

Current management of congenital pulmonary airway malformations. A “European Paediatric Surgeons’ Association” survey.

Francesco Morini¹, Augusto Zani^{2,3}, Andrea Conforti¹, Ernest van Heurn⁴, Simon Eaton⁵, Prem Puri⁶, Risto Rintala⁷, Marija Lukac^{8,9}, Joachim F. Kuebler¹⁰, Florian Friedmacher⁶, Rene Wijnen¹¹, Juan A. Tovar¹², Michael E. Hoellwarth¹³, Agostino Pierro², Pietro Bagolan¹, on behalf of the EUPSA Network Office

- 1- Neonatal Surgery Unit, Department of Medical and Surgical Neonatology, Ospedale Pediatrico Bambino Gesù, IRCCS, Rome, Italy.
- 2- Department of Paediatric Surgery, The Hospital for Sick Children, Toronto, Canada.
- 3- Department of Paediatric Surgery, Sapienza University of Rome, Rome, Italy.
- 4- Department of Pediatric Surgery, AMC/VUMC, Amsterdam, The Netherlands.
- 5- Department of Paediatric Surgery, University College London Institute of Child Health, London, United Kingdom.
- 6- Department of Paediatric Surgery, National Children's Research Centre, Dublin, Ireland.
- 7- Department of Paediatric Surgery, Hospital for Children and Adolescents, Helsinki, Finland.
- 8- Department of Pediatric Surgery, Faculty of Medicine, Belgrade, Serbia.
- 9- Department of Neonatal Surgery, University Children's Hospital, Belgrade, Serbia.
- 10- Department of Pediatric Surgery, Hannover Medical School, Hannover, Germany.
- 11- Department of Pediatric Surgery Sophia Children's Hospital, ErasmusMC, Rotterdam, The Netherlands.
- 12- Department of Pediatric Surgery, Hospital Universitario La Paz, Madrid, Spain
- 13- University Clinic for Pediatric and Adolescent Surgery, Medical University of Graz, Graz, Austria

Corresponding author:

Dr. Pietro Bagolan

Department of Medical and Surgical Neonatology
Bambino Gesù Children’s Hospital, IRCCS
Piazza S. Onofrio, 4 00165, Rome, Italy
Tel. +39 06 68592523 – fax +39 06 68592513
email: pietro.bagolan@opbg.net

Abstract

Aim of the study: To define current management of congenital pulmonary airway malformation (CPAM). **Methods:** 181 EUPSA members (91% senior) from 48 countries completed an online questionnaire. **Main results:** Prenatal: 93% respondents work in centres with prenatal diagnosis facilities, and 27% in centres offering *in-utero* surgery. Prenatal counselling is performed by 86% respondents, 22% of whom see >10 cases per year. Risk of single pre-/postnatal complications is deemed low (<5%) by over 60% of respondents. 86% respondents do not offer pregnancy termination for prenatally diagnosed CPAM. Fetal hydrops is the most frequent indication for termination (87%), followed by parental willingness (52%). Prenatal surgery is an option for 44% respondents, preferring thoraco-amniotic shunt (82%, Figure A). 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 symptom development (62%) are indications for surgery in asymptomatic CPAM. 63% prefer a thoracotomy. Lobectomy is the preferred procedure (58% respondents, Figure B). Motivations against surgery include lesion <1cm (64%), risk of post-operative complications (37%), and lack of evidence favouring surgery (27%). 17% respondents have seen at least one CPAM patient with lung cancer, 89% within the CPAM. 83% and 22% respondents offer dedicated follow-up and genetic screening, respectively.

Conclusions: 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; prenatal; postnatal; surgery

Introduction

Congenital pulmonary airway malformations (CPAM), 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 reported case of congenital cystic disease of the lung is granted to Thomas Bartholin in 1687,² while the first surviving infant following a resection of a CPAM (right upper and middle bilobectomy) was reported by Fischer and co-workers 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's 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 congenital pulmonary malformations from 1 in 35,000 – 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 that 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 congenital pulmonary malformations 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 vs. observation, but involves also the optimal age for

surgery and surgical approach, we performed a survey of members of the European Paediatric 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 via email and asked to fill out a questionnaire on the management of CPAM using SurveyMonkey (SurveyMonkey, Palo Alto, California), 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

One hundred eighty one 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.

CPAM-associated risks:

The risk of complications was stratified as “none”, below 5%, 5-40%, and above 40%. Specific complications included in the survey were: risk of fetal demise, risk of neonatal death, risk of severe symptoms at birth, risk of malignant transformation. The majority of respondents (78%) consider that the risk of prenatal complications is below 5% (“none”: 19%; <5% 59%). **Figure 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; 2 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 pleuro-pulmonary 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% 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), 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 **Figure 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% over 10 patients with CPAM per year. Asymptomatic CPAM patients 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). **Figure 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 post-operative complications (37% 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. Over 83% respondents offer a dedicated follow-up program for CPAM patients (both for operated on and non-operated on 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 UK/Ireland.^{11,12} The Canadian survey explored specifically the post-natal management of prenatally detected asymptomatic CPAM.¹¹ The proportion of respondents favoring prophylactic surgery (67%) was similar to that of the present survey (75%). Also the preferred age for prophylactic surgery was similar to that of the present survey, with 48% respondents preferring the 6-12 months of age period. However, a substantial proportion of the respondents (52% in the Canadian survey and 38% on present survey) prefer to perform prophylactic surgery either before 6 months or after 12 months of age. In the UK/Ireland survey,¹² the proportion of surgeons against prophylactic surgery (24%) was similar to that of present 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 while 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 present 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 (Figure 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 UK/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 present survey. Prenatally detected CPAM may seem to disappear during pregnancy and may not be visible on post-natal X-rays. Therefore, higher level (CT scan or MRI) 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 UK/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 the present survey, thoracotomy was the preferred approach for 63% respondents, in the Canadian survey for 61% respondents,¹¹ and in the UK/Ireland survey for 65% respondents.¹² Similarly, the procedure of choice remained lobectomy (83% respondents in the Canadian survey ¹¹ vs. 58% in the present survey), although other procedures (atypical lobectomy, segmentectomy) gained popularity over time.

Prenatal aspects were only analyzed by the UK/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 the present survey, 33% respondents could offer prenatal treatment and, like in the UK/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 and coworkers found that termination of pregnancy was recommended in first level consultation in approximately 50% of families.¹³

In present survey, 83% respondents offer a dedicated follow-up program to CPAM patients, irrespective of whether they were observed or operated. However, we did not investigate in this aspect deeper. Looking at previous surveys, follow-up was reported only for observed patients in the Canadian Survey¹¹ and for all patients in the UK/Ireland survey.¹² In both 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 the present 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 the present survey (36% vs 69% for the Canadian survey¹¹ and 24% of analyzed responses for the UK/Ireland survey¹²), present 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 UK/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. The present 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 vs. 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, of 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 UK) represents a valid alternative to fill this gap in knowledge.

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Figure legends

Figure 1:

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

Figure 2:

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

Figure 3:

Indications for surgery in asymptomatic CPAM patients (146 respondents). More than one answer was allowed. Note that total % approximates 330%, indicating more than one answer chosen by several respondents.





