	Quality
Krosnar and Baxter [105]	Retrospective	NS	8 TRs	7	The mean OT was 164.4 m and late complications included 2 leaks, 2 strictures, 1 patient with reflux symptoms and 1 procedure-associated mortality	10
Lee et al. [8]	Retrospective	Type C	22 TRs	16	The average OT was 179 m and there was one conversion to OR. Post-op complications included 2 leaks, 10 strictures requiring dilatations and 8 cases of chronic reflux requiring 5 fundoplication procedures	10
MacKinlay [106]	Retrospective	6 Type A, 20 Type C	26 TRs	13	There were 7 cases of anastomotic leaks, 1 recurrent fistula and 9 esophageal strictures. There were 3 mortalities all due to comorbidities independent of the EA	10
Martinez-Ferro et al. [107]	Retrospective	Type C	9 TRs	3	The mean OT was 105 m; there were no conversions to OR. Post-op complications included 2 leaks and 3 strictures	10
Miyano et al. [108]	Retrospective	Type A	4 TRs	No major anomalies	The mean OT was 9.6 h; 3 sequential elongation procedures on average were needed to obtain a close enough gap. Post-op complications included 2 leaks, 4 strictures and 4 fundoplications	10
Mortellaro et al. [109]	Retrospective	NS	12 TRs	NS	The mean OT was 216 m	12
Nachulewicz et al. [110]	Retrospective	Type C	10 TRs	4	The mean OT was 140 m. There were two conversions to OR. Post-op complications included 1 leak and 1 stricture	10

Table 1 (continued)

References	Study design	EA type	*N*	Associated anomalies	Findings	Quality
Nguyen et al. [111]	Retrospective	Type C	6 TRs	3	The mean OT was 143.3 m; there was one conversion to OR. Post-op complications included 1 stricture and 1 death due to respiratory failure	10
Okuyama et al. [112]	Retrospective	NS	58 TRs	NS	The OT ranged from 115 to 428 m; 6 of the procedures were converted to OR. Post-op complications included 11 leaks, 28 strictures requiring dilatation, 3 recurrent fistulas and 13 patients requiring fundoplication. There was 1 mortality not associated with the EA	10
Patkowski et al. [113]	Retrospective	NS	23 TRs	9	The OT declined with experience, with a mean of 131 m. There were 2 accidental injuries to the trachea during the procedure and no conversions to OR. Post-op complications included 3 leaks, 4 strictures requiring dilatation and 3 patients managed conservatively for reflux. There were 3 deaths not associated with the surgery	10
Robie [114]	Retrospective	7 Type C, 1 Type D	8 TRs	NS	The mean length of operation was 207 m; there was one conversion to OR. Post-op complications included 1 stricture requiring dilatation	10
Rothenberg [115]	Retrospective	9 Type A, 52 Type C	61 TRs	22 cardiac, 3 imperforate anus, 1 cloaca	The mean OT was 85 m; there was one conversion to OR. Post-op complications included 3 leaks, 12 strictures requiring dilatation and 18 patients requiring subsequent fundoplication	10

Table 1 (continued)

References	Study design	EA type	*N*	Associated anomalies	Findings	Quality
Rothenberg and Flake [49]	Retrospective	Type A	15 TRs	6 patients with anomalies	Operative times: 60–135 m. There were two anastomotic leaks, 8 required fundoplication	7
Tainaka et al. [98]	Retrospective	Type A:3 Type C: 1 Type D: 1	5 TRs	3 patients with associated anomalies	There were 2 cases of anastomotic leakage. No conversions to OR, and no mortalities	9
Tytgat et al. [124]	Retrospective	Type C	15 TRs	8 patients with associated anomalies	OT ranged from 126 to 387 m	
van der Zee et al. [116]	Retrospective	Type A	10 TRs	3	There were 2 leaks and 9 patients with strictures that required dilation and subsequent fundoplication procedures	12
van der Zee et al. [9]	Retrospective	Type C	72 TRs	44	There were 4 conversions to OR. Post-op complications included 11 leaks, 22 strictures and 2 recurrent fistulas. There were 2 deaths with 1 occurring during the operation	10

CR cervicotomy, *d* days, *EA* esophageal atresia, *h* hours, *HTN* hypertension, *intra-op* intra-operative, *m* minutes, *NS* not specified, *OR* open approach, *OT* operative time, *post-op* post-operative, *pre-op* pre-operative, *RCT* randomized control trial, *SR* systematic review, *TR* thoracoscopy approach, *VACTERL* vertebral, anal, cardiac, renal limb anomalies

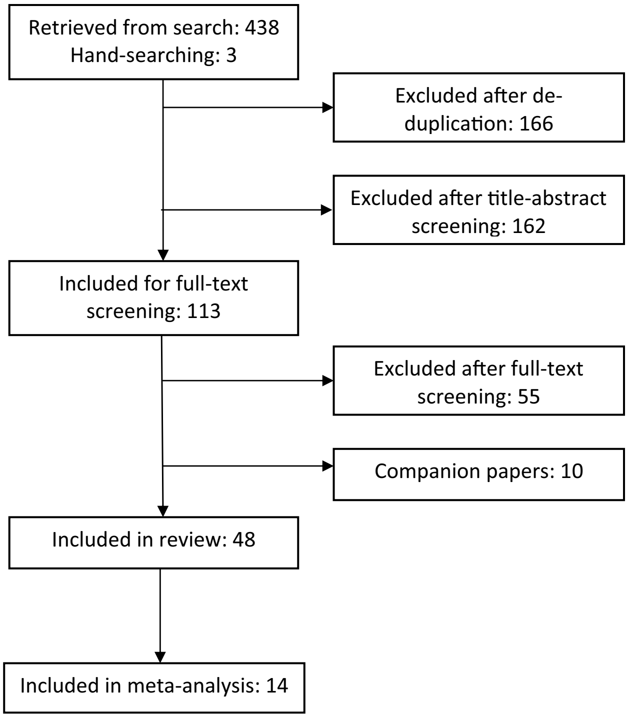

Fig. 1 PRISMA flow chart

was commonly reported was the formation of esophageal stricture following anastomoses that required at least one dilation [6, 7, 87–90, 94–97]; MA revealed no significant difference between thoracoscopic and open approach dilations (OR 1.92, [0.93, 3.98], $p=0.08$; Fig. 4). Six studies reported useable data on mean operative time [26, 88, 90, 91, 94, 97], which was significantly longer in the thoracoscopy group (MD 30.68, [4.35, 57.01], $p=0.02$; Fig. 5). Four of the studies also followed patients long enough to report on the need for fundoplication following EA repair [7, 88, 89, 92]; there was no significant difference between the two surgical approaches (OR 1.22, [0.39, 3.75], $p=0.73$; Fig. 6).

Outcomes that either were not reported by enough studies or lacked the proper data to perform MA included days to extubation, length of hospital stay, time to full oral feeds, length of narcotic use, volume of blood loss, peri-operative injury, wound infection, post-operative cosmesis/musculo-skeletal deformity, and fistula recurrence. Three studies found significantly fewer days to extubation when a thoracoscopic approach was taken [7, 90, 91]. The difference in length of hospital stay was variable among studies. One study found an apparently large reduction in hospital stay with the thoracoscopy group, however, no *p* value was calculated [6]. Another study found a 10-day shorter duration of hospital stay with the thoracoscopic group, however, this was not quite statistically significant [7]. A third study reported significantly shorter hospitalization for thoracoscopy ($p<0.01$) when the authors excluded patients with associated anomalies [90]. Two other studies showed no real difference in length of hospital stay [88, 91]. The length of narcotic use was shorter with thoracoscopy in four studies [6, 87, 88, 90], one of which found a statistically significant difference between the two groups ($p<0.001$ [90]; length of narcotic use ranged from a difference of 1.3 days [88] to 17 days [6]. Similarly, four studies reported shorter times to full oral feeds associated with thoracoscopy; however, no statistical inference could be drawn [6, 7, 88, 90]. Six studies reported on blood loss during surgery [6, 7, 90, 91, 95, 98], four of which reported less blood loss with thoracoscopy [7, 90, 95, 98]. Three studies reported on fistula reoccurrence following surgery, of which there were 0/50 in the thoracoscopy group and 3/61 in the open group [7, 88, 93].

A few of the comparative studies also reported on intra-operative tolerance to the selected procedure, assessed through arterial blood gas (ABG) measurements of maximum pCO_2 and pH levels. We could not conduct a meta-analysis on the data; however, some trends were observed. Three studies found higher intra-operative pCO_2 levels and more acidic pH levels in patients undergoing a thoracoscopic approach, although the differences were small and

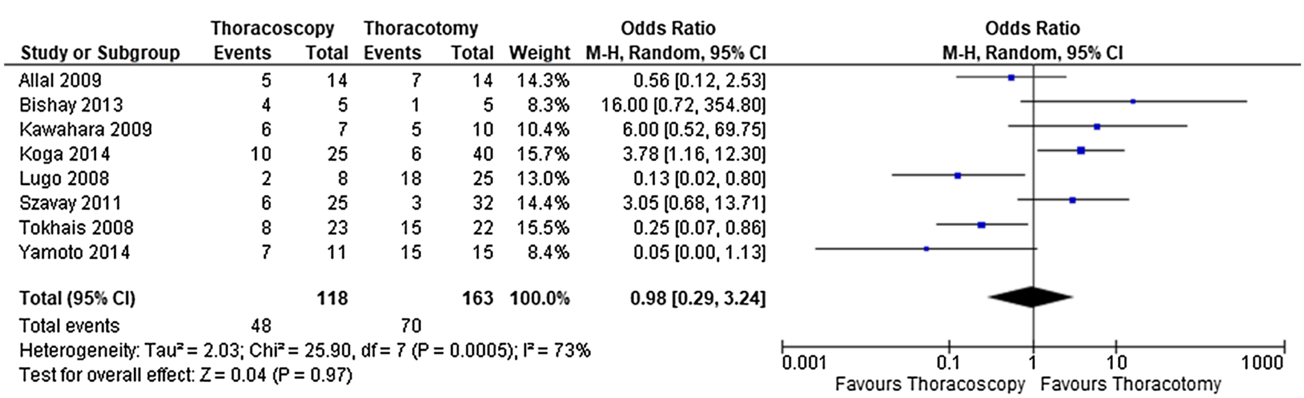

Fig. 2 Meta-analysis of total complications associated with thoracoscopy versus thoracotomy

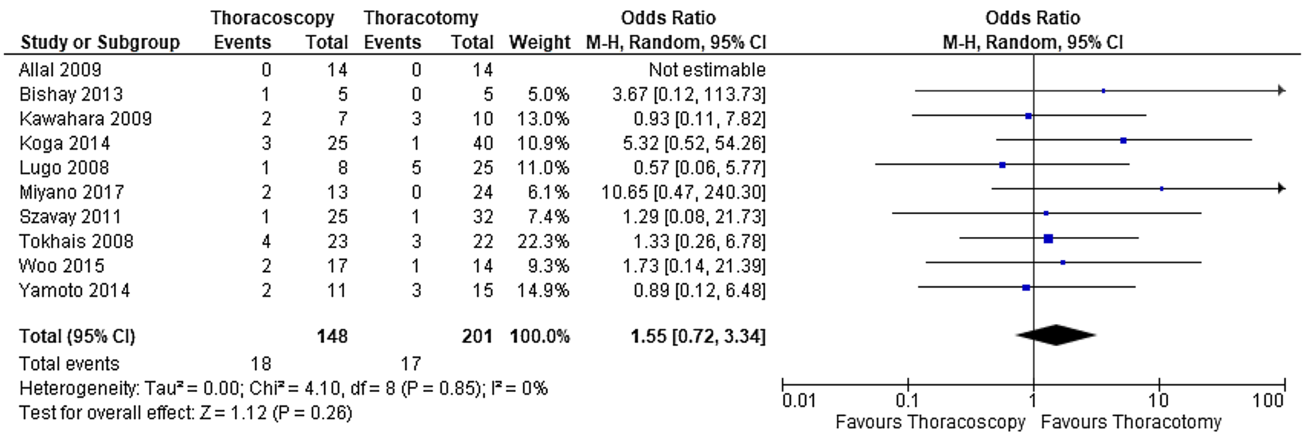

Fig. 3 Meta-analysis of anastomotic leak associated with thoracoscopy versus thoracotomy

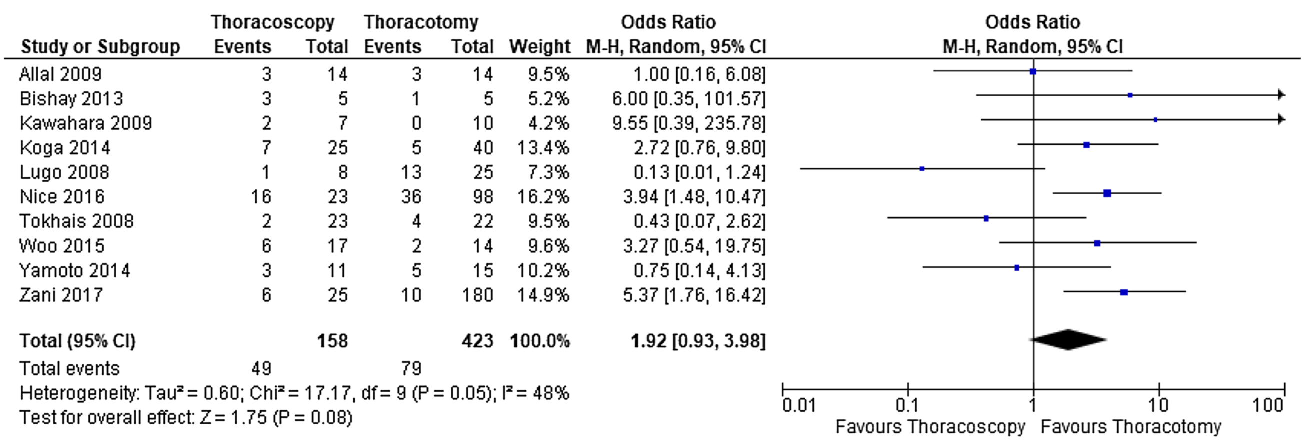

Fig. 4 Meta-analysis of esophageal stricture associated with thoracoscopy versus thoracotomy

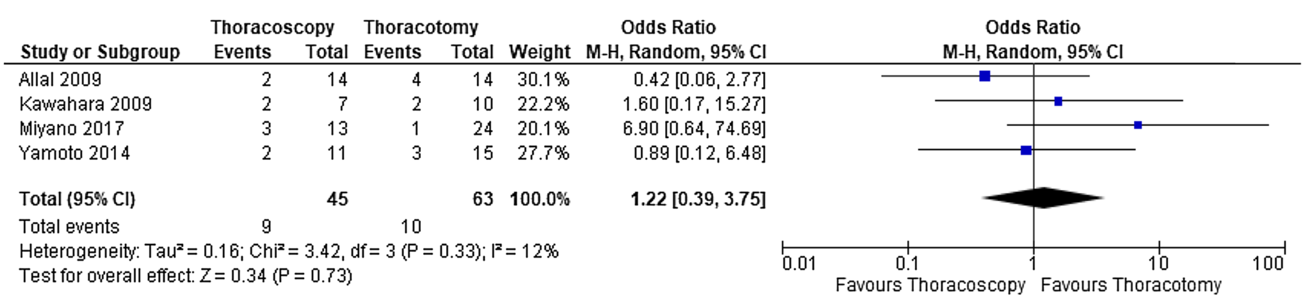

Fig. 5 Meta-analysis of need for fundoplication associated with thoracoscopy versus thoracotomy

not statistically significant [7, 87, 91]; two studies found a significantly higher intra-operative pCO_2 level in patients who underwent thoracoscopy [90, 93]. It is noteworthy, however, that no intra-operative mortalities were reported in these studies, and when measured post-operatively, the pCO_2 and pH levels were equivalent between the approaches [90, 91, 93].

Safety and efficacy of thoracoscopy

Additionally, our literature search identified 20 non-comparative studies that solely looked at the surgical outcomes of patients who underwent thoracoscopic repair of EA [8, 9, 99–116]. To assess the overall efficacy and safety of thoracoscopy for the repair of EA, we combined data

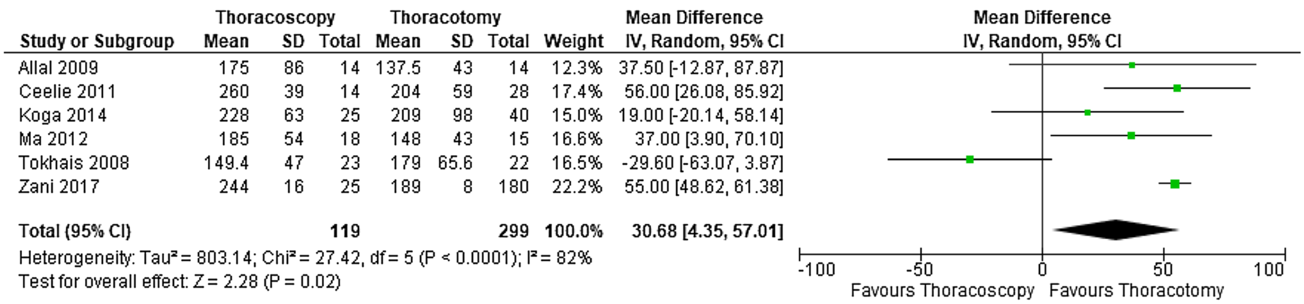

Fig. 6 Meta-analysis of operative time associated with thoracoscopy versus thoracotomy

on thoracoscopy patients from the comparative and non-comparative articles (Table 2). Most of the studies in the table include only type C EA cases (659 patients); however, a handful of studies included data on a limited number of other types (64 patients) [49, 95, 98, 100–102, 106, 108, 114–116] or did not specify the type (175 patients) [92, 96, 99, 102, 105, 109, 112, 113, 117]. We have presented the length of hospital stay and surgery as ranges due to variability in the expression of data among articles. The length of surgery ranged from 54 to 428 min when all articles were included, however, this wide range was primarily due to the results of one study [112]; when excluded, the range was 55–268 min.

The number of patients converted to an open procedure was reported in all comparative and non-comparative articles, and for our purposes was considered a surgical complication. Interestingly, the incidence of intra-operative complications was found to be rare (1.2%); however, this is likely an underestimation as we would consider many of the reasons for conversion to an open procedure to be an intra-operative complication, which was obviously not reported as such. Overall mortality in patients related to the procedure was low at 3.2%. Most patient deaths were attributable to complication of an associated anomaly (i.e., VACTERL) and not the EA repair itself. The incidence of esophageal stricture requiring at least one endoscopic dilation was 30.6%, while subsequent fundoplication was required in 23.1% of patients. The next most common complication was a leak at the anastomosis in 12.5%, which was managed conservatively in almost all cases and did not require further surgery. There were very few cases of recurrent fistula (2.7%).

Other types of EA

By far the most common pathology of EA is type C with a distal TEF, making up 85–90% of EA anomalies [19]. As a consequence, most of the literature focuses on these cases. We only found 67 cases of other types of EA in our literature search, most from non-comparative studies. Of the less well-observed forms of EA, Type A was the second most prevalent (65 cases). This type does not contain a TEF, but often a rather long gap between esophageal pouches that require lengthening before anastomosis can be attempted. These procedures are more complicated and take longer to

Table 2 List of characteristics and outcomes of patients who underwent thoracoscopic repair of esophageal atresia

	Number of included studies	Number of patients	Number of events (range)	% Incidence
Length of hospital stay	8 [6, 7, 9, 89, 97, 115, 117, 122]	166	(11–317 days)	NA
Length of surgery	21 [6, 7, 49, 86, 89, 92, 93, 97, 99, 100, 103, 104, 106, 109–114, 117, 122]	395	(54–428 min)	NA
Conversion to open	39 [6–9, 26, 49, 86–117, 122]	833	83	9.9
Intra-op complications	8 [6, 7, 90, 91, 98, 106, 108, 111, 112, 117]	171	2	1.2
Anastomotic leak	32 [6–9, 49, 86–89, 92–94, 97–107, 109–117, 122]	728	91	12.5
Esophageal stricture	30 [6–9, 86–89, 93–98, 100–107, 109–113, 116, 117, 122]	660	202	30.6
Recurrent fistula	14 [7, 9, 91, 100–103, 105, 107, 109–111, 117, 122]	414	11	2.7
Fundoplication	16 [7, 8, 49, 87, 88, 91, 99–103, 107, 109–111, 117]	341	79	23.1
Time to full oral feeds	7 [6, 7, 89, 93, 97, 117, 122]	107	(4.6–60)	NA
Mortality	29 [6–9, 88, 90–94, 97–107, 109–113, 115–117, 122]	761	24	3.2

NA not applicable

perform compared to surgery for Type C, with an average operative time of over 9 h [108]. The complication rate also tends to be much higher in these cases. In a recent study, out of ten Type A patients undergoing thoracoscopic repair, two had leaks and nine had subsequent strictures requiring fundoplication [116]. Similarly, all four patients in one study had strictures requiring fundoplication [108], while all six patients in another study had strictures requiring dilation (fundoplication rates were not reported) [106]. One SR reported on cervicotomy vs. thoracotomy vs. thoracoscopy for the repair of type E (TEF with no EA present) [86]. The authors found that over 90% of cases were approached by cervicotomy, while thoracoscopy was only performed in six patients and only if the TEF was at or below the T2 spinal level. No statistical comparisons of surgical outcomes could be made due to the small sample size [86].

Discussion

Based on an international survey on the management of EA/TEF and pure EA in 2014, Zani et al. concluded that there is need for consensus on the optimal surgical treatment of pediatric patients with these anomalies [10]; results of our own survey of experts in the field concurred. By conducting this systematic review, we endeavoured to determine whether a minimally invasive approach could in fact achieve similar or superior surgical outcomes and post-operative complication rates to that of the well-established thoracotomy approach.

All six existing SRs included a limited number of studies. Two of these SRs, which focused on type C EA malformations, conducted meta-analyses, which yielded consistent conclusions [81, 82]: while the minimally invasive approach had longer operative times, it had similar complication rates when compared to the open approach. However, both SRs noted that thoracoscopy may reduce time to first oral feeds as well as length of hospital stay. Again, these SRs were assessed to be of high quality (AMSTAR: 7 [82]; 6 [81]).

Our MAs yielded similar findings, examining our primary outcome of total complications related to the procedure as well the secondary outcomes of anastomotic leak, stricture rate, operation length, and need for future fundoplication. While strictures occurred slightly more frequently in the thoracoscopic group, this may be due to inconsistencies in the reporting of stricture, as studies differ in the length of follow-up. Another explanation may be the varying surgical experience when performing the repair. As a result, to confirm this observation, a randomized clinical trial with adequate follow-up is required.

The results of our MAs showed no significant differences between the minimally invasive approach and the open procedure, with the exception of operative time. As thoracoscopic repair of EA and TEF have only recently become more prevalent, we hypothesize longer operative times may be due to a lack of familiarity with the technique. As surgeons become more experienced in performing this type of procedure, we expect operative times to decrease. To complement the comparative study results, we tabulated the results of 47 non-comparative studies that looked at the surgical outcomes of patients who underwent thoracoscopic repair of EA to assess the overall efficacy and safety of thoracoscopy. Of note, mortality in patients was low at 3.2% and in most cases was due to an associated anomaly of the VACTERL type. The incidence of esophageal stricture requiring at least one endoscopic dilation and subsequent fundoplication was approximately 25%. The next most common complication was a leak at the anastomosis, which was managed conservatively in most cases. Very few cases of recurrent fistula occurred; indicating that ligation of the fistula was quite effective.

An additional concern with thoracoscopy is that single lung ventilation, as required in this approach, has the potential to contribute added risk to the newborn. Several of the comparative studies reported on the neonate's intra-operative tolerance via ABG measurements, the general consensus being that there were no significant differences between groups, with the exception of one study finding a significantly higher intra-operative maximum pCO_2 level in patients who underwent thoracoscopy [93]. Even in this study, however, there was no ongoing morbidity associated with this finding and all post-operative ABG levels were equivalent regardless of the surgical approach. That being said, the respiratory status of the patient should be considered when determining which method to use, as patients with pre-existing respirator compromise could suffer additional risks with the deflation of one lung [103, 110].

Theoretically, we would expect minimally invasive surgery to carry advantages over a more intrusive open procedure in outcomes such as length of hospital stay, time to full oral feeds, blood loss, and narcotic use, and to reduce further long-term complications such as cosmetic and musculo-skeletal deformities. Unfortunately, due to small sample sizes, a limited number of studies, and relatively short follow-up periods, it was impossible to conduct meta-analyses on these outcomes. It is noteworthy that only two of the included studies looked at cosmesis following surgical intervention for EA [49, 92]. The limited data that do exist appears to favour a thoracoscopic approach as expected; however, more data will be needed to verify this finding [72, 73, 77, 118]. Fewer sequelae are the ultimate rationale behind the shift towards a minimally invasive surgical approach [3–5].

Our results are reassuring for proponents of thoracoscopy, as they suggest that surgeons can correct EA with TEF using a thoracoscopic technique with at least the same efficacy as an open procedure, while not exposing the infant to increased rates of post-operative complications. This appears to be true despite the potential difficulties related to the confinements of a neonate's body habitus [103] and the steep learning curve associated with thoracoscopic surgery [8, 9]. In fact, operative times for thoracoscopy may shorten as this method becomes more mainstream and is taught in residency programs by surgeons with extensive experience in minimally invasive surgery.

Of course, our systematic review is not without limitations. The non-randomized design of the majority of included studies introduces some potential biases, particularly related to the selection of study participants and the reporting of results [119–121]. However, we considered it important to include evidence from non-randomized studies due to the general lack of RCTs available in the literature as well as the usefulness of non-randomized studies in reviews of effectiveness [120]. Furthermore, the quality of non-RCTs was quite good according to the MINORS criteria. According to the developers, gold standard RCTs score 23–24, while top rated comparative non-RCTs typically score 19–20 out of a possible 24. Ten of the comparative studies in this SR scored fair (12–16) and four scored strong (18) out of a possible 24. A total of 20/27 non-comparative non-RCTs were fair quality with scores ranging from 10 to 12 out of a possible 16. The remaining non-comparative, non-RCTs were poor quality, ranging from 5 to 9 out of a possible 16. Publication bias may also have influenced our results, as we did not specifically search for grey literature. In addition, we may have missed some pertinent data due to language limitations.

Conclusion

Thoracoscopic approach for the repair of EA/TEF is safe, with no increased morbidity when compared with the open approach. Although operative times were longer with thoracoscopic repair, rates for complications, anastomotic leak, stricture, and need for fundoplication were similar between open and thoracoscopic repair. A large-scale randomized controlled trial would help to determine the true value of this newer approach, with a full evaluation of possible acute and chronic complications and sequelae. In many areas of surgery, a natural progression is being made towards minimally invasive techniques, and we appear to be at the brink of this advancement with EA/TEF management.

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Compliance with ethical standards

Conflict of interest The authors declare no conflict of interest.

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