Current Management of Congenital Pulmonary Airway Malformations: A "European Pediatric Surgeons' Association" Survey

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Abstract

Aim To define current management of congenital pulmonary airway malformation (CPAM).

Methods A total of 181 European Pediatric Surgeons' Association members (91% senior) from 48 countries completed an online questionnaire.

Main Results Prenatal: 93% respondents work in centers with prenatal diagnosis facilities, and 27% in centers offering in utero surgery. Prenatal counseling is performed by 86% respondents, 22% of whom see >10 cases per year. Risk of single pre-/postnatal complications is deemed low (<5%) by more than 60% of respondents. Eighty-six percent respondents do not offer pregnancy termination for prenatally diagnosed CPAM. Fetal hydrops is the most frequent indication for termination (87%), followed by

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parental willingness (52%). Prenatal surgery is an option for 44% respondents, preferring thoracoamniotic shunt (82%).
Postnatal: 75% respondents operate on asymptomatic patients, 18% before 6 months of age, 62% between 6 and 12 months of age, and 20% after 12 months of age. Risk of infection (86%), cancer (63%), and symptoms development (62%) are indications for surgery in asymptomatic CPAM. Sixty-three percent prefer a thoracotomy. Lobectomy is the preferred procedure (58% respondents). Motivations against surgery include lesion <1 cm (64%), risk of postoperative complications (37%), and lack of evidence favoring surgery (27%). Seventeen percent respondents have seen at least one patient with CPAM with lung cancer, in 89% of the cases within the CPAM. Of all the respondents, 83% and 22% offered dedicated follow-up and genetic screening, respectively.
Conclusion Current pre- and postnatal management of CPAM lacks uniformity, particularly for surgical indication, timing, and approach. Efforts should be made toward standardization. Risk of CPAM-associated cancer is not clear.

Keywords
- congenital lung anomalies
- observation
- postnatal
- prenatal
- surgery

Introduction

Congenital pulmonary airway malformations (CPAMs), formerly known as congenital cystic adenomatoid malformations of the lung, encompass a variety of congenital anomalies of the lung considered the result of different developmental pathogenic mechanisms.[1] The first case of congenital cystic disease of the lung was reported by Thomas Bartholin in 1687,[2] whereas the first surviving infant following a resection of a congenital lung malformations (right upper and middle bilobectomy) was reported by Fischer et al in 1943.[3] In the early 1970s, the application of ultrasound examination to obstetrics and gynecology allowed the prenatal identification of congenital anomalies, and that is how the first fetus with a congenital cystic lung lesion was described in 1975.[4] The introduction and development of this diagnostic tool had three major consequences. First, the possibility to implement in utero treatments for selected patients. Second, the rise of the detected incidence of CPAMs from 1 in 35,000 to 8,000[5,6] up to 1 in 2,500 live births.[7] In fact, until the late 1960s and early 1970s, incidental diagnosis in asymptomatic patients was extremely unusual, and the incidence of pulmonary malformations was almost exclusively due to symptomatic cases. The introduction of prenatal ultrasound allowed detecting also those patients who would not have presented with severe clinical manifestations at birth or during infancy. The third consequence was the origin of a controversy with the management of the large number of asymptomatic patients. When asymptomatic patients were rare, they were operated on prophylactically for the risk of infection and development of severe clinical manifestations.[8] When it became clear that the vast majority of patients with CPAMs were asymptomatic at birth and during infancy, the role of prophylactic surgery was challenged, with some authors supporting watchful observation and others purporting prophylactic surgery.[9,10] Since the controversy currently persists, and is not limited to the aspect operation versus observation but involves also the optimal age for surgery and surgical approach, we performed a survey of members of the European Pediatric Surgeons' Association (EUPSA) with the aim to describe the current management of CPAM.

Methods

Following approval of the EUPSA Executive Board and the EUPSA Network Office, 507 members were contacted through e-mail and asked to fill out a questionnaire on the management of CPAM using SurveyMonkey (SurveyMonkey, Palo Alto, California, United States), an online survey platform. The questionnaire contained 31 items focusing on various prenatal and postnatal features of CPAM management, including diagnosis, surgery, and long-term follow-up aspects. The questionnaire was piloted by the EUPSA Network Office. Response anonymity was guaranteed by the fact that survey creators and analyzers worked independently.

Results

A total of 181 EUPSA members completed the survey (response rate: 36%).

Respondents were invited to fill in their position (Head of Department/Permanent Staff, or Consultant/Trainee) and country of practice. Of the 181 respondents, 2 delegates did not disclose their degree, whereas 52 were head of the department (29%), 110 permanent staff/consultants (62%), and 17 trainees (9%). On 177 questionnaires, respondents reported their country of origin: 130 (73%) were from 28 European countries and 47 (27%) from 20 non-European countries.

Congenital Pulmonary Airway Malformation Associated Risks

The risk of complications was stratified as "none," below 5%, 5 to 40%, and above 40%. Specific complications included in

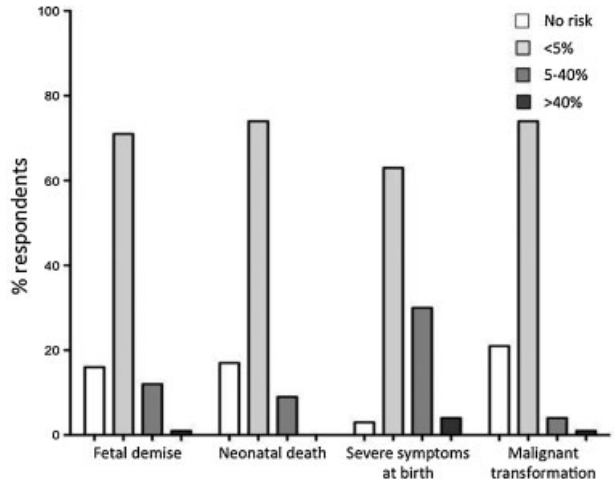

Fig. 1 Alleged risk of fetal demise, neonatal death, severe symptoms at birth, and malignant transformation (159 respondents).

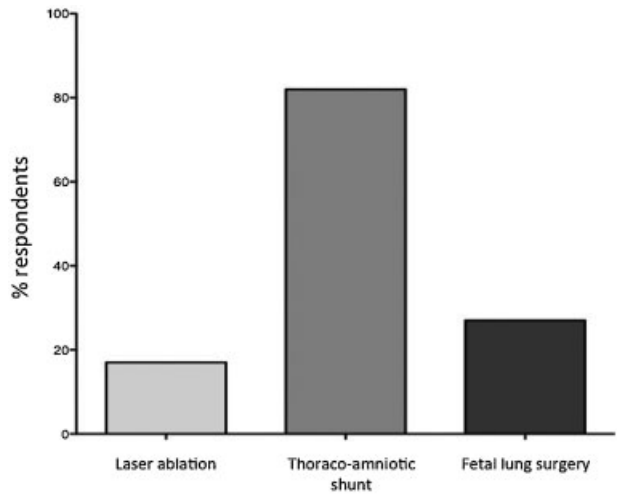

Fig. 2 Preferred prenatal surgical treatment (66 respondents). More than one answer was allowed.

the survey were risk of fetal demise, risk of neonatal death, risk of severe symptoms at birth, and risk of malignant transformation. The majority of respondents (78%) consider that the risk of prenatal complications is below 5% ("none": 19%; "<5%": 59%). ►**Fig. 1** shows the distribution of alleged risk for each complication. CPAM-associated cancer was seen at least once by 17%, before 1 year of age by 6%, between 1 and 5 years of age by 8%, and after 5 years of age by 3% respondents; two respondents have seen at least one CPAM-related cancer with no specific age pattern. In 89% of cancer cases, the lesion was within the CPAM. Genetic screening for pleuropulmonary blastoma (DICER1 mutation) is offered by 22% of respondents.

Prenatal Management

Overall, 93% respondents work in a hospital with prenatal diagnosis facilities, 78% in a hospital with maternal–fetal unit, and 27% in a hospital that offers in utero surgery. Prenatal counseling is performed by 86% of the respondents, half of whom counsel less than 5 cases per month and 22% counsel more than 10. CPAM regression is considered unlikely (<5% probability) by 59% respondents, possible (5–40% probability) by 29% respondents, and probable (>40% probability) by 12% respondents. Termination of pregnancy is considered for selected cases by 14% of the respondents. The indication to consider termination of pregnancy include fetal hydrops (87% respondents), parental willingness (52% respondents), risk of fetal demise (39% respondents), risk of prenatal complications (35% respondents), early diagnosis (before 22 weeks of gestation) and large lesion defined as mediastinal shift (both 26% respondents), and pleural effusion and cystic volume ratio >1.6 (both 13% respondents). The latter parameter is calculated and followed up by 51% respondents. Prenatal surgery is considered an option in selected cases by 44% respondents. Sixty-six respondents specified their preferred prenatal surgical options, which are reported in ►**Fig. 2**. Prenatal treatment is actually offered by 33% respondents.

Postnatal Management

In a year, 46% respondents perform less than 10 lung surgeries, 20% more than 20, the remainder between 10 and 20. Looking specifically at CPAM, 63% respondents operate on less than 5, 31% between 5 and 10, and 6% more than 10 patients with CPAM per year. Asymptomatic patients with CPAM are operated upon by 75% of the respondents, before 6 months of age by 18%, between 6 and 12 months of age by 62%, and over 12 months of age by 20% respondents. Risk of infection is the most frequently reported indication to operate on asymptomatic patients (86% respondents). ►**Fig. 3** shows surgical indications for asymptomatic patients. The arguments against surgery in asymptomatic patients include very small lesion (<1 cm) for 64% respondents, risk of postoperative complications (37%

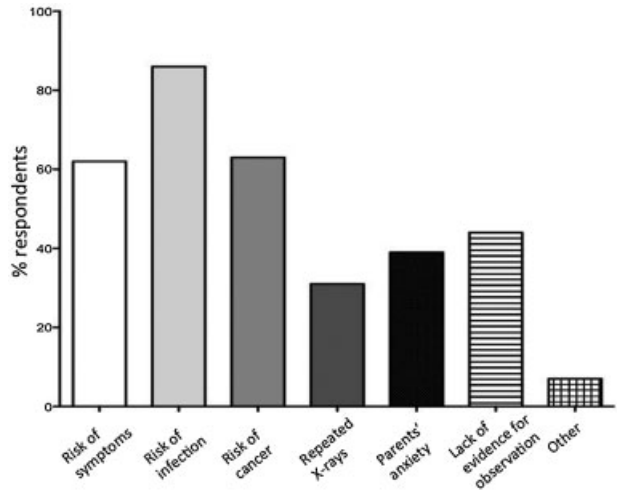

Fig. 3 Indications for surgery in asymptomatic patients with congenital pulmonary airway malformation (146 respondents). More than one answer was allowed. Note that total percentage approximates 330%, indicating more than one answer chosen by several respondents.

respondents), lack of evidence supporting surgery (27% respondents), and other arguments for 9% respondents. Thoracotomy is the preferred approach for 63% respondents (thoracoscopy, 37%), with lobectomy as the procedure of choice for 58% respondents, segmentectomy for 25% respondents, and atypical resection for 17% respondents. More than 83% respondents offer a dedicated follow-up program for patients with CPAM (both for operated and nonoperated patients).

Discussion

We report the results of a survey on CPAM management performed among EUPSA members. Overall, we found lack of consensus in several prenatal and postnatal aspects of CPAM, ranging between considerations on its natural history (risks of fetal demise, neonatal death or severe symptoms, malignant transformation) and management strategies for asymptomatic patients.

Two previous surveys have explored the management of congenital lung malformations, including CPAM: one from Canada and one from United Kingdom/Ireland.[11,12] The Canadian survey explored specifically the postnatal management of prenatally detected asymptomatic CPAM.[11] The proportion of respondents favoring prophylactic surgery (67%) was similar to that of this survey (75%). Also, the preferred age for prophylactic surgery was similar to that of this survey, with 48% respondents preferring the 6 to 12 months of age period. However, a substantial proportion of the respondents (52% in the Canadian survey and 38% in this survey) prefer to perform prophylactic surgery either before 6 months or after 12 months of age. In the United Kingdom/Ireland survey,[12] the proportion of surgeons against prophylactic surgery (24%) was similar to that of this survey (25%). Moreover, the decision for prophylactic surgery seemed more articulated than based on a single factor. In fact, 21% of the respondents stated that they would always resect asymptomatic lesions, whereas 56% respondents would resect only selected asymptomatic patients.[12] The most reported factors influencing the decision to operate on an asymptomatic patient were the size of the lesion, parental anxiety, and the desire to obtain histologic diagnosis. Also, in this survey, the decision to operate on asymptomatic patients was not based on one single factor as suggested by the finding that several respondents chose more than one possible answer to the question on indication for prophylactic surgery (►Fig. 3). The size of the lesion was a factor influencing the decision to operate on an asymptomatic patient also in our survey, as a lesion <1 cm was the mostly cited indication against prophylactic surgery (63% respondents). In the United Kingdom/Ireland survey,[12] very few gave a specific size influencing the decision for/against prophylactic surgery as they stated that other factors in combination would influence their decision. Another factor likely influencing the decision to operate on an asymptomatic patient is the possibility of spontaneous regression, considered not unlikely (>5% probability) by 41% of the respondents of this survey. Prenatally detected CPAM may seem to disappear during pregnancy and may not be visible on postnatal X-rays. Therefore, higher level (CT [computed tomography] scan or MRI [magnetic resonance imaging]) imaging studies are necessary to define persistence or regression of the lesion. As far as the preferred age for prophylactic surgery is considered, 56% respondents of the United Kingdom/Ireland survey state that they prefer the period between 3 and 12 months of age.[12] Nonetheless, a substantial proportion of surgeons (44%) preferred different ages. Thoracotomy remains the preferred approach over time and populations of surgeons surveyed. In fact, in this survey, thoracotomy was the preferred approach for 63% respondents, in the Canadian survey for 61% respondents,[11] and in the United Kingdom/Ireland survey for 65% respondents.[12] Similarly, the procedure of choice remained lobectomy (83% respondents in the Canadian survey[11] vs. 58% in this survey), although other procedures (atypical lobectomy, segmentectomy) gained popularity over time.

Prenatal aspects were only analyzed by the United Kingdom/Ireland survey.[12] Different fetal interventions were used, including (in order of frequency) thoracoamniotic shunts, therapeutic amniocentesis, puncture of cysts/hydrothorax, and lasering of feeding vessels (for sequestrations). However, it was not stated whether all respondents had prenatal treatment facilities or not. In this survey, 33% respondents could offer prenatal treatment, and like in the United Kingdom/Ireland survey, the preferred surgical treatment was thoracoamniotic shunt, although 44% respondents would prefer a different approach. It is difficult to draw robust conclusions from these data as different prenatal treatments (thoracoamniotic shunts, therapeutic amniocentesis, cysts drainage, laser ablation, high-dose corticosteroids) are indicated for different conditions, which were not specified in both surveys. In our survey, 14% respondents consider termination of pregnancy in selected cases of prenatal CPAM. Although this may relate to differences in individual practices and differences among different countries, it is remarkable that 52% respondents consider "parental willingness" as an indication for termination of pregnancy. Parental beliefs are important, but it should be born in mind that they may be directed from the physicians' opinions. In a study on prenatal counseling for CPAM, Aite et al found that termination of pregnancy was recommended in first level consultation in approximately 50% of families.[13]

In this survey, 83% respondents offer a dedicated follow-up program to patients with CPAM, irrespective of whether they were observed or operated. However, we did not investigate this aspect deeper. Looking at previous surveys, follow-up was reported only for observed patients in the Canadian Survey[11] and for all patients in the United Kingdom/Ireland survey.[12] In both the surveys, the follow-up practices varied widely in terms of who actually performs the follow-up (general practitioners vs. respiratory physicians vs. pediatric surgeons), recommended frequency, follow-up radiology (chest X-rays, CT scan, ultrasound, and MRI), and time of follow-up. The risks related to repeat X-rays studies was reported as a concern suggesting prophylactic surgery by 31% of respondents in this survey.

This study has some limitations. The first is the relatively low response rate. The second limitation is that the number of questions in a survey needs to be limited. A too lengthy survey would discourage respondents. As a consequence, survey studies do not allow to go deeply into details but to obtain the general picture.

Notwithstanding a relatively low response rate for this survey (36 vs. 69% for the Canadian survey[11] and 24% of analyzed responses for the United Kingdom/Ireland survey[12]), this survey has two major advantages over the other two. The total number of analyzed respondents (181) is much higher than that of previous surveys (34 in both Canadian and United Kingdom/Ireland surveys). In addition, the composition of the analyzed population is much more heterogeneous, coming from 48 different European and non-European countries. This makes the results more generalizable and possibly less influenced by local policies. This survey confirms the lack of consensus in both prenatal aspects of CPAM (considered risk of fetal demise and neonatal symptoms/death, preferred prenatal surgery) and postnatal features of asymptomatic patients (considered risk of malignant transformation, prophylactic surgery versus observation, follow-up) outlined in previous surveys.[11,12] Most of the controversies are due to the lack of evidence on almost all prenatal and postnatal aspects of CPAM.[14] This, in turn, derives from the substantial lack of knowledge on the natural history of CPAM, finally leaving each physician alone with its experience in the decision-making process when facing an asymptomatic patient. Large prospective studies would be difficult because of the rarity of the disease, CPAM-related cancer or other adverse events, and the necessary long follow-up time required. The development of registries (such as that proposed in the United Kingdom) represents a valid alternative to fill this gap in knowledge.

Conflict of Interest

None.

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Erratum: The author byline has been corrected as per Erratum published on June 5, 2018. DOI of the Erratum is 10.1055/s-0038-1660778.