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REVIEW ARTICLE

Thoracoscopic repair of esophageal atresia

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Abstract
Thoracoscopic repair (TR) of esophageal atresia (EA) has been performed with increasing frequency over the last two decades, with the expectation of improved outcomes by avoiding thoracotomy. To understand the current practice and outcomes of TR of EA, we reviewed the relevant literature, including 15 case series, 7 comparative studies, and 3 meta-analysis comparing TR with conventional open repair (COR). Most of the studies had a retrospective design and small numbers of patients. Although the evidence level is low because of the lack of prospective studies, this review found that TR is as safe as COR, with comparative outcomes. Moreover, there were several advantages of TR over COR, such as less blood loss and a shorter hospital stay. The long-term outcomes of TR remain unclear because of limited data. Moreover, there is a significant learning curve over the first 10–20 TRs performed. We conclude that TR of EA, when conducted by experienced surgeons, is a safe and minimally invasive alternative to COR and may yield better results than COR in appropriately selected patients.

Keywords Esophageal atresia · Thoracoscopic repair · Literature review

Introduction

Lobe et al. [1] performed the first thoracoscopic repair (TR) for esophageal atresia (EA) without trachea-esophageal fistula (TEF) in 1999 and Rothenberg [2] performed the first TR of EA with TEF in 2000. Since then, many reports have described the operative techniques and outcomes of TR of EA. To date, two multi-institutional studies have been conducted. An analysis of over 100 cases by Holcomb et al. [3] concluded that TR was similar to conventional open repair (COR) in terms of outcomes and mortality. A multi-institutional study of 58 cases by Okuyama et al. [4] also found that although TR was associated with a higher incidence of stenosis and longer operative times, the complication rate was similar to that of COR. These single and multi-institutional studies suggested that TR of EA was comparable to COR. Because so few of these operations have been performed by individual practitioners, there is wide variation in the technique and management documented in each series. Consequently, there are no standard indications, procedures, or perioperative management for TR of EA. To understand the current practice and outcomes better, we reviewed the available literature on this subject.

Methods

We performed an electronic keyword literature search of the PubMed database for articles published in English up to the end of 2018. The terms “esophageal atresia” and “thoracoscopic repair” were used as key words in combination. Reference lists of identified articles were screened for additional studies. Articles that did not contain original research data or did not give adequate information about the operation performed were excluded.

Results

We were unable to identify any randomized control studies comparing TR and COR. We found 15 case series, 7 comparative studies, 3 meta-analysis, and 2 multi-institutional studies. Data collected from these studies were analyzed for the indications for TR, anesthesia management, operative procedures, outcomes, comparative studies, and the learning curve.

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Indications for TR

We identified 15 case series of TR of EA that gave adequate information about the operation performed. Table 1 summarizes the data from these case series [5–19]. Although the indications for TR varied widely in each institute, the necessary requirement for TR is that the respiratory and circulation statuses are stable enough to tolerate stimulation of artificial pneumothorax and the prone position, and that the thoracic cavity has enough room to allow the thoracoscopic procedure to be carried out. Therefore, several exclusion criteria for TR, such as low birth weight, major coexisting anomalies, and compromised physiologic status, were reported.

Low birth weight

In the case series, the average body weight at the time of the operation ranged from 2.2 to 3.1 kg. In all series (except for one, in which the lowest body weight after successful TR was 1.2 kg [11]), TR was performed successfully in infants weighing more than 1.8 kg. The lower limit of body weight seems to be about 1.8 kg.

Major coexisting anomalies

Although major cardiac anomalies have been reported as contraindications by two institutes [17, 20], there are no clear definitions of major cardiac anomalies. Because CO_2 insufflation may cause hypoxic spells in patients with cyanotic heart diseases, TR has not been performed in patients with cyanotic cardiac diseases in many case series. On the contrary, Burgmeier et al. [21] reported that thoracoscopic surgery could be performed safely in term and preterm neonates with cardiac anomalies. Our experience also showed that TR could be performed safely in infants with a major cardiac anomaly. These results suggest that once the respiratory and circulation status are stabilized, a major cardiac anomaly is not a contraindication to TR.

Long gap

A long gap between the proximal and distal esophagus was identified by two institutes as an exclusion criterion for TR for EA [18, 22]. Despite the lack of a unified criterion for a long gap, it is not appropriate to exclude these patients from TR. Detailed long gap management is described in the later part of this article.

Anesthesia management

In the case series, single lung ventilation using a bronchial blocker was used in three institutes [5, 11, 19], whereas main stem ventilation was used in the remaining institutes. However, it has been reported that artificial pneumothorax in combination with the prone position can provide an excellent operative field for TR of EA. Therefore, single lung ventilation was not used in the most recent series.

Tytgat et al. [23] reported that intrathoracic CO_2 insufflation caused a reversible decrease in the SpO_2 level and pH and an increase in the $PaCO_2$ level during TR of EA, and that brain oxygenation during TR of EA remained stable and within normal limits during and after CO_2 pneumothorax. Bishay et al. [24] also reported finding no significant difference in the $PaCO_2$ or PaO_2 level or pH in patients undergoing TR of EA. As this was a pilot randomized controlled trial (RCT) including only five neonates in each study, the effect of TR on neonatal physiology was not conclusive. Conversely, Kalfa et al. [25] reported low oxygen saturation levels and high end-tidal pressures of CO_2 in five patients undergoing TR. Li et al. [26] also reported that during TR, hypercarbia and acidosis developed within 1 h after pneumothorax and concluded that CO_2 insufflation had an additional influence on the respiratory function of newborns. A major limitation of all these studies was the small number of patients in each. None of their findings were conclusive, so further large case series with long-term follow-up are necessary.

Operative procedures

Patient's position and port placement

In previous case series, TR of EA was performed uniformly via the right intrapleural approach. Briefly, the patient was placed in a modified prone position, with the right side elevated at approximately 30°–45° to allow the lung to fall away from the posterior mediastinum. The surgeons and assistants stood in front of the patient and TR was performed using three ports; however, the insertion of a fourth port was necessary to retract the lung occasionally. An initial camera port (3 or 5 mm) was placed in the fifth intercostal space, posterior to the tip of the scapula. A 30° lens allowed the surgeons to look down on the operative field. Two additional working ports were placed to achieve an angle of 90° at the presumed site of the anastomosis. The upper port size was 5 mm to allow the introduction of a clip applier and an energy device. The lower port was placed one or two intercostal spaces below and slightly posterior to the camera port.

Azygos vein, TEF closure, and anastomosis

The azygos vein was divided using a vessel-sealing device or an electric cautery machine in all institutes, except two, in which it was preserved [10, 16]. Because TEFs and the vagal nerve are usually located just behind the azygos vein,

Table 1 Reported case series of thoracoscopic repair of esophageal atresia

Authors	Year	Case # Type C/A	BW @op (kg)	Age (day)	Pneumothorax (mmHg)	Azygos vein	TEF closure	Anastomosis (# of stiches)	Op time (min)	Conversion	leak	Stenosis	TEF recurrence	Death
Lovvorn et al. [5]	2001	2/8	2.1–3.6	N/A	4	Divided	Clip	Interrupted	55–120	1	2 (20%)	3 (30%)	0	0
Marchero et al. [6]	2002	9/0	2.7 (1.9–3.3)	N/A	5	Divided	Clip	Interrupted	105 (70–189)	0	2 (22%)	3 (33%)	0	0
Allal et al. [7]	2005	4/1	2.7 (2.3–3.6)	N/A	6	Divided	Ligate	Interrupted	100 (9–110)	2 (40%)	0	0	0	0
Nguyen et al. [8]	2006	6/0	2.6 (1.7–3.4)	N/A	5	Divided	Ligate	Interrupted	143 (75–215)	1/6 (17%)	0	1 (17%)	0	1/6 (13%)
MacKinlay [9]	2009	20/6	1.4–3.9	0–5	6	Divided	Clip/ligate	Interrupted	N/A	0	7/26 (27%)	9/26 (35%)	1/20 (5%)	2/26 (8%)
Patkowsk et al. [10]	2009	23/0	1.1–3.4	N/A	5–6	Not divided	Clip	Interrupted	131 (55–245)	0	3	4	0	3(not related)
Rothenberg [11]	2012	49/0	2.4 (1.2–3.8)	1	4–8	N/A	Clip	Interrupted	75 (50–120)	1/49 (2%)	2 (4%)	16 (33%)	1/20 (5%)	0
van der Zee et al. [12]	2012	72/0	2.64	N/A	5	Divided	Ligate	Running sutures	155–160	4/72 (6%)	11/72 (15%)	22/72 (31%)	2/72 (3%)	2/72 (3%)
Huang et al. [13]	2012	33/0	2.58	3 (1–11)	4	Divided	Clip/ligate	Interrupted	146	2/33	3	7	1/20 (5%)	2
Digemann and Ure [14]	2013	19/1	2.78 (2.0–4.0)	0–5	3–5	Divided	Ligate	Interrupted	142 (75–220)	2/20 (10%)	0	4 (20%)	1/20 (5%)	0
Lee et al. [15]	2014	23/0	2.6 ± 0.5	2 (1–28)	5	Divided	Ligate	Interrupted	179 ± 81	1 (4%)	2/22 (9%)	10/22 (45%)	0	1/23 (4%)
Nachulewicz et al. [16]	2015	10/0	2.2 (1.8–2.2)	1–4	N/A	Not divided	Clip	Interrupted	140 (110–225)	2/10 (20%)	1 (redo1) (10%)	1 (10%)	0	0
Hiradfar et al. [17]	2016	24/0	2.8 ± 0.9	2.1 ± 1.6	5	Divided	Ligate	Interrupted	220 ± 76	14/24 (58%)	2/10 (20%)	4/10 (40%)	0	1/24 (4%)
Kanojia et al. [18]	2016	29/0	2.6 (1.8–3.2)	2.8 (2–6)	4–6	N/A	N/A	Interrupted	N/A	4/29 (14%)	4/29 (14%)	2/29 (7%)	0	6/29 (21%)
Okuyama et al. [19]	2018	11/0	2.8 (2.5–3.7)	1 (1–3)	5	Divided	Clip	Interrupted	230 (164–383)	0	0	1 (9%)	2/72 (3%)	0

dividing the azygos vein can help find the distal esophagus. After TEF dissection up to the insertion into the trachea, the TEF was occluded using suture ligature in six institutes, clips in six institutes, and both ligature and clips in three institutes. The type of TEF occlusion had no influence on the outcomes, including anastomotic leak, stenosis, and TEF recurrence. Anastomosis was performed using interrupted sutures in all institutes except one, where a running suture was used whenever possible to secure a watertight anastomosis [12].

Long gap

In most cases of a long gap, TR was converted to COR to allow extensive dissection for the primary anastomosis. Recently, however, there have been several reports of thoracoscopic procedures for long gaps. Table 2 summarizes six identified articles describing TR of long gap EA [27–32]. Rothenberg et al. [30] reported 14 cases of long-gap EA with or without TEF, in which TR was completed with excessive thoracoscopic dissection. They concluded that TR of long-gap EA was safe and effective because of its improved visualization and easy access to the upper and lower pouches. Most recently, Sun et al. [28] reported delayed primary anastomosis for long gap by TR and described performing tension-free anastomosis using a bougienage stretching technique.

Multi-stage thoracoscopic procedures for long gaps have also been reported. van der Zee et al. [31] reported 10 cases of long gaps, in which TR was performed using the thoracoscopic traction technique. Tainaka et al. [29] and Bogusz et al. [27] reported similar cases, in which two-stage TR was performed using internal esophageal traction. Thoracoscopic esophagostomy after sequential extrathoracic esophageal elongation (Kimura procedure) was also described for four cases of long gap EA [32]. According to these reports, multi-stage TR is a surgical option for long-gap EA, as well as primary TR using elongation techniques and excessive dissection.

EA with a right-sided aortic arch (RAA)

The optimal approach for the management of EA with RAA remains controversial. Parolini et al. [33] concluded that a left-sided transpleural approach for EA with RAA can provide safe and easy access to the proximal and distal esophagus without obstructing the right-sided aorta. There are two previous reports of TR of EA with RAA. Wong et al. [34] reported two cases of EA with RAA, in which TR was performed through the right side of the chest. In contrast, Oshima et al. [35] reported a case of EA with RAA, in which two-stage TR was performed through the left side of the chest. It is necessary to accumulate cases of EA with RAA to establish whether one approach is superior to the other.

Outcomes of TR

Table 1 summarizes the operative data collected from the case series on TR of EA.

Open conversion and mortality

The open conversion rate ranged from 0 to 58% (average 10.4%; 31/296). The cause of open conversion included prematurity, long gaps, technical difficulties, and unstable physiology. The mortality rate for TR has been reported to range from 0 to 21% (average 4.4%; 13/296). The mortality rate was 0% in eight case series. These results suggest that TR of EA is compatible with COR in terms of feasibility and safety.

Operative time

The operative time of TR for EA varied among the case series. The average (median) operative time for TR ranged from 100 to 230 min. Anatomical factors, such as small body weight, tiny distal esophagus, and long gaps, accounted for the longer operative time. Because of the significant learning curve for TR for EA [19], the experience of the surgical team would be another factor affecting the operative time.

Table 2 Reported case series of thoracoscopic repair of long gap esophageal atresia

Authors	Year	Patient #	Procedures	Results
Bogusz et al. [27]	2018	4	Staged (internal traction)	Completed in 3 of 4
Sun et al. [28]	2018	7	Delayed primary	Completed in all
Tainaka et al. [29]	2017	5	Staged (internal traction)	Completed in all
Rothenberg and Flake [30]	2015	14	Excessive horacoscopic dissection	Completed in all
van der Zee et al. [31]	2015	10	Staged (internal traction)	Completed in 8 of 10
Miyano et al. [32]	2013	4	Staged (extrathoracic elongation)	Completed in all

Operative complications

The anastomotic leakage rate ranged from 0 to 20% (average 12.2%; 36/296). In most cases, the leak resolved with conservative management, but in one case, re-operation was required [16]. The anastomotic stenosis rate ranged from 10 to 43% (average 26.6%; 79/296). Although the incidence of anastomotic stenosis was high after TR, one or two endoscopic dilatations were successful in most cases. Woo et al. [36] reported that TR had a higher rate of vocal cord paresis than COR and that thoracoscopic deep neck dissection up to the thoracic inlet caused the complication. However, there were no other reports of a high incidence of vocal cord paresis after TR. It is likely that vocal cord paresis can be avoided under magnified thoracoscopic view.

Long-term outcomes

A few studies investigated the long-term outcomes of TR of EA. Spoel et al. [37] reported that lung function during the first year was similar in infants with EA repaired by thoracotomy or thoracoscopy. Although TR is expected to reduce the risk of postoperative musculoskeletal deformities, the effects of TR on long-term musculoskeletal deformities and functional outcomes remain unclear. Miyano et al. [38] assessed the quality of life (QOL) of patients after surgery for EA by comparing COR and TR 1 year postoperatively and then after starting school. The initial QOL scores were significantly lower after TR, but were similar by school age. Kawahara et al. [39] reported that there were no benefits of TR in terms of postoperative esophageal motor function. However, further studies are necessary to identify whether the long-term functional outcomes of TR are superior to those of other procedures.

Comparative studies (TR versus COR)

To our knowledge, there are no RCTs comparing TR with COR. Table 3 summarizes the data collected from the seven studies comparing TR and COR [20, 22, 26, 36, 40–42]. These studies did not identify any differences in mortality or intraoperative complications between TR and COR. In three studies, the operative time was longer for TR than for COR and in the other three studies, the estimated blood loss was less in TR than in COR. In addition to these studies, there are two meta-analyses comparing TR with COR. One meta-analysis of four studies (166 patients) did not show any significant differences in the intra- and postoperative complication rates between TR and COR [43]. The other meta-analysis, which included eight studies (452 patients), found that TR and COR yielded similar complication rates, although TR had the advantages of less blood loss and shorter hospital stay [44]. Although a large selection bias exists, these studies and reviews conclude that TR is a comparable alternative to COR. RCTs with long-term follow-ups are necessary to establish whether TR is better than COR.

Learning curve and simulator

A few reports have discussed the learning curve for TR of EA with TEF. Lee et al. [15] reported that the mean operative time was significantly longer for the first 13 cases than

Table 3 Published studies comparing thoracoscopic repair vs. conventional open repair

Authors	Year	case # TR COR	Gestational age (week) TR COR	Body weight (kg) TR COR	Operative time (min) TR COR	Blood loss (ml) TR COR	Leak (%) TR COR	Stenosis (%) TR COR	Death (%) TR COR
Lugo et al. [22]	2008	8	36.9 (28–40)	2.7 (1.7–3.4)	156 (75–240)	N/A	14	14	0
		25	36.7 (30–41)	2.4 (1.2–3.3)	123 (82–205)		20	52	0
Al Tokhais et al. [40]	2008	23	36.3	2.7 ± 0.7	149 ± 047	N/A	17.4	8.7	4.4
		22	36.3	2.4 ± 0.7	179 ± 66		13.6	18.8	9.1
Szavay et al. [41]	2011	25	N/A	2.7 (1.5–3.5)	134 (119,150)	N/A	4	N/A	0
		32		2.1 (0.8–3.3)	106 (91, 123)*		3		0
Ma et al. [26]	2012	18	39.0 ± 2.7	2.6 ± 0.8	185 ± 54	N/A	N/A	N/A	0
		15	39.7 ± 2	2.3 ± 0.6 8	148 ± 43*				0
Yamoto et al. [20]	2014	11	38.6 (36–40)	2.6 (2.1–3.1)	175(135–260)	1 (0–10)	18	27	0
		15	38.5 (37–40)	2.7 (2.2–3.1)	155(120–190)*	12 (5–20)*	20	33	0
Koga et al. [42]	2014	25	38.1 ± 1.7	2.6 ± 0.4	228 ± 63	3.1 ± 3.2	12	28	0
		40	38.6 ± 1.3	2.6 ± 0.4	209 ± 98	11.5 ± 6.9*	2.5	12.5	0
Woo et al. [36]	2015	17	38.5 ± 26.5	2843 ± 803	N/A	1.9 ± 1.9	12	35	0
		14	31.6 ± 21.4*	2079 ± 590*		5.3 ± 5.0*	7	14	0

*$p < 0.05$ vs TR

for the subsequent 9 cases and also noted that leaks and stenoses occurred less frequently in the later cases. Hiradfar et al. [17] reported that the open conversion rate decreased from 58.3 to 35.7% after the first 10 cases. van der Zee et al. [12] compared 41 earlier cases with 31 later cases of TR. The mean operative time remained relatively unchanged, although in the later part of their series, the operations were performed by junior surgeons who were less experienced with the procedure. Most recently, Okuyama et al. [19] reported that the operative time decreased significantly as the number of consecutive cases increased. According to these reports, the learning curve exists for the first 10–20 cases of TR.

As TR of EA needs advanced minimally invasive techniques, training with the aid of a simulator is expected to shorten the learning curve. There were several reports of neonatal TR simulators using synthetic tissues and a rib cage. These simulators are reported to be useful for practicing neonatal TR of EA [45–49].

Discussion

An International Pediatric Endosurgery Group (IPEG) survey on the current patterns of TR of EA, completed by 170 surgeons from 31 countries, revealed that half of the respondents utilized TR [50]. However, because the online-based survey was limited to IPEG members, there could be a large bias in terms of surgeons' preference. Another multicenter survey on the best surgical approach for EA revealed that TR for EA was performed in 21% of 18 hospitals in Belgium and Luxembourg, [51]. The limited number of institutes where TR is the standard procedure for EA highlights the necessity to standardize it.

Considering the indications for TR, this review showed that the lower limit of the body weight for TR of EA is about 1.8 kg, depending on the size of available thoracoscopic instruments. On the contrary, major coexisting anomalies are not always considered contraindications. Physiologic stabilization seems to be a more important factor in defining the indications for TR. This review also identified that there is a variability in the technical aspects of the operation. However, the differences in operative procedures do not influence the operative results. As the number of cases in each institute is limited, it is thought that TR of EA will become the best operative maneuver. Technical and instrumental advances are expected to widen the inclusion criteria for TR and improve its outcomes.

A long gap was thought to be a contraindication for TR; however, this review showed that there are several TR approaches for long gaps. As the thoracoscopic approach can allow easier esophageal dissection, TR might have several advantages for long gap management. Single lung ventilation was used for the anesthesia management in the early case series of TR; however, this review identified that stable artificial pneumothorax in combination with the prone position can provide an excellent operative field for TR. Therefore, main stem ventilation seems to be standard for TR of EA.

This review also showed that the overall outcomes, including the mortality and complication rates of TR, are similar to those of COR. Although there are several disadvantages of TR, including longer operative time and higher stenosis rate, a significant learning curve exists in the first 10–20 cases. As most of the previous case series are thought to be on the learning curve, improved outcomes can be expected.

Previous reports on COR described a high incidence of musculoskeletal deformities, including winged scapulae, asymmetry of the thoracic wall, and severe scoliosis. The primary advantages of TR lie in its potential role of reducing the musculoskeletal sequelae arising from thoracotomy during infancy. As data on the long-term outcomes of TR are limited, further studies are necessary.

Conclusion

This review revealed considerable variability in the indications, surgical techniques, and long gap management in TR of EA and that the outcomes of TR are comparable to those of COR. We conclude that TR of EA is a safe and less invasive alternative to COR and may yield better results in appropriately selected patients.

Compliance with ethical standards

Conflict of interest No competing financial interests exist.

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