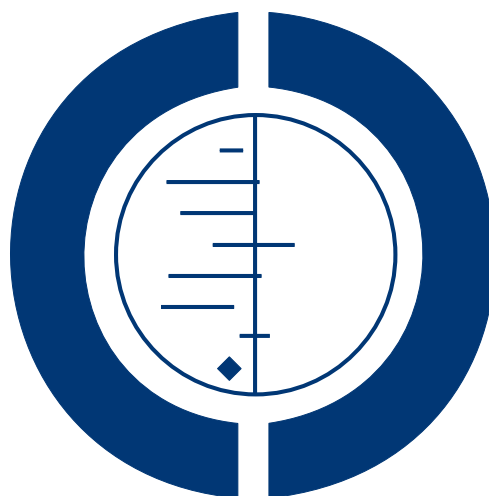


Interventions for primary (intrinsic) tracheomalacia in children (Review)

Masters IB, Chang AB



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[Intervention Review]

Interventions for primary (intrinsic) tracheomalacia in children

I Brent Masters¹, Anne B Chang²

¹Respiratory Medicine, Royal Children's Hospital, Brisbane, Australia. ²Respiratory Medicine Level 3 Woolworths Bldg, Royal Children's Hospital, Brisbane and Menzies School of Health Research, CDU, Darwin, Brisbane, Australia

Contact address: I Brent Masters, Respiratory Medicine, Royal Children's Hospital, Herston Rd, Herston, Brisbane, Queensland, 4029, Australia. brent_masters@health.qld.gov.au.

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ABSTRACT

Background

Tracheomalacia, a disorder of the large airways where the trachea is deformed or malformed during respiration is commonly seen in tertiary paediatric practice. It is associated with a wide spectrum of respiratory symptoms from life threatening recurrent apnea to common respiratory symptoms such as chronic cough and wheeze. Current practice following diagnosis of tracheomalacia include medical approaches aimed at reducing associated symptoms of tracheomalacia, ventilation modalities of continuous positive airway pressure (CPAP) and bi-level positive airway pressure (BiPAP) and, surgical approaches aimed at improving the caliber of the airway (airway stenting, aortopexy, tracheopexy).

Objectives

To evaluate the efficacy of medical and surgical therapies for children with intrinsic (primary) tracheomalacia.

Search methods

The Cochrane Central Register of Controlled Trials (CENTRAL), the Cochrane Airways Group Specialised Register, MEDLINE and EMBASE databases were searched by the Cochrane Airways Group. The latest searches were performed in February 2008.

Selection criteria

All randomised controlled trials of therapies related to symptoms associated with primary or intrinsic tracheomalacia.

Data collection and analysis

Results of searches were reviewed against pre-determined criteria for inclusion. No eligible trials were identified and thus no data were available for analysis.

Main results

No randomised controlled trials (RCTs) that examined therapies for intrinsic tracheomalacia were found. Eight of the more recent (last 11 years) non randomised controlled trials reported a benefit from the various surgical interventions. The success was however not universal and in some studies severe adverse events occurred.

Authors' conclusions

There is currently an absence of evidence to support any of the therapies currently utilised for management of intrinsic tracheomalacia. It is unlikely that any RCT on surgically based management will ever be available for children with severe life threatening illness associated with tracheomalacia. For those with less severe disease, RCTs are clearly needed. Outcomes of these RCTs should include measurements of the trachea and physiological outcomes in addition to clinical outcomes.

PLAIN LANGUAGE SUMMARY

Interventions for primary (intrinsic) tracheomalacia in children

The clinical spectrum of tracheomalacia in children ranges from minimal symptoms to severe life threatening disease. Available medical and surgical approaches to treat symptoms associated with tracheomalacia range from simple medical therapies, ventilation, tracheostomy and stents to direct surgical approaches such as aorta/tracheopexy. Using the standard search module of the Cochrane Airways Group, no randomised controlled trials that assessed any therapy for intrinsic tracheomalacia were found. With the lack of evidence, the routine use of any therapies for intrinsic tracheomalacia cannot be assessed. The decision to subject a child to any surgical or medical based therapies will have to be made on an individual basis, with careful consideration of the risk-benefit ratio for each individual situation.

BACKGROUND

Tracheomalacia is a disorder of the large airways where the trachea is deformed or malformed during respiration (Masters 2002). Tracheomalacia is commonly seen in tertiary paediatric practice (Masters 2002) and many of the children are only referred for assessment after repeated failures of therapy which include asthma drug therapies (Gormley 1999, Thomson 2002). This large airway disorder can be classified as primary (intrinsic abnormality of the airway) or secondary (related to compression of trachea by another structure such as a mass). Primary tracheomalacia may occur in isolation, or in association with other malacia disorders (laryngomalacia and bronchomalacia), as part of a syndrome (e.g. Downs syndrome, Ehlers-Danlos syndrome), or with other congenital non-syndromic disorders (e.g. cardiac abnormalities, tracheoesophageal fistula etc) (Austin 2003, Masters 2002). Some have classified tracheomalacia associated with other abnormalities as secondary tracheomalacia assuming that it is related to the compression effects. However, as embryologically these tracheomalacia are related to a developmental abnormality with the associated condition (as opposed to because of the associated condition) (Beasley 1998) and in general do not totally resolve after correction of the associated problem (such as in tracheo-oesophageal fistula (Kovesi 2004) or after thoracic vascular surgery (Horvath 1992, van 1993), we have classified these types of tracheomalacia as primary tracheomalacia with associated abnormalities. True secondary tracheomalacia generally resolves on removal of the of-

fending agent (such as a mediastinal mass or lymph node) and thus will not be discussed in this review.

Tracheomalacia may be diagnosed by flexible and rigid bronchoscopy, radiological airway screening, chest computed tomography (CT) scan, magnetic resonance imaging or tracheo-bronchogram. The current gold standard of diagnosing tracheomalacia is by visual assessment during bronchoscopy (Wright 2003) and flexible bronchoscopy is superior to rigid bronchoscopy for evaluation of tracheo-bronchomalacia (Midulla 2003). Flexible bronchoscopy provides the best assessment for the dynamic airway changes found in tracheo-bronchomalacia (Midulla 2003). The other methods of diagnosis are less reliable and/or have major pitfalls. During flexible bronchoscopy, different visual descriptions of tracheomalacia have been described (Masters 2002). However the associated symptoms are similar (Masters 2002). The most common symptoms at presentation are persistent respiratory symptoms in particular chronic cough and wheeze. These symptoms cover most of the common respiratory symptoms seen in children and thus it not surprising that diagnosis is often delayed (Masters 2002, Wood 1997, Gormley 1999). Gormley and colleagues described that 75% of children with congenital tracheomalacia secondary to congenital vascular anomaly had persistent cough at presentation (Gormley 1999). As these symptoms overlap with other respiratory disorders, it is also not surprising that the diagnosis and management of tracheomalacia is often sub-optimal (Gormley 1999). Other respiratory symptoms include recurrent infections and pneumonia, recurrent cyanosis, stridor, exertional dyspnoea

and effort intolerance. Severe tracheomalacia may also be associated with difficult anaesthesia (Austin 2003) and increased CO₂ value during flexible bronchoscopy under general anaesthesia is associated with these airway lesions (Chang 2004). Non respiratory symptoms related to tracheomalacia have also been described and these include dysphagia (Agrawal 1999) and gastroesophageal reflux (Bibi 2001).

The respiratory symptoms attributed to tracheomalacia are most likely primarily to be related to the effect of a narrowed airway generating altered airflow. Wheeze is generated from altered flow through a narrowed tube. Misdiagnosis of asthma in children with airway malacia disorders has been well described (Finder 1997). Cough is likely related to reduction of muco-ciliary clearance as the compressed airway impedes clearance of secretions (Finder 1997) which sets up a bronchitic process distal to the lesion. Exactly why this occurs is unknown but the possibility of a more subtle process that involves functional abnormalities in the development of the neuro-vascular and airway immunological, smooth muscle and epithelial cell lines would be biologically possible, but have not been described. Thus, it is also plausible that a change in anatomical improvement (if possible) may not necessary result in symptomatic improvement.

Current practice following diagnosis of tracheomalacia include medical approaches aimed at reducing associated symptoms of tracheomalacia and surgical approaches aimed at improving the caliber of the airway (airway stenting, aortopexy) and thus reducing associated symptoms. These interventions may have serious and significant adverse events. Hence, there is a need for systematic evaluation of the effects of interventions aimed at reducing the respiratory symptoms related to tracheomalacia.

OBJECTIVES

To evaluate the efficacy of medical and surgical therapies for children with intrinsic (primary) tracheomalacia.

METHODS

Criteria for considering studies for this review

Types of studies

All randomised controlled trials of therapies related to symptoms associated with primary or intrinsic tracheomalacia.

Types of participants

Children aged < 15 years with tracheomalacia with associated respiratory symptoms.

Exclusion criteria: secondary tracheomalacia.

Types of interventions

All randomised controlled comparisons of therapies for symptoms associated with primary or intrinsic tracheomalacia. Trials that included the use of other medications or interventions were included if all participants had equal access to such medications or interventions.

Types of outcome measures

It was planned to obtain data on at least one of the following outcome measures:

Primary outcome:

a) proportions of participants who were not cured or not substantially improved at follow up (clinical failure)

Secondary outcomes:

b) proportions of participants who were not cured at follow up
c) proportions of participants who not substantially improved at follow up

d) mean difference in number of respiratory episodes (defined by diary cards or acute respiratory illness score)

e) proportions requiring hospitalisation for respiratory illness

f) mean difference in symptoms and signs (mean improvement in clinical state)

g) proportions developing new respiratory complications such as bronchiectasis, bronchiolitis obliterans, etc.

h) proportions requiring acute or complicated airway intervention (prolonged intubation, tracheostomy, etc.)

i) proportions experiencing adverse effects of the intervention (e.g. death from surgery, surgical complications etc.)

The proportions of participants who failed to improve on treatment and the mean clinical improvement were to be determined using the following hierarchy of assessment measures (i.e. where two or more assessment measures are reported in the same study, the outcome measure that is listed first in the hierarchy would be used).

i) Objective measurements of cough indices (cough frequency)

ii) Symptomatic (Quality of life, Likert scale, visual analogue scale, level of interference of respiratory symptoms such as cough, wheeze, cyanotic events etc using diaries) - assessed by child

iii) Symptomatic (Quality of life, Likert scale, visual analogue scale, level of interference of respiratory symptoms such as cough, wheeze, cyanotic events etc using diaries) - assessed by the parents/ carers

iv) Symptomatic (Likert scale, visual analogue scale, level of interference of respiratory symptoms such as cough, wheeze, cyanotic events etc using diaries) - assessed by clinicians

- v) Pulmonary function tests
- vi) Bronchoscopic assessment of tracheomalacia (using flexible bronchoscopy)
- vii) Relevant airway markers consistent with neutrophilic inflammation

Search methods for identification of studies

The following topic search strategy was used to identify the relevant randomised controlled trials listed on the electronic databases:

("tracheomalacia" OR "tracheo-malacia" OR "malacia" OR "trachea abnormalities" OR "tracheal diseases" all as (text word) or (MeSH)) AND ("child" OR "children" OR "infant" as (text word) or (MeSH))

The full search strategies are shown in [Table 1](#) and [Table 2](#).

Trials were identified from the following sources:

1. The Cochrane Controlled Trials Register (CENTRAL) which includes the Airways Collaborative Review Group Specialised Trials Register
2. MEDLINE 1966-2004. Topic search strategy combined with the MEDLINE randomised controlled trial search filter as outlined in the Airways Group module
3. OLDMEDLINE 1951-1965. Topic search strategy combined with the MEDLINE randomised controlled trial search filter as outlined in the Airways Group module
4. EMBASE 1980-2004. Topic search strategy combined with the EMBASE randomised controlled trial search filter as outlined in the Airways Group module
5. The list of references in relevant publications
6. Written communication with the authors of trials included in the review when necessary

The latest searches were performed in February 2008

Data collection and analysis

Study Selection

Retrieval of studies: From the title, abstract or descriptions, two reviewers independently reviewed literature searches to identify potentially relevant trials for full review. Searches of bibliographies and texts were conducted to identify additional studies. From the full text using specific criteria, the same two reviewers independently selected trials for inclusion. Agreement would have been measured using Kappa statistics. Disagreement would have been resolved by consensus.

Assessment of Quality

Studies included in the review would have undergone quality assessment performed independently by both reviewers. Four components of quality would have been assessed:

1. Allocation concealment. Trials would have been scored as: Grade A: Adequate concealment, Grade B: Unclear, Grade C: Clearly

inadequate concealment (Grade A = high quality)

2. Blinding. Trials would have been scored as: Grade A: Participant and care provider and outcome assessor blinded, Grade B: Outcome assessor blinded, Grade C: Unclear, Grade D: No blinding of outcome assessor (Grade A, B = high quality)

3. Reporting of participants by allocation group. Trials would have been scored as: Grade A: The progress of all randomised children in each group described, Grade B: Unclear or no mention of withdrawals or dropouts, Grade C: The progress of all randomised children in each group clearly not described (Grade A = high quality)

4. Follow-up. Trials would have been scored as: Grade A: Outcomes measured in >90% (where withdrawals due to complications and side-effects are categorised as treatment failures), Grade B: Outcomes measured in 80 to 90%, Grade C: Unclear, Grade D: Outcomes measured in <80% (Grade A = high quality)

While only the allocation concealment quality would have been displayed in the meta-analysis figures, all assessments would have been included in the 'Characteristics of included studies' table. Inter-reviewer reliability for the identification of high quality studies for each component would have been measured by the Kappa statistic.

Each study would have been assessed using a one to five scale described by Jadad ([Jadad 1996](#)) and summarised as follows:

Was the study described as randomised? (1 = yes; 0 = no)

Was the study described as double blind? (1 = yes; 0 = no)

Was there a description of withdrawals and dropouts? (1 = yes; 0 = no)

Was the method of randomisation clearly described and appropriate? (1 = yes; 0 = no)

Was the method of double blinding well described and appropriate? (1 = yes; 0 = no)

Data Extraction

Trials that satisfy the inclusion criteria would have been reviewed and the following information recorded: study setting, year of study, source of funding, patient recruitment details (including number of eligible children), inclusion and exclusion criteria, randomisation and allocation concealment method, numbers of participants randomised, blinding (masking) of participants, care providers and outcome assessors, intervention (duration and type), control, co-morbidities (all medical problems with particular attention to genetic syndromes and co-morbidities), existing respiratory problems, co-interventions, numbers of patients not followed up, reasons for withdrawals from study protocol (clinical, side-effects, refusal and other), details on side-effects of therapy, and whether intention-to-treat analyses were possible. Data would have been extracted on the outcomes described previously. Further information would have been requested from the authors where required.

Data Analysis

For the dichotomous outcome variables of each individual study, relative and absolute risk reductions would have been calculated using a modified intention-to-treat analysis. This analysis assumes

that children not available for outcome assessment have not improved (and probably represents a conservative estimate of effect). An initial qualitative comparison of all the individually analysed studies would examine whether pooling of results (meta-analysis) is reasonable. This would take into account differences in study populations, inclusion/exclusion criteria, interventions, outcome assessment and estimated effect size.

The results from studies that meet the inclusion criteria and reported any of the outcomes of interest would have been included in the subsequent meta-analysis. The summary weighted risk ratio and 95% confidence interval (fixed-effect model) would have been calculated using the inverse of the variance of each study result for weighting (Cochrane statistical package, RevMan 4.2). Numbers needed to treat (NNT) would have been calculated from the pooled OR and its 95% CI applied to a specified baseline risk using an online calculator (Cates 2003). This calculator converts the risk in the placebo group to the corresponding odds, applies the OR to estimate the odds in the treated group, and converts that odds to the corresponding risk and calculates the risk difference, the inverse of which is the NNT. The outcome indices would have been assumed to be normally distributed continuous variables so the mean difference in outcomes can be estimated (weighted mean difference). If studies reported outcomes using different measurement scales, the standardised mean difference would have been estimated. In cross-over trials, if data is combined with parallel studies only data from the first arm would have been used (Elbourne 2002). In addition, for pooled cross-over studies, mean treatment differences would have been calculated from raw data, extracted or imputed and entered as fixed effects generic inverse variance (GIV) outcome to give weighted SD unit difference and 95% confidence intervals (RevMan 4.2). Heterogeneity between the study results would have been tested to see if it reached statistical significance using a chi squared test, and the proportion of heterogeneity arising from between study differences would have been assessed with the I^2 statistic (Higgins 2003). The 95% confidence interval estimated using a random-effects model would have been included whenever there are concerns about statistical heterogeneity.

SUB-GROUP ANALYSIS:

An a priori subgroup analysis was planned for

1. Age: infants (<12 months) or children (aged 1-14 years)
2. Presence of congenital (cardiac, tracheoesophageal fistula) or syndromes
3. Medical therapies
4. Surgical therapies

Sensitivity analyses was planned to assess the impact of the potentially important factors on the overall outcomes:

- a) study quality
- b) study size
- c) variation in the inclusion criteria
- d) differences in other medications used in the intervention and comparison groups
- e) differences in outcome measures

- f) analysis using random-effects model
 - g) analysis by 'treatment received'
 - h) analysis by 'intention-to-treat'
 - i) analysis by study design: parallel and cross over studies
- Publication bias would have been tested using a funnel plot.

RESULTS

Description of studies

See: [Characteristics of excluded studies](#).

The searches identified 13 potential studies but none fulfilled the study eligibility criteria. An update search run in February 2008 yielded 41 references of which none met the eligibility criteria of the review.

Risk of bias in included studies

Not applicable.

Effects of interventions

The Airways Group search identified 757 potentially relevant titles. After assessing the abstracts, 13 studies were considered for inclusion into review but none fulfilled the study eligibility criteria. Eight of the more recent non controlled studies are summarised in the excluded table.

DISCUSSION

No randomised controlled trials of therapies for symptoms associated with primary or intrinsic tracheomalacia were identified. There are numerous cohort descriptive studies with varying numbers of patients that reported on a variety of interventions (mainly surgical) to increase the airway caliber. Most of these children managed surgically had presumably the severe end of the clinical spectrum, with life threatening apnoea episodes. These cohort studies (see excluded table) have highlighted the importance of interventions in terms of clinical improvement. However these surgical procedures (tracheopexy, aortopexy and/or stenting) are not universally successful and have associated morbidity and mortality (Valerie 2005). CPAP alters forced expiratory flow in infants but the authors did not describe clinical correlates (Davis 1998). There are no studies that quantitatively defined severity either anatomically or clinically. Also, when tracheomalacia is associated with a vascular compression, surgical correction of the vascular compression alleviates major respiratory symptoms in most (68%) but

not in a significant number of children (Bonnard 2003, Benjamin 1976).

Physiological measurement studies of lung function have shown short-term benefits in function in lung mechanics and improvement in spirometric parameters for selective children managed with surgical intervention (Zinman 1995) and CPAP (Davis 1998). However there are no quantitative assessments of severity of the tracheomalacia at the entry or end point. Interpretation of lung function may be limited unless paired (pre and post intervention) data are obtained, as children with these airway abnormalities may have reduced lung growth (Agrawal 1999). At the mild end of the spectrum there are no studies that have assessed the disease impact, the management of intercurrent respiratory illness or symptoms associated with tracheomalacia.

AUTHORS' CONCLUSIONS

Implications for practice

With the lack of evidence, recommendations for the routine use

of any therapies for intrinsic tracheomalacia cannot be made. The decision to subject a child to surgical and/or medical based therapies will have to be made on an individual basis, with careful consideration of the risk-benefit ratio for each individual situation.

Implications for research

It is unlikely that any RCT on surgically based management will ever be available for children with severe life threatening illness associated with tracheomalacia. For those with less severe disease, RCTs are clearly needed. In these RCTs, outcomes should include measurements of the trachea and physiological based outcomes in addition to clinical outcomes.

ACKNOWLEDGEMENTS

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Corbally 1993 *{published data only}*

Corbally MT, Spitz L, Kiely E, Breerton RJ, Drake DP. Aortopexy for tracheomalacia in oesophageal anomalies. *European Journal of Pediatric Surgery* 1993;**3**(5):264–6.

Davis 1998 *{published data only}*

Davis S, Jones M, Kisling J, Angelicchio C, Tepper RS. Effect of continuous positive airway pressure on forced expiratory flows in infants with tracheomalacia. *American Journal of Respiratory & Critical Care Medicine* 1998;**158**(1):148–52.

Filler 1993 *{published data only}*

Filler RM, Forte V, Chait P, Weber TR, Othersen HB, Tracy TF, et al. Tracheobronchial stenting for the treatment of airway obstruction. *Journal of Pediatric Surgery* 1993;**33**(2):304–11.

McCarthy 1997 *{published data only}*

McCarthy JF, Hurley JP, Neligan MC, Wood AE. Surgical relief of tracheobronchial obstruction in infants and children. *European Journal of Cardio-Thoracic Surgery* 1997;**11**(6):1017–22.

Nicolai 2001 *{published data only}*

Nicolai T, Huber RM, Reiter K, Merckenschlager A, Hautmann H, Mantel K. Metal airway stent implantation in children: follow-up of seven children. *Pediatric Pulmonology* 2001;**31**(4):289–96.

Vazquez-Jimenez 2001 *{published data only}*

Vazquez-Jimenez JF, Sachweh JS, Liakopoulos OJ, Hugel W, Holzki J, von Bernuth G, Messmer BJ. Aortopexy in severe tracheal instability: short-term and long-term outcome in 29 infants and children. *Annals of Thoracic Surgery* 2001;**72**(6):1898–901.

Vinograd 1994 *{published data only}*

Vinograd I, Klin B, Efrati Y, Barr J, Behar M, Eshel G. Airway obstruction in neonates and children: surgical treatment. *Journal of Cardiovascular Surgery* 1994;**35**(6 Suppl 1):7–12.

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Higgins 2003

Higgins JPT, Thompson SG, Deeks JD, Altman G. Measuring inconsistency in meta-analysis. *BMJ* 2003;**327**: 557–60.

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Wright 2003

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Zinman 1995

Zinman R. Tracheal stenting improves airway mechanics in infants with tracheobronchomalacia. *Pediatric Pulmonology* 1995;**19**(5):275–81.

* Indicates the major publication for the study

CHARACTERISTICS OF STUDIES

Characteristics of excluded studies *[ordered by study ID]*

Study	Reason for exclusion
Abdel-Rahman 2002	Non controlled study. Authors reported on effect of aortopexy on 16 infants and children with tracheomalacia. No intraoperative or postoperative mortality occurred and 13 (81%) had permanent relief of symptoms
Corbally 1993	Non controlled study. Authors reported on 48 patients with repaired congenital oesophageal anomaly who underwent aortopexy for significant tracheomalacia. Indications for aortopexy included recurrent apnoea/cyanosis, near fatal episodes, recurrent respiratory distress and infection and worsening stridor. Aortopexy cured near fatal episodes in all patients and resulted in improvement of airway obstruction in 95%. The procedure failed in 2 patients due to unrecognised bronchomalacia and phrenic nerve palsy
Davis 1998	Non controlled study. Continuous positive airway pressure (CPAP) was used to minimize airway collapse in infants with tracheomalacia. Forced expiratory flows increased with CPAP use
Filler 1993	Non controlled study. The authors reported on their 5-year experience of inserting the Palmaz stent into infants and children who had a variety of major airway obstructions, including tracheomalacia in 8 children. Granulation tissue developed over the stents in five of eight cases. Obstructing granulations were removed by scraping or balloon compression in three and resulted in earlier than the planned removal in two
McCarthy 1997	Non controlled study. Twenty-four infants and children with various causes of airway obstruction including tracheomalacia. Hospital mortality was 8.7%, 19 (79.2%) patients were alive and symptom free. The single most important predictor of mortality was the presence of associated cardiac anomalies
Nicolai 2001	Non controlled study. Authors reported on 7 children with extreme structural central airway obstruction (6 were mechanically ventilated). All patients showed marked improvement of their respiratory obstruction; 6 were weaned at least temporarily from ventilation. Three children are well and at home
Vazquez-Jimenez 2001	Non controlled study. Authors reported on 29 children operated for tracheomalacia associated with oesophageal atresia. No early nor late mortality occurred. Surgery associated morbidity were: reversible lesion of the phrenic nerve was observed in 2 patients, a pneumothorax in 3, and secondary wound healing in 1. In all but one patient symptoms improved markedly or disappeared within days or within the first 3 months postoperatively. An increased susceptibility to respiratory infections was observed in long-term follow-up of children
Vinograd 1994	Non controlled study. Authors reported on surgical management (aortopexy) of 54 children with airway problems, of whom 20 had tracheomalacia. No operative deaths occurred

DATA AND ANALYSES

This review has no analyses.

ADDITIONAL TABLES

Table 1. MEDLINE search strategy

1. tracheomalac\$.mp.
2. tracheo-malac\$.mp.
3. (trache\$ adj5 malac\$).mp.
4. malacia\$.mp.
5. exp Tracheal Diseases/dt, su, th [Drug Therapy, Surgery, Therapy]
6. exp TRACHEA/ab, su [Abnormalities, Surgery]
7. exp BRONCHI/ab [Abnormalities]
8. (trache\$ adj5 abnormal\$).mp.
9. or/1-8
10. ADOLESCENT/ or exp CHILD/ or exp INFANT/ or exp PEDIATRICS/
11. (child\$ or paediat\$ or pediat\$ or adolesc\$ or infan\$ or toddler\$ or bab\$ or young\$ or preschool\$ or pre school\$ or pre-school\$ or newborn\$ or new born\$ or new-born\$ or neo-nat\$ or neonat\$).mp
12. 10 or 11
13. 9 and 12

Table 2. EMBASE search strategy

1. tracheomalac\$.mp.
2. tracheo-malac\$.mp.
3. (trache\$ adj5 malac\$).mp.
4. malacia\$.mp.
5. (trache\$ adj5 abnormal\$).mp.
6. exp TRACHEOMALACIA/
7. or/1-6
8. exp pediatrics/
9. exp CHILD/ or exp INFANT/ or exp ADOLESCENT/
10. (child\$ or paediat\$ or pediat\$ or adolesc\$ or infan\$ or toddler\$ or bab\$ or young\$ or preschool\$ or pre school\$ or pre-school\$ or newborn\$ or new born\$ or new-born\$ or neo-nat\$ or neonat\$).mp.
11. 8 or 9 or 10
12. 7 and 11

WHAT'S NEW

Last assessed as up-to-date: 31 January 2008.

Date	Event	Description
7 April 2008	Amended	Search re-run; no new studies identified for inclusion in the review

HISTORY

Protocol first published: Issue 2, 2005

Review first published: Issue 4, 2005

Date	Event	Description
7 April 2008	Amended	Converted to new review format.
25 July 2005	New citation required and conclusions have changed	Substantive amendment

CONTRIBUTIONS OF AUTHORS

IBM: formulation and writing of protocol. AC: initiation, formulation and writing of protocol. For the review- both IBM and AC: review and selection of studies from search, data extraction and writing of review.

DECLARATIONS OF INTEREST

None known.

SOURCES OF SUPPORT

Internal sources

- Royal Children's Hospital Foundation, Brisbane, Australia.

External sources

- National Health and Medical Research Council, Australia.

INDEX TERMS

Medical Subject Headings (MeSH)

Adolescent; Trachea [*abnormalities]; Tracheal Diseases [*therapy]

MeSH check words

Child; Humans