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Review Article

Surgical versus conservative management of congenital pulmonary airway malformation in children: A systematic review and meta-analysis

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ABSTRACT

Background: The ideal management of infants born with asymptomatic congenital pulmonary airway malformation (CPAM) is controversial. We performed a systematic review and meta-analysis comparing elective resection versus expectant management.
Methods: We searched CENTRAL, MEDLINE, EMBASE, CINAHL, and PubMed for studies describing the management of asymptomatic CPAM and reporting on postoperative morbidity, mortality, and length of hospital stay (LOS). We performed meta-analyses when possible and provide a narrative summary of results.
Results: One nonrandomized prospective and eight retrospective studies met our inclusion criteria. Out of 168 patients, 70 underwent surgery before symptoms developed with seven experiencing postoperative complications (10.0%); 63 developed symptoms while being managed expectantly and subsequently underwent surgery with 20 complications (31.8%). Thirty-five patients continued to be followed nonsurgically (three months to nine years of follow-up). Morbidity was higher with surgery after symptom development (6 studies; odds ratio 4.59, 95% confidence interval (CI) 1.40 to 15.11, $P < 0.01$); there was no difference in LOS (3 studies; mean difference 4.96, 95% CI −1.75 to 11.67, $P = 0.15$). There were no related deaths.
Conclusions: Elective resection of asymptomatic CPAM lesions is safe and prevents the risk of symptom development, which may result in a more complicated surgery and recovery.

Congenital pulmonary airway malformation (CPAM) is a relatively rare congenital disorder characterized by replacement of a portion of lung by a nonfunctioning cystic section of abnormal tissue [1,2]. CPAM represent 25% to 30% of all congenital lung malformations, with a slight male predominance [3]. While the prevalence is estimated to be between 1 in 10,000 and 1 in 35,000 pregnancies [1,3,4], the true prevalence is difficult to discern given the portion that go undiagnosed owing to a lack of clinical symptoms.

There is much variation in the presentation and evolution of CPAM, ranging from prenatal death to respiratory distress in early life to entirely asymptomatic lesions [2,5]. An increasing proportion of neonates are now presenting asymptomatically, as many are identified on antenatal ultrasound. Clinical presentation typically dictates treatment, however when cases of known CPAM are asymptomatic, optimal management is less defined [6,7].

Arguments favoring either elective surgery or expectant management of asymptomatic lesions are many. They include estimates that delaying surgery until symptom onset will result in a more complicated procedure with worse surgical outcomes [8–13], as well as counterarguments stating that, as rates of symptom development are largely unknown [14,15], intervening before symptoms appear may result in exposure of healthy patients to unnecessary surgical risks [15]. These differing viewpoints illustrate the lack of consensus as to whether surgical management or an expectant approach for asymptomatic CPAM is associated with a smaller risk of morbidity in the short and long term.

Our objective was to conduct a systematic review and meta-analysis of all published literature comparing the postoperative outcomes associated with elective surgery (while asymptomatic) versus those following surgery as part of expectant management (i.e., performing surgery only upon the development of symptoms) in children born with asymptomatic CPAM lesions. This research was carried out for the Canadian Association of Pediatric Surgeons (CAPS) Evidence-Based Resource [16], the aim of which is to encourage evidence-based practice in pediatric surgery by making up-to-date evidence easily accessible.

1. Methods

1.1. Selection of study topic

We used a Dephi-like method [17] to determine the issues of greatest concern to pediatric surgeons regarding the surgical management of CPAM.

1.1.1. First round

We sent an online survey to 18 experts with proficiency in this area, identified primarily on the basis of a literature search. This survey was

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hosted on the CAPS website and consisted of the following open-ended question: "In your practice with the surgical management of congenital pulmonary airway malformation, what issues do you find to be controversial and in need of further research and/or consensus?"

1.1.2. Second round

We developed a questionnaire listing all issues raised by the experts in the first round. We sent this questionnaire to the respondents from the first round, asking them to select the three issues which they felt were the most important. The issue that received the highest number of votes is the focus of this review.

1.2. Literature search

To identify all studies on elective surgery and expectant management of asymptomatic CPAM lesions, we conducted an electronic literature search of the Cochrane Central Register of Controlled Trials (CENTRAL), MEDLINE (1966 onwards), EMBASE (1980 onwards), CINAHL (1982 onwards), and PubMed (1966 onwards) in January 2015. We used the search terms ("asymptomatic" AND "congenital" AND "cystic" AND "adenomatoid malformation") OR ("lung" AND "lesion") AND ("management" OR "treatment" OR "therapy."). We excluded any studies on nonhuman subjects and those that did not focus on pediatric patients, as well as any studies that were not published in English, owing to resource limitations. We also excluded editorials, case reviews, any studies that did not evaluate postoperative outcomes, and any studies where it was not possible to extract data only on patients who were asymptomatic at birth. Finally, we hand-searched the reference sections of all relevant articles to identify additional studies. Two independent reviewers conducted all article screening; where consensus on an article could not be reached, a third reviewer was consulted.

1.3. Outcomes

Our primary outcome of interest was postoperative morbidity including respiratory distress, respiratory infection, pneumonia, pneumothorax, and death. Our secondary outcome of interest was length of stay in hospital following surgery (LOS).

1.4. Quality assessment

We used the Methodological Index for Non-Randomized Studies (MINORS) to assess the quality of the included studies, as all were nonrandomized [18]. The MINORS criteria comprise 12 items, each of which is assigned a score of 0, 1 or 2, for a maximum total score of 24 (comparison studies) or 16 (noncomparison studies). Higher scores are indicative of greater methodological quality. Two researchers independently assessed each study using the MINORS criteria and discussed their score for each item to reach a consensus. When consensus could not be reached, a third researcher was consulted. Had we identified any, we would have used the Cochrane "Risk of bias" tool to assess randomized controlled trials [19].

1.5. Data extraction

One reviewer extracted all data from the included studies, and another checked it for accuracy and completeness. We extracted the following data exclusively on patients who were asymptomatic at birth: number of patients undergoing elective surgery, number undergoing surgery as part of expectant management (after symptom development), age at symptom development if applicable, postoperative complications, mortalities, and total length of postoperative hospital stay, as well as number of patients successfully managed conservatively at the end of follow-up, and length of follow-up for these patients.

1.6. Statistical analysis

We conducted our meta-analyses using Review Manager 5.3 [20], using random-effects models [21], to produce an odds ratio (OR) for morbidity, as this is a categorical variable, and a mean difference (MD) for length of stay, as this is a continuous variable, along with 95% confidence intervals (CIs). We produced Chi^2 and I^2 values to assess homogeneity. Had we included a sufficient number of studies, we would have created funnel plots to help assess the risk of reporting and other biases [19,22].

2. Results

2.1. Studies included

Our electronic search yielded 342 studies. After applying our exclusion criteria to titles and abstracts, 63 studies remained. Full-text review resulted in eight of these studies being included, while an additional one was identified from hand-searching the reference sections of included articles; nine studies were ultimately included [10–12,14,23–27]. Seven of these were amenable to inclusion in meta-analyses [10–12,14,23–25] (Fig. 1).

2.2. Study characteristics

We did not identify any RCTs; all but one of the included nine studies were retrospective [26]. Studies were published between 1996 and 2011 and were conducted in Australia [14,27], Belgium [25], Canada [23], China [24], Israel [26], Italy [10], Japan [12], and the United States of America [11]. The MINORS scores for our included studies ranged from 7 to 14, with a median score of 9 (Table 1).

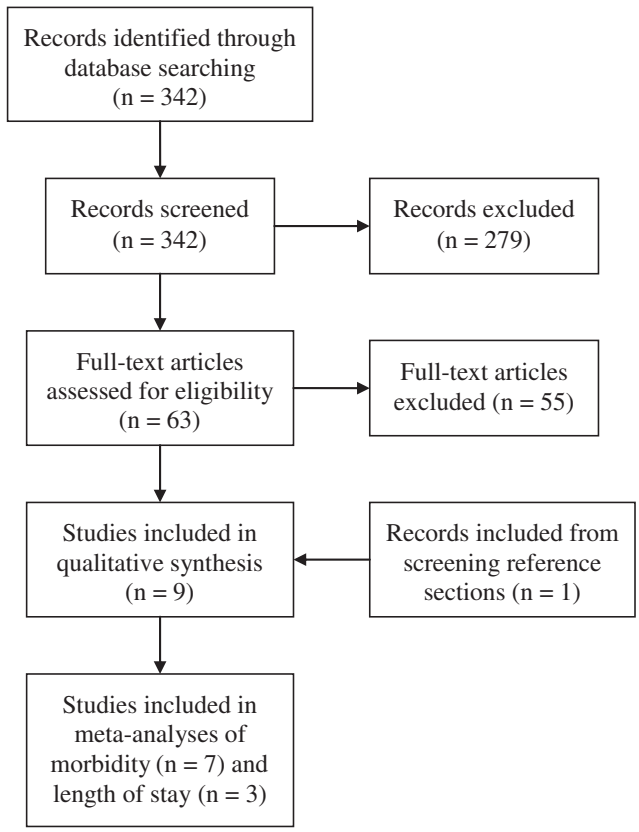

Fig. 1. Flow diagram of search and screening process.