17

Systematic Review of the Literature: Comparison of Open and Minimal Access Surgery (Thoracoscopic Repair) of Esophageal Atresia with Tracheo-Esophageal Fistula (EA-TEF)

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1. Introduction

Surgical correction of esophageal atresia with tracheo-esophageal fistula (EA-TEF) has been performed since 1943 (Cameron Haight) via postero-lateral thoracotomy using an extra-pleural approach in most cases. This procedure can be considered as the standard treatment of EA. The pitfalls of the operation, the incidence of complications and the outcomes, both short term and long term, have been analysed and reported by many pediatric surgeons around the world.

Since 1999, minimal access surgery (MAS) has been practised for the correction of EA [1]. The risk of complications and short term outcomes have been reported as equal to the open approach. MAS has been advocated because of a possibly reduced risk of impairment of shoulder function, and a possible reduction in occurrence of postoperative scoliosis. Next to that, it has been postulated the MAS repair might lead to a better cosmesis.

Several advantages and disadvantages of both procedures have been described. The open approach is well standardized and is resorted to in difficult cases. Disadvantages of the open approach are the presence of a scar, possible chest wall deformities and rib fusion. The occurrence of scoliosis and possible shoulder function impairment has been related to the open approach as well.

The thoracoscopic approach has the advantage of magnification of view. Next to that the chance on a postoperative scoliosis and impaired shoulder function may be reduced due to the small incisions which also might lead to better cosmesis. Technically, the thoracoscopic approach is more demanding than the open approach which has consequences for training and education.

So far, it seems that there is no difference between open and MAS approach in the frequency of anastomotic leakages, strictures, recurrent fistulas, tracheomalacie or GERD.

In 2005, Holcomb et al presented their results of MAS (thoracoscopic) EA-TEF repair in 104 patients in multiple centres. This landmark paper has been extensively discussed by leaders

in the field and highlights the need for a randomized clinical trial. Since that discussion, several more articles have been published on MAS repair of EA-TEF, but no prospective comparative studies, let alone RCT's. The Clinical Trials Register (www.clinicaltrials.gov) does not list a study on this subject.

	Al Thokais,2008 MAS	Al Thokais,2008 open	Szavay 2011MAS	Szavay 2011 open	Kawahara MAS	Kawahara open	Lugo MAS	Lugo open
no of patients	21	22	25	43	7	10	8	25
type EA	C (dist fist)	C (dist fist)	C (dist fist)	C (dist fist)	C (dist fist)	C (dist fist)	C (dist fist)	C (dist fist)
ass malform	9(39.1%)	13(59.1%)	47%	47% (all only)			87,50%	72%
weight at op	2735±744	2427±726	2720	2090	2.814(2.46-3.71)	2.45(1.46-2.9)	2,7	2,4
age at op			1 (median)	1 (median) (all only)	2(0-12)		36,9	36,7
gestat age	36,3	36,3	35	35 (all only)	38(33-41)	34.5-41.6		
anastom leak	4 (18%)	3(14%)			3(30%)	2(25%)	14%	20%
dilat >1	2 (9%)	4 (18%)			1	2	14%	52%
recurr fist	NR	NR						
mortality related	0	2(9%)					0	0
duration op	149±47	179±65	141(median)	106(median)			156(75-240)	123(82-205)
post ventil	no difference						4.6(1-12)	19(3-150)
l.o.s	NR	NR					21.8(11-38)	66(8-280)
conversion rate	3(14%)	NR					1	
antireflux	NR	NR			2	2		
aortopexy	NR	NR						
follow-up	14.4(6-46)mo	29.8(6-119)mo						
other	incl 2 A				antirefluxstudy	antirefluxstudy		
pCO2 max intraop.			62	48				
pCO2 max postop.			53	47				
Base excess postop.			-1	-3				
PH postop.			7.16	7.20				

Table 1.

2. Methods

Search strategy:
EmBase and PubMed (Medline) search using keywords (MESH terms): <Minimal access surgery> OR <thoracoscopic surgery> OR <thoracoscopy> AND <esophageal atresia>
Only full text papers in English were included. If more than one paper had been published by the same author or group of authors [2], only the most recent paper was included in order to avoid duplications.
Two authors reviewed all papers and selected those that contained sufficient data on patients characteristics and outcome parameters to enable comparison with reports on open repair of EA-TEF of patients operated after 1995.
Parameters recorded are represented in table 1.
Three categories can be discerned

1. patients' characteristics
2. intra-operative and post-operative data, including complications
3. follow-up data

3. Results

The initial search resulted in 55 articles. After critical review by two independent reviewers twenty-one articles were included, based on the criteria stated above.

There were no RCT's or prospective studies. All papers were based on retrospective analysis, mostly single center cohort or case studies. The largest population was reported in a multicenter review by experts in minimally invasive pediatric surgery combining the experience in 104 patients.

Together the 22 articles contained 332 patients who had (type C) EA-TEF repair via the thoracoscopic approach, 11 patients with isolated (type A) [3,4,5,6] and one case report of type D (proximal and distal fistula) [7].

At a closer look there are different study-designs in those 22 articles in which only four papers [4,8,9,10] did a retrospective analysis with historic [4] or contemporary [8,9,10] open approaches as controls. (Table 1) Seven papers reported the results of thoracoscopic EA-TEF repair containing at least 20 patients per report for a total of 312 patients [4,11,5,12,13,2,10]. (Table 2)

Several papers, particularly in the early period, concentrated on technical and feasibility aspects dealing with the initial diagnosis of esophageal atresie. Other studies highlighted special characteristics of the patients, like cardiac malformations [14]. Also on anesthesiological subjects, including the effects of CO2 inflation [15,16] and pain after thoracoscopic repair was studied [17].

	Author,year						
	Holcomb,2005	Al Thokais,2008 MAS	Rothenberg	MacKinlay,2009	Patkowski,2009	vanderZee, 2007	Szavay 2011MAS
no of patients	104	21	26	20	23	50	25
type EA	C (dist fist)	C (dist fist)	C	C (dist fist)	C (dist fist)	C (dist fist)	C (dist fist)
ass malform		9(39.1%)	50%	13(65%)	9(38%)	31(61%)	47%
weight at op	2.6±0.5	2735±744	1.8-3.8	1,4-3.9	1070-3390	2620(1025-4030)	2720
age at op	1.2±1.1					1-7 d	1 (median)
gestat age		36,3		31-41		37.2(31.3-42.2)	35
anastom leak	8 (8%)	4 (18%)	3.6%	7(35%)	3 (13%)	9 (18%)	
dilat >1	21 (21%)	2 (9%)	30%	3(15%)	4 (18%)	22 (45%)	
recurr fist	2 (1.9)	NR	0	1(5%)	NR	2 (4%)	
mortality related	1(1%)	0		1(5%)		1(2%)	
duration op	129.9±55.5	149±47	95(55-120)	NR	131(55-245)	178(90-390)	141(median)
post ventil	3.6±5.8	no difference	1-4dd	NR	NR	4(1-95) med	
l.o.s	18.1±18.6	NR		NR	NR	16.5(7-150) med	
conversion rate	5 (5%)	3(14%)	1	1 (5%)		2(4%)	
antireflux	26 (25%)	NR		NR		11(22%)	
aortopexy	7 (6.8%)	NR		NR	1(4%)	6(12%)	
follow-up		14.4(6-46)mo		NR	14 (1.5-33)mo	27(10-145)	
other	Rt arch 6	incl 2 A			2 trach perf		
pCO2 max intraop.							62
pCO2 max postop.							53
Base excess postop.							-1
PH postop.							7.16

Table 2.

To compare the results of the minimal invasive operations with open operations, data were distilled from the literature (Table 3). This represents the results from textbooks and standard papers on open repair of EA-TEF. Also these results on open approach are based on retrospective studies and did not comprise RCT's or prospective studies.

	Ashcraft	Prem Puri	Engu m	Spitz	Randolph	Mannin g	Yancha r
no of patients			174	148	39	63	90
type EA							
ass malform							
weight at op							
age at op							
gestat age							
anastom leak	17%	11-21%		21%	10.2%	17%	16.6%
stricture	17-59%	37-55%	32.7%	17.7 %	33.3%	4.3%	17%
recurr fist	3-15%	5-15%	2.2%	12%	5.1%	6.4%	3.3%
mortality EA/TEF related			4.5%	14.8 %	0%	3.1%	1.1%
duration op							
post ventil							
l.o.s						24(9-174)	
GER	40%	40-50%					
antireflux-operatie	20%	6-45%	25.2%	18%	15.3%	16.9%	32.2%
aortopexy				16%		4.8%	

Table 3.

4. Patiens' characteristics

The *gestational age and the birth weight* of MAS patients were not different from open repairs in the comparative studies (2.7-2.8 kg MAS vs 2.0-2.4 open Table 1). In the minimal invasive group the thoracoscopic approach was succesfully performed even in premature babies with weights below 1500 g [18,5,2] but these are not different from data in the literature for open repair ([19] , mean 2557 with range 1100-4460 g).

Concerning the *associated malformations and risk classification* only Holcomb [11] et al present data on Waterston classification(A 62, B 30 and C12) respectively. The reported associated malformations were seen in up to 87.5% [9] of the thoracoscopically repaired babies, but in the comparative studies no difference is seen between MAS (39-87%) and open (47-72%) concerning these associated malformations

5. Perioperative data

Mean *duration of operation* was recorded in 12 articles and ranged between 95 and 260 minutes. In the comparative studies the paper of Szavay [10] reveals a significantly longer operation time (open 106 min versus MAS 141). But Al Tokhais [4] and Lugo [9] did not find a significant difference in operation time between them with 179 and 123 min open and 149 and 156 min.for MAS.

The conversion rate was reported in 15 papers, in which no conversion was done in 9 papers and in the remaining 6 papers the rates varied between 5 and 16%.

The *duration of postoperative ventilation* was mentioned in 10 papers. One reported no difference between open and MAS patients [4], others reported mean duration of 4 days post-

operative ventilation [11,3,20,9,13] (range 1-4.6). Of interest is the paper of Krosnar [16] where, although in a small number, a comparison between open and MAS approach is done concerning extubation time (extt) and discharge to PICU(DPICU) .
These results were for an open approach with an extt of 54 hrs and DPICU discharge of 3.4 days and for the MAS approch extt 37.6 hrs and DPICU of 2.75 days. This numbers suggest a better postoperative recovery of the MAS approach.
Length of hospital stay was reported in 7 articles, some giving mean, others median values so a good comparison of these numbers is not justified. The mean length of stay in Hollcombs' paper compares favorably with open repairs as reported by Manning [21] 18.1 days for MAS and 24 for the open method. This historic group however might not be representative for present l.o.s so the evidence is not clear. Also Lugo [9] found a difference in l.o.s as it is 21 days in MAS (n=8) and 66 days in the open approach (n=25) but in here hard evidence seems to be scarce as the numbers are small. *Mortality* related to the procedure was recorded in 14 articles and 11 reported no mortality; in the other three it varied between 1 and 16%. But these were small numbers also [18]. In the series reported by Holcomb the mortality rate was 0.9 %. Yanchar [22], reported 1.1 % mortality after open repair in 90 patients. For this parameter no difference could be demonstrated.

6. Complications

The main short term complications are leakage of the anastomosis, anastomotic strictures and recurrent TEF. (Table 1, 2, 3)
Anastomotic leakage was reported in 18 papers. Important is that the definition may differ between the papers depending on whether routine esophagograms were performed or not. Most leaks were described as minor and healed spontaneously. The incidence varies between 0 and 30% with a median 15%. There is no difference with the reported leak rates in the open thoracotomies in the papers [8,9,23,24,22] and in the literature.(Table 3)
A clear definition of *anastomotic stricture* is an important factor. Most authors define stricture by the need for (repeated) dilatations however others state that narrowing of more than 50% of the lumen or every narrowing detected on an esophagram with a symptomatic patient can be seen as an anastomic stricture [25,26]. Sixteen papers reported an incidence between 9 and 45%, with a median of 22%. This incidence is comparable to the rates reported after open repair (6-52%) by Holland [24] and in the literature (Table 3).
The incidence of the serious complication of a *recurrent tracheo-oesophageal fistula* was noted in 8 articles. The incidence varied between 0 (in 5 papers) and 4%. In the open repair series and in the literature, similar incidences have been reported (Table 3).

7. Other complications

Allthough *gastro-oesophageal reflux* is often seen after repair of esophageal atresia with TEF, the need for anti-reflux surgery was mentioned in 4 articles. The incidence of anti-reflux surgery varied from 22 to 50% (1,3,4,19). Procedures performed, if reported, were Thal or Nissen-fundoplication. Antireflux surgery numbers after open approach was performed in 18 to 32.2% of cases [19,27,28,21,22].
The need for aortopexy in case of a severe *tracheomalacia* is mentioned in only one paper [11] were it was performed in 6.8% of the cases. This is compatible with the rate of 4.7% and 16% after open repair [21,27].

There were no reports on any cosmetic benefit in any of the papers on MAS. And although there is more awareness of the effect of thoracotomy on shoulder-function and *scoliosis* this was not reported in any of these papers.
The duration of follow-up after discharge from the hospital was reported in 7 papers with means varying between 6 and 30 months. No further *long-term complications* as dysphagia, late pulmonary disease both restrictive and obstructive and late sequelae from GER are reported.

8. Discussion

In summary a total of 22 papers reporting on 332 EA-TEF repairs performed via MAS revealed no prospective studies and only four comparative studies with historic and contemporary open repairs as controls.
The focus of this chapter is on the type C, or esophageal atresia with fistula (TEF) as this is the most common form in esophageal atresia. Even with these numbers data are sometimes scarce and difficult to compare.
Allthough it is not the aim of this chapter a special mention has to be made of the role of MAS in correction of type A (long gap) EA. In some of the reviewed papers, these patients have been included because a esophago-esophagostomy was performed 3,5,6. And there are a number of other reports on the role of MAS in esophageal replacement. For example Stanwell 29 describes 7 patients in whom gastric transposition was performed and were laparoscopically assisted. In this study five of these had a long gap EA. Esteves 30 reported on laparoscopically assisted colon interposition in 5 children with long gap EA. Nevertheless because of the small numbers in these studies, the different nature and the conflicting views on the various procedures (primary anastomosis vs replacement by stomach, colon or jejunum), these papers have not been included in this review.

9. Clinical outcomes

When analyzing the results on *patients characteristics* it does not appear that there is a difference in the selection of patients in favour of any of the procedures. The gestational age, birth weight and associated malformations were similar to data recorded in open repair.
There is a wide variety between reports when focusing on post-operative results and complications. Consistent differences are lacking when compared with results reported for open thoracotomies as is seen in Table 1 and 2. The biggest problem however is the definition of a complication in these cases like anastomotic leakage and anastomotic stricture. For example esophagrams are not made routinely everywhere. Therefore, a difference in the incidence of esophageal strictures is likely to be present due to the difference in classification and not due to an incidence of occurrence of anastomotic strictures.
Also the follow-up data on MAS repair of EA-TEF is scarce, but again, they do not indicate that the incidence of *gastro-oesophageal reflux (GER)* and GER requiring anti-reflux surgery is different from that in patients who had open repairs of the esophageal atresia with TEF. Kawahara [8]et al studied the influence of MAS on esophageal motor function and gastro-esophageal reflux in 7 patients in comparison to 10 patients who had an open repair.

Manometry and 24-hours pH monitoring did not demonstrate any differences between MAS and open repair.
There is only one paper [11] mentioning the consequences of *tracheomalacia* requiring aortopexy. There seem to be no differences between MAS and studies after open repair.

10. Studies on systemic effects of MAS

In several papers the systemic effects of thoracoscopy in neonates are emphasized. In the findings of Bishay [15] (6 Congenital Diafragmatic Hernias and 2 EA-TEF) on decreased cerebral oxygen saturation measured by Near Infra Red Spectrometry (NIRS) might cause concern. These changes and also the decreased arterial pH values had not recovered after 24 hours. However the real value of NIRS is still not clear and is extensively discussed in a study by Pennekamp [31]. So far, the long term effect on brain development remains unknown but will have to be followed very carefully.
In the study by Kalfa et al [32] a cohort of 49 neonates who underwent MAS was investigated, among them five with esophageal atresia. They also found decreased values of saturation due to thoracic insufflation of CO2. Some other data are reported, such as thermic loss, which is proportional to duration of operation, and a decreased systolic arterial pressure, responding to vascular expansion. But these data are not comparative to open surgery.
Krosnar [16] also noted a decrease of oxygen saturation, and their patients required 100% inspired oxygen in order to maintain the saturation above 85%. They also experienced difficulties in end-tidal CO2 monitoring. But on the other hand Szavay [10] in his retrospective comparative analysis in 68 patients of which 25 were operated via MAS showed no differences in postoperative pCO2 max levels as in postoperative PH and base excess.
What do these findings mean?
To begin with, all papers are retrospective studies with inconsistent reporting of results. Obviously, the multi-center study by Holcomb [11] et al should be seen as the standard at this moment with only few institutions reporting on datasets of more than 20 MAS procedures [5,13,2,10,12,4] of which one comparative multicenter study [4]. Even if these papers are compiled no consistent pattern arises to show superiority or inferiority of MAS versus open repair in terms of early post-operative results.
Secondly, almost all reports come from pioneers in this field who have endeavoured with great zeal to advance the skills in pediatric MAS. On one hand, this implies that these studies represent early experiences and learning curves. On the other hand, these results were obtained by the experts and therefore may be difficult to attain by less experienced surgeons. There is still a world to win in MAS as spreading of MAS is possible in centres without pioneers. After passing their learning curves their results would become better and the patients could benefit from it. Already from adult literature we know that there are benefits of minimal invasive surgery when compared with open surgery by means of better cosmesis, body-image, lenght of stay and reduced postoperative complications [33 34 35].
One of the reasons to advocate MAS for EA-TEF repair is the cosmesis and elimination of shoulder function disturbances and scoliosis, that in the past has been reported after open thoracotomies. But until now hard evidence is not available for either for the contention that MAS gives better cosmetic and functional results, or for the better results of muscle-sparing thoracotomies in children. It is interesting that also breast-development, chronic pain (in 50%) and even paraplegia is reported after thoracotomy [36,37,38].

Another argument for MAS could be the reduced need for opioid administration postoperatively.The effects of MAS on *post-operative pain* as measured by opioid requirements were studied by Ceelie [17] et al in 10 CDH and 14 EA patients. No differences were found compared to matched controls (20 CDH and 28 EA) concerning cumulative opioid doses at different time points postoperatively.

An improved esophageal function after thoracoscopic repair, represented by more effective motility and less gastro-esophageal reflux have not been demonstrated in the patients series of Kawahara [8].

Could MAS have negative influences in comparison to open repair?

The insufflation of the pleural cavity appears to have greater impact on arterial oxygen saturation particularly in cerebro than open repair, as demonstrated by Bishay [15] using NIRS. But as mentioned earlier no comparative study has been done and the validation in open surgery for EA with TEF has not been done.

In summary, making up the balance between MAS and open repair, there appear to be no differences in short term results, both in terms of complications and postoperative pain or ICU-stay. Little is known about the long term outcomes, but again, no differences have been recorded. So far there is no data available on the cosmetic or shoulder/spine/chestwall outcomes after MAS. However Holcomb is mentioning that ample literature is now available about long term sequelae from thoracotomies such as, besides scoliosis, mammary maldevelopment and chronic postoperative pain, even after muscle-sparing thoracotomy [39]. Some concern has been raised about the harmful effects of MAS in newborns on cerebral perfusion and subsequent development.

This emphasises the need for a prospective, randomised trial as has already been stated by Holcomb [11] in 2005.

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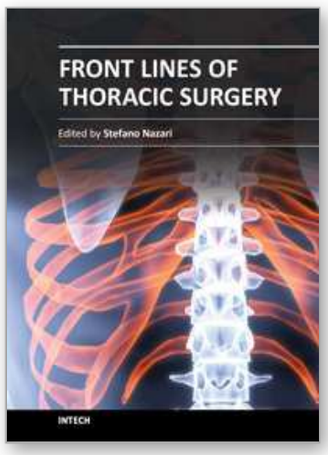

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Front Lines of Thoracic Surgery collects up-to-date contributions on some of the most debated topics in today's clinical practice of cardiac, aortic, and general thoracic surgery,and anesthesia as viewed by authors personally involved in their evolution. The strong and genuine enthusiasm of the authors was clearly perceptible in all their contributions and I'm sure that will further stimulate the reader to understand their messages. Moreover, the strict adhesion of the authors' original observations and findings to the evidence base proves that facts are the best guarantee of scientific value. This is not a standard textbook where the whole discipline is organically presented, but authors' contributions are simply listed in their pertaining subclasses of Thoracic Surgery. I'm sure that this original and very promising editorial format which has and free availability at its core further increases this book's value and it will be of interest to healthcare professionals and scientists dedicated to this field.

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