Journal of Pediatric Surgery 52 (2017) 247–251

Contents lists available at ScienceDirect

Journal of Pediatric Surgery

journal homepage: www.elsevier.com/locate/jpedsurg

Does thoracoscopy have advantages over open surgery for asymptomatic congenital lung malformations? An analysis of 1626 resections

Stephen Adams [a], Matthew Jobson [a], Patarawan Sangnawakij [b], Adam Heetun [a], Anthony Thaventhiran [a], Navroop Johal [a], Dankmar Böhning [b], Michael P. Stanton [a,*]

[a] Department of Paediatric Surgery, University Hospital Southampton NHS Foundation Trust, Southampton, Hampshire, UK
[b] Southampton Statistical Sciences Research Institute, University of Southampton, Southampton, Hampshire, UK

ARTICLE INFO

Article history:
Received 2 November 2016
Accepted 8 November 2016

Key words:
Congenital lung lesion
Congenital cystic adenomatoid malformation
Surgery thoracoscopic
Meta-analysis

ABSTRACT

Aim: The apparent incidence of antenatally diagnosed congenital lung malformations (CLM) is rising (1 in 3000), and the majority undergo elective resection even if asymptomatic. Thoracoscopy has been popularized, but early series report high conversion rates and significant complications. We aimed to perform systematic review/meta-analysis of outcomes of thoracoscopic *vs* open excision of asymptomatic CLMs.
Methods: A systematic review according to PRISMA guidelines was performed. Data were extracted for all relevant studies (2004–2015) and Rangel quality scores calculated. Analysis was on 'intention to treat' basis for thoracoscopy and asymptomatic lung lesions. Meta-analysis was performed using the addon package METAN of the statistical package STATA14™; $p < 0.05$ was considered significant.
Results: 36 studies were eligible, describing 1626 CLM resections (904 thoracoscopic, 722 open). There were no randomized controlled trials. Median quality score was 14/45 (IQR 6.5) 'poor'. 92/904 (10%) thoracoscopic procedures were converted to open. No deaths were reported. Meta-analysis showed that regarding thoracoscopic procedures, the total number of complications was significantly less (OR 0.63, 95% CI 0.43, 0.92 $p < 0.02$, 12 eligible series, 912 patients, 404 thoracoscopic). Length of stay was 1.4 days shorter (95%CI 2.40, 0.37 $p < 0.01$). Length of operation was 37 min longer (95% CI 18.96, 54.99 $p < 0.01$). Age, weight, and number of chest tube days were similar. There was heterogeneity (I^2 30%, $p = 0.15$) and no publication bias seen.
Conclusions: A reduced total complication rate favors thoracoscopic excision over thoracotomy for asymptomatic antenatally diagnosed CLMs. Although operative time was longer, and open conversion may be anticipated in 1/10, the overall length of hospital stay was reduced by more than 1 day.
Level of evidence: 4 (based on lowest level of article analyzed in meta-analysis/systematic review).

Although controversy exists as to the management of antenatally diagnosed congenital lung malformations (CLM), published series describe that elective surgery is undertaken in the majority (70%), even if they have been asymptomatic [1–3]. The apparent incidence of CLM has risen dramatically from previous reports of 1 in 30,000, to one recent fetal register and population study estimating as high as 1 in 2500, largely because of improvements in prenatal sonography [4]. Therefore, increasing numbers of infants worldwide currently undergo pre-emptive surgical resection, usually lobectomy.

There are several examples of pediatric conditions where minimally invasive surgery has demonstrable benefits in terms of analgesia requirements, smaller scars and shorter lengths of stay. However, there are also specific examples where laparoscopic surgery may have worse long-term outcomes [5]. Reports of thoracoscopic lobectomy for CLM vary and some have described high conversion rates (up to 20%) and significant complications [6–8].

The only previous meta-analysis of thoracoscopic and open CLM resection included 216 patients from six reports (all pre-2010), two of which described only four patients in each treatment arm [9–11]. Since this report, there has been a large number of high-volume case series of CLM resection. In addition there are a significant number of studies including only thoracoscopic or open CLM resections without comparison.

In view of the increase in both the incidence and available data on surgical outcomes, we aimed to perform a systematic review and meta-analysis of the published results of thoracoscopic and open CLM resections. We chose to focus on the outcomes of surgery for asymptomatic cases—the patients in whom controversy remains as to whether conservative or surgical management should be undertaken. This focus was also to try and minimize possible selection bias of patients who were symptomatic being considered less suitable preoperatively for a thoracoscopic approach. In order to include as many patient outcomes as possible we also aimed to further develop meta-analysis methodology. This ensured that reports including only means and sample sizes of

* Corresponding author at: Department of Paediatric Surgery, University Hospital Southampton NHS Foundation Trust, Southampton, Hampshire, SO16 6YD, UK. Tel.: +44 2381 206489; fax: +44 2381 204750.
E-mail address: Michael.stanton@uhs.nhs.uk (M.P. Stanton).

http://dx.doi.org/10.1016/j.jpedsurg.2016.11.014
0022-3468/

Table 1
Inclusion/exclusion criteria, search terms and dataset for systematic review.

Inclusion criteria	Exclusion criteria
Published in peer reviewed journal	Age < 28 days old
Congenital lung lesion	Age > 18 years
Asymptomatic child >28 days old	Respiratory symptoms/pneumonia
All languages	Case reports
	Abstracts with unpublished papers
Search terms	
Congenital cystic adenomatous malformation or CCAM	Congenital pulmonary airways malformation or CPAM
Thoracocotomy	Segmentectomy
Thoracoscopy	Bronchogenic cyst
Bronchopulmonary sequestration or BPS	Video-assisted thoracoscopic surgery or VATS
Minimally invasive surgery or MIS	Congenital lung lesion
Pulmonary sequestration	Prenatal lung lesion
Minimal access surgery	Congenital lobar emphysema (or CLE)
Lobectomy	Echogenic lung lesion
Dataset	
Age, sex, weight	Complications
Length of follow-up	Total, death, malignancy on histology
Number of thoracoscopic cases	Early: bleeding, wound infection, chest infection, tracheal injury, prolong air leak,
Conversions to open	pneumothorax, unplanned return to theater, other
Number of open cases	Late: recurrence/inadequate resection, chest wall deformity, scoliosis, other
Types of lesions excised	
Length of operation Length of stay	

both treatment possibilities could be compared, anticipating that most series would not include an estimate of variability.

1. Methods

A systematic review was undertaken following PRISMA guidelines [12]. Two independent reviewers searched PubMed, EmBASE and Google Scholar databases using the search terms and inclusion/exclusion criteria as detailed in Table 1 for the period 2004–2015. The abstracts were assessed for relevance and reviewed in committee to arbitrate inclusion as necessary. Full text articles were obtained and an agreed dataset (Table 1) was collected from each included paper, specifically focusing on operative outcomes of patients who were asymptomatic. A further two independent reviewers assessed the quality of all

Table 2
Results of systematic review and quality scoring.

Ref	Author	Year	Country	Total number	Thoracoscopic	Open	Conversion to open	Age at surgery (months)	Rangel score
[14]	Aziz et al.	2004	Canada	15	0	15	N/A	9	14.5 (poor)
[11]	Tölg et al.	2005	France	8	4	4	1 (25%)	66	12.5 (poor)
[15]	de Lagausie et al.	2005	France	8	8	0	2 (25%)	10	11 (poor)
[16]	Jesch et al.	2005	Germany	5	5	0	0 (0%)	1	13.5 (poor)
[17]	Truitt et al.	2006	USA	12	12	0	0 (0%)	10	5.5 (poor)
[18]	Cano et al.	2006	USA	6	6	0	0 (0%)	10	8.5 (poor)
[19]	Diamond et al.	2007	Canada	36	12	24	2 (17%)	7	21 (fair)
[20]	Sundararajan and Parikh	2007	UK	29	20	9	7 (35%)	14	16.5 (fair)
[21]	Albanese and Rothenberg	2007	USA	144	144	0	3 (2%)	Not recorded	18 (fair)
[22]	Calvert and Lakhoo	2007	UK	16	0	16	N/A	8	7 (poor)
[23]	Chow et al.	2007	Hong Kong	6	0	6	N/A	4	8 (poor)
[24]	Vu et al.	2008	USA	36	12	24	6 (50%)	5	20.5 (fair)
[25]	Rothenberg	2008	USA	97	97	0	4 (4%)	46	11 (poor)
[26]	Sueyoshi et al.	2008	Japan	8	0	8	N/A	1	11 (poor)
[27]	Tsai et al.	2008	USA	105	0	105	N/A	3	12.5 (poor)
[28]	Rahman and Lakhoo	2009	UK	28	14	14	1 (7%)	9	18 (fair)
[29]	Zeidan et al.	2009	France	6	6	0	1 (17%)	5	10.5 (poor)
[30]	Nagata et al.	2009	Japan	5	0	5	N/A	5	8.5 (poor)
[31]	Tarrado et al.	2010	Spain	6	6	0	0 (0%)	9	5 (poor)
[32]	Kaneko et al.	2010	Japan	7	7	0	0 (0%)	1	14 (poor)
[33]	Ferreira et al.	2010	Brazil	35	0	35	N/A	17	13 (poor)
[34]	Rothenberg et al.	2011	USA	75	75	0	1 (1%)	4	12 (poor)
[35]	Boubnova et al.	2011	France	30	30	0	6 (20%)	4	21.5 (fair)
[36]	Johnson et al.	2011	USA	15	15	0	0 (0%)	Not recorded	11 (poor)
[37]	Raychaudhuri et al.	2011	Australia	14	0	14	N/A	8	12.5 (poor)
[38]	Reismann et al.	2012	Germany	22	14	8	3 (21%)	4	17 (fair)
[39]	Muller et al.	2012	France	12	12	0	0 (0%)	12	17.5 (fair)
[40]	Cho et al.	2012	Korea	34	7	27	0 (0%)	61	20 (fair)
[41]	Fievet et al.	2012	France	11	9	2	0 (0%)	Not recorded	11.5 (poor)
[6]	Seong et al.	2013	Korea	0	50	0	9 (18%)	38	16.5 (fair)
[42]	Tanaka et al.	2013	Japan	12	12	0	0 (0%)	66	15.5 (poor)
[43]	Lau et al.	2013	Hong Kong	67	39	28	13 (33%)	11	22 (fair)
[44]	Fascetti-Leon et al.	2013	Italy	54	26	28	18 (69%)	Not recorded	14.5 (poor)
[45]	Kunisaki et al.	2014	USA	62	49	13	0 (0%)	12	22 (fair)
[46]	Kulaylat et al.	2015	USA	258	112	146	3 (3%)	3	19 (fair)
[47]	Laje et al.	2015	USA	288	100	188	12 (12%)	2	21 (fair)
	Total			1626	904 (56%)	722	92 (10%)	15	13.8 (Poor)

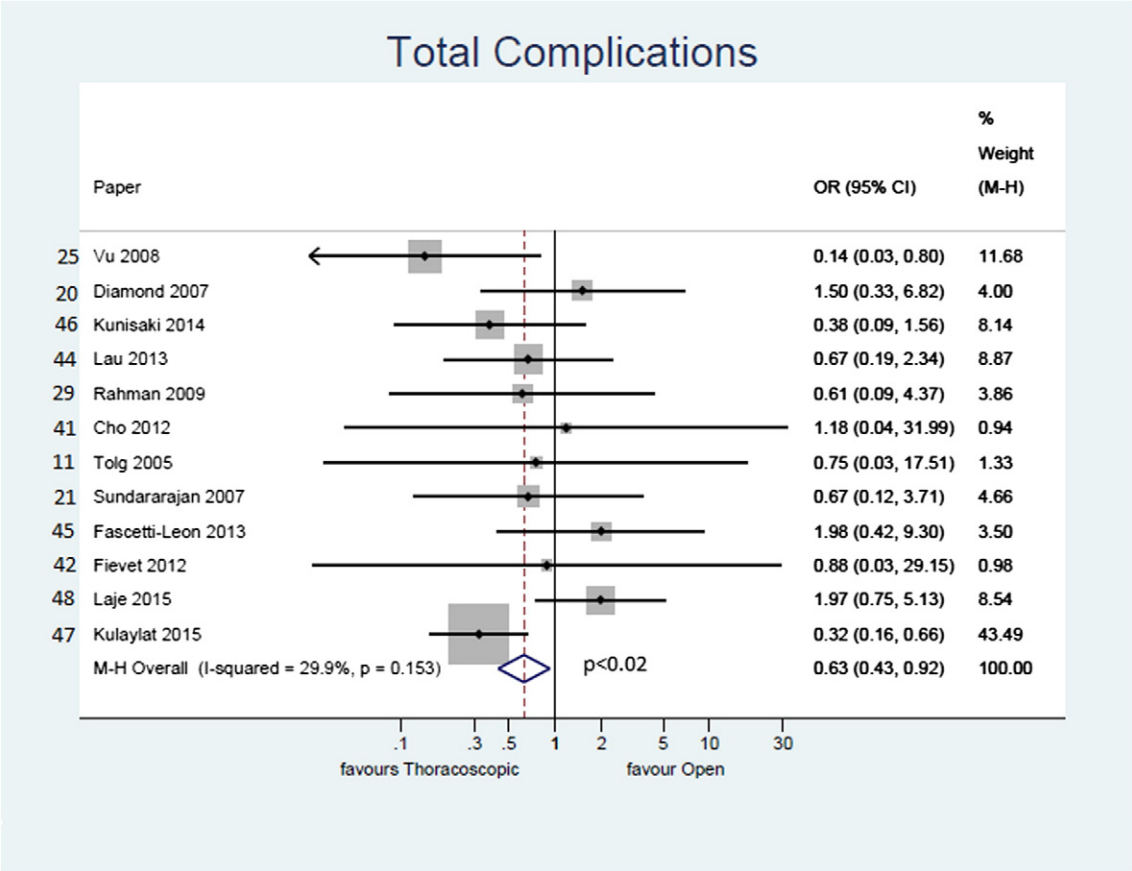

Fig. 1. Forest plot for total complications.

included articles using the Rangel scoring system, a validated quality assessment scale (published in 2003) for assessing retrospective pediatric surgical case series [13]. The mean of these scores was used to rank articles as 'poor' (0–15), 'fair' (16–30) or 'good' (31–45) quality.

Studies with comparative data of open to thoracoscopic lung lesion resection that were included in the systematic review were submitted to meta-analysis. Data were analyzed using Excel™ and STATA14™ with METAN add-on. Analysis was on an intention to treat basis for asymptomatic lung lesions and also on the same basis for thoracoscopic *vs* open operation. A fixed effects model (Mantel–Haenszel) was used. Forest plots were produced and heterogeneity testing (I^2 test) undertaken. Funnel plots were used to assess for publication bias. Results were expressed as odds ratio or actual difference with 95% confidence intervals and *p*-value. Statistical significance was taken as $p < 0.05$.

Having undertaken data collection it became apparent that the majority of studies available did not include a measure of variance in the publication. When the measure of interest is a frequency, for example, when looking at the number of complications, it is possible to compute an estimate of the variance of the measure of interest such as the risk ratio from the frequency data. However, for a quantitative outcome such as the length of hospital stay or number of chest tube days, it is not possible to derive an estimate of the variance of the mean only on the basis of the mean itself and the sample size. We required this in order to be able to state if there are any significant differences between the treatment groups.

Given a set of independent studies such as those in this study, it is possible to construct an estimate of the variance by means of cross-study information using the assumption that the study data follow a normal distribution. Hence we are able to say, for the summary estimator across studies as well as for the individual studies, whether there are significant differences between treatments.

2. Results

2.1. Systematic review

36 studies were included, describing 1626 CLM resections (904 thoracoscopic, 722 open). There were no randomized controlled trials. The summary data are reviewed in Table 2. The quality of these studies was rated as poor on average (median range score 13.8; IQR 6.5) although 14/36 (39%) papers rated 'fair', none achieved 'good'. Follow-up data were not universally available, but averaged 403 days in the minimally invasive group and 268 days for open resection.

Average age at resection was 17 months for thoracoscopy and 13 months for thoracotomy. 92/904 (10%) of thoracoscopic operations were converted to open. 195/1626 (12%) of patients were reported to have developed respiratory symptoms preoperatively, these ranged from wheeze to recurrent infections. These patients were included in the analysis on the basis that resection of the antenatally diagnosed lung lesion was planned irrespective of symptom development. There were no deaths and no reported cases of malignancy in antenatally diagnosed lesions in this series.

2.2. Meta-analysis

12/36 papers were included in the meta-analysis representing 887 CLM resections; 404 thoracoscopic and 483 open. There was no evidence of publication bias. Heterogeneity assessment was negative ($I^2 = 30\%$, $p = 0.15$). Age was not significantly different between the groups, mean 15 months, 1.4 (−8 to 10.9) months older in the open group ($p = 0.8$). Weight was similar in each group, mean 8 kg, 0.4 (−0.2 to 1.0) kg less in the open group ($p = 0.2$).

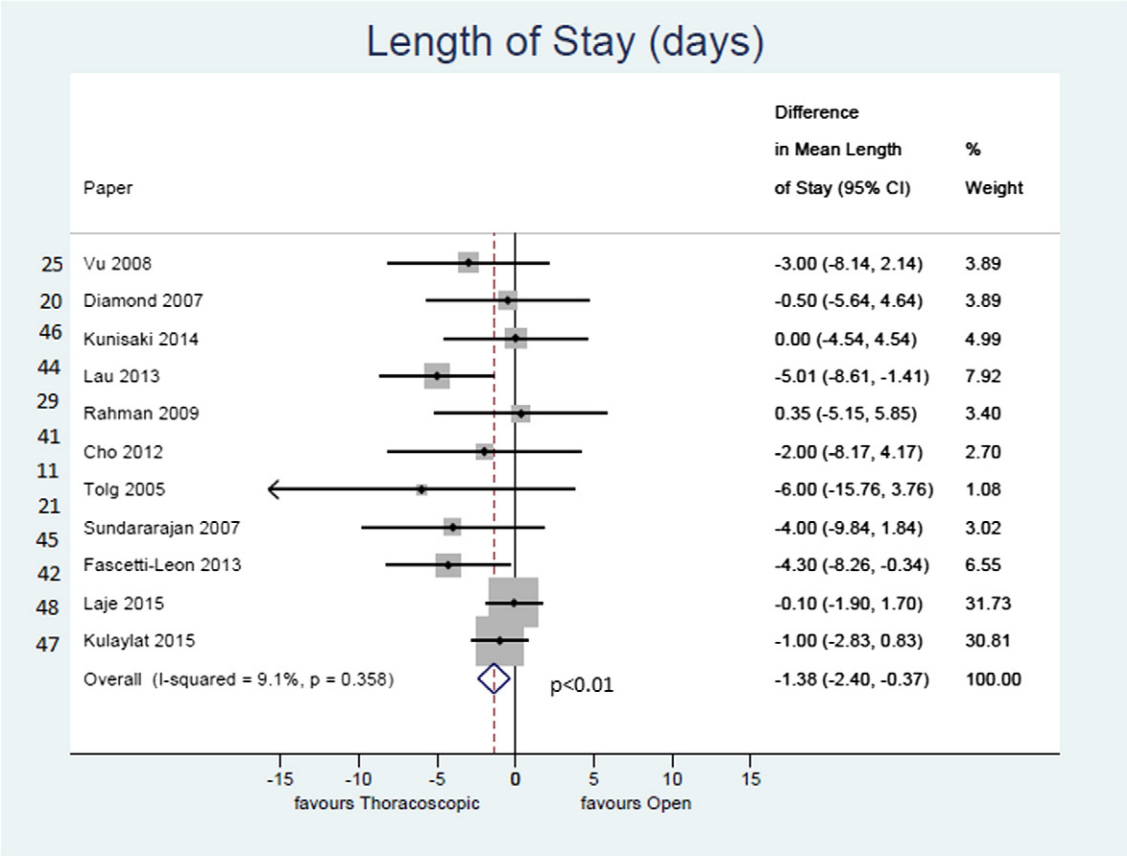

Fig. 2. Forest plot for length of stay in hospital.

Total complications occurred in 63/404 (16%) of the analyzed thoracoscopic operations and in 87/483 (18%) of open. Total complications were significantly less frequent in the thoracoscopic group, OR 0.69 (0.41–1.17, $p = 0.018$) (Fig. 1). Individual complications were infrequent enough to preclude further analysis. Mean length of stay was 5.5 days, the forest plot showing a hospital stay 1.4 (0.4–2.4) days shorter in the minimally invasive group ($p = 0.008$) (Fig. 2). Operative time averaged 142 min and was 37 (19–55) min longer for thoracoscopy ($p < 0.0005$). Chest tube days were similar between the groups, averaging 3.3 days, being a nonsignificant 0.79 (−0.02 to 1.59, $p = 0.055$) days shorter in the thoracoscopic group.

3. Discussion

This study has demonstrated that, on the basis of available literature, thoracoscopic resection is at least as safe as open surgery for asymptomatic antenatally-diagnosed CLMs. We found the total complication rate and length of stay favored thoracoscopy. Although we have demonstrated a significant difference in the total complication rates of open and thoracoscopic resections, these were in fact quite similar (18% *vs* 16% respectively). In our view, this could be viewed as demonstrating that thoracoscopy does not have a higher associated complication rate.

Thoracoscopy was associated with a longer operative time (by 37 min), this was off-set by a shorter hospital stay of 1.4 days. Approximately 10% of cases started thoracoscopically were converted to open thoracotomy.

The strength of this study lies in being able to analyze a relatively large number of patient outcomes (904 thoracoscopic *vs* 722 open thoracotomy, with a total of 1626 patients). The only previous meta-analysis on thoracoscopic CLM resection was published by Nasr and Bass in 2012. For this study, 6 studies were analyzed with a total of 216 patients; in two series, very small numbers were compared—4 in each treatment arm.

A greater number of papers have become available since 2010. We have developed a meta-analysis theory to allow estimates of variance from studies which only reported mean values and sample sizes. Thus we were able to compare a much larger number of series and patients.

The weakness of this study lies in the quality of available reported data. No randomized controlled trials have been published on this subject, so we relied largely on retrospective case series. According to Rangel scoring, overall study quality was on average 'poor'. Inherent bias in reporting may be present. It is possible, for example that cases considered likely to be relatively simple, *i.e.,* small malformations, would be more likely to be offered thoracoscopy than patients with larger, complex cysts. Our focus was on asymptomatic cases, mainly as this is the group at the center of the controversy of surgery *vs* conservative management. In all series, elective resection was planned for all included patients, however 11.5% of patients from the systematic review had respiratory symptoms preoperatively. Respiratory symptoms varied from wheeze to recurrent chest infections. This has been proposed potentially to influence not only the choice of approach, but also the complexity of surgery (and outcomes) [28].

4. Conclusion

On the basis of available reported data, thoracoscopic resection of asymptomatic antenatally diagnosed congenital lung malformations is associated with a (slightly) lower total complication rate, a shorter hospital stay and a longer operative time. Thoracoscopic resection is, therefore, not associated with more risks than open surgery. These data should be of use in counseling parents preoperatively if resection of asymptomatic lung lesions is felt to be necessary.

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