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Journal: International journal of pediatric otorhinolaryngology

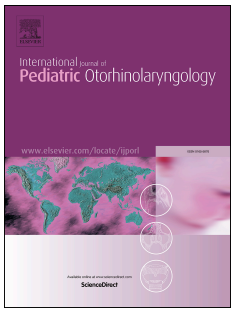
Year: 2018 Nov

Issue: 114

Pages: 80-86

DOI: 10.1016/j.ijporl.2018.08.031

Accepted Manuscript



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PII: S0165-5876(18)30437-3

DOI: 10.1016/j.ijporl.2018.08.031

Reference: PEDOT 9156

To appear in: *International Journal of Pediatric Otorhinolaryngology*

Received Date: 28 April 2018

Revised Date: 9 August 2018

Accepted Date: 24 August 2018

Please cite this article as: M. Kapitanova, J.-F. Knebel, O. El Ezzi, M. Artaz, A.S. de Buys Roessingh, C. Richard, Influence of infancy care strategy on hearing in children and adolescents: a longitudinal study of children with unilateral lip and /or cleft palate, *International Journal of Pediatric Otorhinolaryngology* (2018), doi: 10.1016/j.ijporl.2018.08.031.

Influence of infancy care strategy on hearing in children and adolescents: a longitudinal study of children with unilateral lip and /or cleft palate

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Influence of infancy care strategy on hearing in children and adolescents: a longitudinal study of children with unilateral lip and /or cleft palate

ABSTRACT

Objectives: To evaluate the relation between ventilation tube insertion, otitis media with effusion duration and otologic outcomes in unilateral cleft lip and/or cleft palate children from infancy to teenage age.

Design and Population: Retrospective longitudinal charts review of patients from the multidisciplinary cleft team of the University Hospital of Lausanne over a 30-year period. 146 charts from consecutive patients with non-syndromic unilateral cleft lip and/or cleft palate who were born between January 1986 and January 2003 were included.

Results:

The earlier in life a cleft child experience his first otitis media with effusion (OME), the worse his long-term hearing will be. Along with the age of onset of OME, we disclosed an influence of the duration of OME without ventilation tube (VT) insertion on short and long-term hearing outcomes. Different patterns were observed between cleft palate (CP) and cleft lip palate children (CLP), with a higher incidence of otitis media with effusion for the CLP group than the CP group. Direct positive relationship between VT insertion and hearing were disclosed and evaluation of long-term complications did not reveal significant relation with VT insertion.

Of note, OME in CLP children led to a higher rate (but not statistically significant) of chronic ear complications than in the CP group, that may indicate more persistent OME or different adverse effect on the middle ear mucosa between CP and CLP children.

Conclusions:

Individualized counseling should take into account different factors such as the type of cleft, the age of onset of OME and duration of OME, keeping in mind the adverse effect of persistent middle ear fluid. In the present report, results prone an early ventilation tube insertion to prevent short and long-term injury to the middle ear homeostasis, hearing loss and related issues.

Keywords: unilateral cleft lip and palate, hearing loss, complications, long-term outcomes

INTRODUCTION

Orofacial clefting is a congenital anomaly that encompasses a wide range of malformation, including unilateral or bilateral cleft lip (CL), unilateral of bilateral cleft lip and palate (CLP) and cleft palate (CP), isolated or associated to a syndrome. In Switzerland, the birth prevalence of CL with or without CP is between 0.83 to 0.96 and for isolated cleft palate from 0.59 to 0.69 per 1000 live-born babies.[1] The incidence of unilateral cleft is nine times higher than bilateral clefts and unilateral clefts are more frequently on the left than on the right side. Isolated CP more frequently concerns females whereas CLP predominantly affects males.

Otitis media with effusion (OME) is a common pathology of childhood defined as the presence of fluid (build-up of mucus or liquid) in the middle ear without signs or symptoms of acute ear infection whereas its persistence over a 3 month-period defines a chronic OME.[2] In the general population, 50% of children are reported to experience at least one OME in the first year of life, increasing to 60% by the age of 2.[3] However children with CP and CLP experience a greater number of OME than the general population[4] and chronic secretory otitis media is suggested to develop in almost all infants with cleft palate within the first month of life.[5] Of the different predisposing factors, the Eustachian tube dysfunction plays a major role in the pathogenesis of the OME in infants with CP and CLP.[6] The structure of the Eustachian tube in cleft children presents differences as compared with general specimens[7] and the lack of insertion of the tensor and levator palate muscles into the midline palate prevents normal opening of the nasopharyngeal end of the Eustachian tube, efficient pressure regulation and secretion clearance.[8,9] Cleft patients are at higher risk of middle ear effusion in comparison with general population and the prevalence of OME remains high even in teenage age with 13% to 49% of adolescents with CLP reported with OME.[10] Based on these observations, several authors advocate early ventilation tube (VT) insertion during the primary palatal repair to limit the impact of hearing loss on speech and language development and to prevent long-lasting effects of chronic OME.[11,12] A VT allows the fluid to drain and decreases secretion from the mucosa by providing aeration and equalization of pressure to the middle ear cavity.[13] Albeit a positive effect on short term hearing, VT insertion is for some authors not devoid of adverse effects: [14] a 2005 Cochrane review of randomized controlled trials[15] comparing effectiveness of short-term ventilation tube insertion with myringotomy or nonsurgical treatment in non-cleft children with middle ear effusion, concluded that the effect

of short-term ventilation tube on hearing was small and diminished over the first year. Such findings led some groups to focus on the use of possible hearing aids to avoid problems associated with repeated VT insertion.[16]

Close follow-up is required from birth until adulthood as affected children present higher morbidity and mortality throughout life than the general population.[17,18] Especially recurrent middle ear problems have to be carefully monitored during the critically period of speech and language acquisition, social behavior development and for years as complications and long-lasting hearing loss can occur.[14,19] Since 1986, we adopted a multidisciplinary team approach strategy, including pediatric surgery, nursing, maxillofacial surgery, otolaryngology, audiology, speech therapy, psychology, genetics, orthodontics, and thus provided children with a centralized care strategy. However, despite growing interest towards long-lasting adverse effects in CLP and CP children, evidence for the effective management of OME in these children is still incomplete and uncertainties among clinicians remain.[20,21]

The aim of this study was to evaluate the potential benefits and harms of our care strategy (VT insertion or watchful waiting) at different ages from childhood until 15 years. The 15 years ending time-point was chosen in reference to the end of normal school in Switzerland, a transition from teenage to adulthood.

We examined the relation between VT insertion, OME duration and otologic outcomes in our cohort of non-syndromic CP and CLP children longitudinally followed over time in the same tertiary care center to assess a better picture of prevalence and factor influences at 2, 4, 6, 8 10 and 15 years of age.

SUBJECTS AND METHODS

Design

This study involved a detailed longitudinal retrospective chart review from a consecutive series of children over a 30-year period. Data pertaining to the clinical characteristics of the children were collected for all children from the multidisciplinary cleft palate team at the Lausanne University Hospital. This study was approved by the ethic comity of Canton de Vaud (CER_VD 2016-00862).

Participants and setting

This study was undertaken at a single institution, the Lausanne University Hospital, Switzerland, a tertiary care medical facility where comprehensive orofacial cleft services including assessment, speech therapy, surgery, audiologic and early rehabilitation intervention have been in place since 1986. As part of standard care, children with orofacial cleft undergo a comprehensive interdisciplinary team assessment with professionals representing pediatric surgery, maxilla-facial surgery, audiology, speech-language intervention, otolaryngology, and psychology as well as other developmental and medical services (e.g. developmental pediatrician) if required.

Data were collected from a consecutive series of children treated within the same centralizing service over a 30-year period. Inclusion criteria comprised the following:

- Children born with unilateral cleft lip and palate (CLP) and children with only cleft palate (CP) without associated syndrome, chromosomal abnormality or sequence
- Children born between January 1986 and January 2002 and followed from birth to 15 years of age by the multidisciplinary cleft palate team.
- Data available from birth to 15 years of age during multidisciplinary consultations and clinical ENT visits.

Children with cleft lips only, children who had undergone cleft repair at an outside hospital or had an intact secondary palate, children lost from the follow up, children with co-existing syndrome or children with sensorineural or mixed hearing loss were excluded from the study.

Surgical, clinical treatment and outcome measures:

Surgical intervention strategy was performed according to the von Langenbeck procedure.[22] Timing of primary surgical repair did not vary significantly across population. Children with

a CLP underwent palatal surgery at a mean age of 4.8 months (SD = 3.1) and CP children underwent palatoplasty around 6.4 months of life (SD = 3.3; mean = 6.3 months for the group with less than half of the roof involved and 6.7 months for the other subgroup).

Hearing assessments were performed at the Audiology clinic and included otomicroscopy, tympanometry and pure-tone audiometry by the same experienced pediatric otolaryngologist. Otomicroscopy findings were classified as normal or abnormal (OME, tympanic retraction, tympanic perforation, cholesteatoma, tympanosclerosis) and completed with tympanometry evaluation. Middle ear effusion was classified as untreated if no short-term ventilation tube was present within the 5-days period prior or after its diagnosis. Middle ear impedance was assessed using a Grason-Stadler GSI28A tympanometer and hearing thresholds were ascertained from 500 to 4000 Hz for each ear using pure-tones under headphones with an GrasonStadler GSI-16 earphone audiometer (Grason-Stadler, Littleton, MA, USA). For young children, the experienced audiologists chose the most appropriate testing between behavioral, visually reinforced, or conditioned-play audiometry to obtain ear and frequency specific thresholds. Hearing loss was defined as >20 dB and thresholds were classified as normal for responses at intensities ≤ 20 dB HL, mild hearing loss was diagnosed for thresholds between 21 to 40 dB HL whereas moderate hearing loss was considered for thresholds between 41 and 60 dB HL. Tympanostomy tubes were placed in case of persistence of otitis media with effusion (*i.e.* at least 3 months) and conductive hearing loss on sequential evaluations (>5 dB conductive loss with >20 dB pure tone average). Details related to the presence or absence of middle ear effusion, the number of VT, including age at insertion and complications, were computed at each visit.

Data analysis

The data are presented primarily descriptively using means, medians, or proportions as appropriate. Statistical analyses were conducted using Anaconda 2.7, a free distribution of the Python programming language (Python Software Foundation). Python Language Reference, version 2.7.), the python module Rpy2 (Available at https://pypi.python.org/pypi/rpy2) to link python with R 3.1.3 (R Core Team (2015). R: A language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria. URL http://www.R-project.org/). A multivariate analysis using logistic regression was performed, Odds ratio were calculated to assess the relationship between the following variables: duration of middle ear effusion without short-term ventilation tube insertion and hearing outcomes at 2, 4, 6, 8, 10 and 15 years. Results were significant if the *P*-value was <0.05.

Statistics were reviewed by an experienced statistician listed as one of the co-authors.

RESULTS

Sample description

Two hundred eleven non-syndromic patients with either unilateral cleft lip and palate (CLP) or only cleft palate (CP) were identified from our database. Examination of their medical records showed that 65 of the 211 children were referred after their first year of life or were lost before 15 years of follow-up and 4 children presented with submucous cleft palate. Table I shows the demographics of the 146 children included in the present report.

Age of onset of middle ear effusion

The earlier onset of middle ear effusion was reported at 0.7 month in the CLP group, 0.2 in the CP group involving more than half of the roof and 2.7 months in the CP group involving less than half of the roof. No statistically significant difference was found between groups. Analyses did not reveal any significant relationship between age of onset of OME and hearing outcomes at 2, 4, 6 and 8 years of age. However, multivariate logistic regression between age of onset of OME and pathology revealed a trend (p = 0.056) between the pathology and the hearing at 15 years of age and a significant effect between age of onset OME and hearing at 15 years old. It revealed that the youngest a child experience his first OME the worse his hearing will be at 15 years of age (p = 0.043, OR = 0.750, CI = 0.557-0.978).

Duration of OME without VT insertion:

To assess the effect of lasting OME on hearing, we noted the OME episodes lasting more than 3 months and for which no VT insertion was performed during the following 7 days (Table IIa). Multiple logistic regressions focusing on the influence of OME duration without VT insertion, pathology (CP; CLP) at 2, 4, 6, 8, 10 and 15 years of age (Table IIb) revealed significant effect of OME without VT insertion at 8 years of age (p = 0.005, OR = 1.027) and a significant effect of the pathology at 10 years (p = 0.047, OR = 2.777). For 15 years of age, both the pathology (p = 0.018, OR = 5.346) and the OME duration without VT insertion (p = 0.004, OR = 1.013) disclosed significant relationship. Children from the CLP group presented with a significant risk of hearing loss at 8 years (p = 0.016, OR = 1.032), at 15 years (p = 0.014, OR = 1.020) and a trend at 10 and 15 years of age (p = 0.085). As the duration is disclosed in months, it means that a CLP child with OME will have a risk of abnormal

hearing increasing by 1.032 every month. Moreover, for a given child, suffering from a cleft lip palate increased drastically their risk of presenting an abnormal hearing at 15 years old with an Odds ratio of 5.33 times that of a child presenting with a cleft palate (p = 0.013, CI = 1.584-24.423).

Incidence of persistent OME and short-term ventilation tube insertion frequency:

The measure of persistent otitis media with effusion frequency by cleft type during different periods from childhood to teenage (cumulative incidence or incidence proportion) is presented in table III. By the time CP and CLP children reached 4-year-old age group, the majority (62% and 75% respectively) had presented persistent middle ear effusion at some stage. Overall, cumulative incidence showed a great increase between 2 and 6 years of age for both group (CP and CLP) and stabilizes from 10 years of age. The incidence of persistent OME for the first 2 years after birth was quite similar between CP and CLP groups (with 36% and 37% respectively). Of these patients, 10% of the CP and 14% of the CLP with OME had ventilation tube insertion before 2 years of age with these percentages increasing until 8-years-old and stabilizing until 15 years of age. Of the 73 CP children (Table III), 41 (56%) did not benefit from ventilation tube insertion until 15 years of age. However, 20 out of those children had undergone one episode of middle ear effusion and 2 children experienced two episodes of otitis media with effusion. At 15 years of age, 40% (29/73) of the CPL and 22% (16/73) of the CP children had benefited from more than one VT insertion with a mean number of VT insertion of respectively 1.95 and 1.87 in the CPL and CP population (min = 0, max = 5 for both groups).

The cumulative incidence of OME doubled between 2 and 4 years of age, with an incidence of OME higher in the CLP group compared to the CP groups (Table III).

Hearing and short-term ventilation tube insertion related to the age of the child:

A peak incidence for hearing problems is seen in the 2-to 4 year olds who did not benefit from ventilation tube insertion (Table III, Figure 1&2). This hearing loss was classified as mild for 95% of the 2-year-old CLP children and 98% of the 2-year-old CP children. As shown in Figure 1a, until 6 years of age, CP children with VT exhibited better hearing outcomes than their pairs who did not benefit from VT insertion. Of the noticeable number of CP children who exhibited abnormal hearing at 8 years despite VT insertion (Fig.2, 95%

classified as mild and 5 % as moderate hearing loss), charts review revealed recurrent obstructed VT in the majority of these patients.

Significant hearing improvements from VT insertion are disclosed for CLP children (Fig. 1b), with emphasize regarding the 0-6-year-olds (at 2 years of age: $p = 0.06$; at 4 years of age: $p = 0.019$ and at 6 years of age $p = 0.009$). Although not statistically significant difference was observed after 6, a trend is still visible until 7 years of age. At 15 years old, 67% of CLP children had VT versus only 44% in the CP group, with a higher proportion of children suffering from abnormal hearing in the CLP group (mild hearing loss, Fig.2). Figure 1 depicts slightly different trends between CP and CLP children: influence of ventilation tube insertion is not blatant at 6 years of age and later (Fig. 1a) while it remains clear for the CLP children from birth to 7 years of age (Fig. 1b). Of note, CP children presented with a decreasing incidence of middle ear problems earlier in life than CLP children (Table III).

To appraise the relative influence of VT insertion on hearing, we ran a logistic regression analysis focusing on the impact of undergoing at least one VT insertion on the hearing at 2, 4, 6, 8, 10 and 15 years of age in the CP and CLP populations. When considering the CP children, the analysis did not disclose any statistically significant relation between VT and hearing. On the other hand, undergoing at least one VT insertion for a given CLP child who had experienced OME decreased his risk of abnormal hearing at the age of 4 ($p = 0.036$; $OR = 0.167$). Similar results were observed for the CLP population at 6 years of age ($p = 0.010$; $OR = 0.158$) but not at 8 years of age.

Long-term middle ear complications:

Otologic complications at 15 years of age are represented in Table IV. Tympanosclerosis is the most frequent complication for both groups whether the children had undergone or not VT insertions. Incidence of tympanosclerosis in the CLP group was 5 time higher in the subgroup of children that had undergone ventilation tube insertion, but without any statistical difference (t-test, $p = 0.5$). Of note, 7 (33%) of the 21 CLP children, who experienced VT insertion, had abnormal hearing at 15 years of age (mild hearing loss, Table IV). Noteworthy, the severity of the tympanosclerosis varied with the population considered. All children from the CLP group who had VT insertion and presented with hearing below normal at 15 years of age, suffered from severe (more than 80 % of the tympanic membrane involved) tympanosclerosis whereas all CP children with tympanosclerosis (39 children, 53%) had normal hearing at 15 years of age (Table IV).

Retracted tympanic membrane was the second most frequent chronic ear complication for both groups of children (Table IV). Regarding this condition, there was no statistical correlation between improvement in hearing outcomes at 15 years of age and forgoing of VT insertion procedure for the CLP nor the CP groups. Of the 9 CLP children who had complications without any VT insertion, all had a history of OME whereas 7 out of the 15 CLP children with normal tympanic membrane TM and no VT insertion had a history of OME. Of note of the 12 CP children presenting with complications but without any VT insertion, 5 had history of OME and 17 of the 29 CP children with normal TM and no VT insertion had experienced OME (Table IV).

DISCUSSION

Despite numerous progress, long-term adverse outcomes of children born with cleft palate CP or cleft lip palate CLP remain a burden on the child's health and social transition to adulthood. Herein, we took advantage of the multidisciplinary team approach provided from birth to adulthood in our tertiary care center to evaluate the influence of OME management on short and long-term for CP and CLP children. Such strategy enabled patients to benefit from the same standards of care for years and permitted detailed records of these children to be maintained. Retrospective data gathering is likely to be less accurate than data gathered prospectively. However, the population referred to the multidisciplinary consultation in our tertiary referral center came from a narrowed geographical area and all the patients included were followed by the multidisciplinary team and did not attend a consultation with an otorhinolaryngologist nor a pediatric surgeon at another hospital. Although a prospective study would be preferred, the population included is representative of the population referred to our consultation. It also has the advantage of a large enough longitudinal cohort providing valuable and useful information and accruing patients over a 30-year period to assess long-term follow-up seemed most likely difficult. Moreover, when analyzing outcomes, the process of care has to be consistent so that reports can be useful by providing comparative data.

In line with previous studies, the overall incidence of OME decreases with increasing age,[23–26] and children with cleft lip and palate presented with a higher incidence of middle ear effusion than that for children with cleft palate only.[26] The incidence variation of OME with age and cleft type (CP versus CLP) is in accordance with tympanometric studies that showed a higher frequency of type B tympanograms at the ages of one to three in the CLP children than in the CP group, decreasing at 7 to 12.[23] These findings may suggest that the

characteristic conditions of each type of cleft (CP or CLP) will promote different patterns of middle ear disease development. Another consideration is the conflicting evidence previously reported regarding incidence of OME across ages for CLP children,[12,24] in our report increasing cumulative incidence until 15 years of age with peak incidence between 2 and 4 years of age. Indeed, incidence of OME among children without clefts varies with age and Eustachian tube morphology, exhibiting a peak between 2 and 6 years of age.[27] Variation with age is directly related to the morphological changes of the Eustachian tube that lead to better tubal function. For CP children, decrease of OME was noted in previous studies following the age of 15 years[23,24] whereas in the present report, CP children exhibited peak incidence between 2 and 4 years of age and increased cumulative incidence of OME from 2 to 10 years of age with a stabilization of the cumulative incidence after 10 years of age. Such difference may be due to methodology differences: the previous studies focused on cross sectional analysis of different group ages whereas our report represents longitudinal data from the same population of children. OME is often associated with a conductive hearing loss. As previously noted by Flynn *et al.*[26] in their longitudinal study on hearing loss and cleft type across different age groups, we observed a decrease in prevalence of hearing loss between 10 and 15 years in all type of cleft. Herein, we revealed hearing loss to vary with cleft type and age, with the CLP children more prone to abnormal hearing than in the CP group.

Another relevant point was the VT insertion in relation to OME and the effect on hearing. Surprisingly, we observed a high incidence of hearing issue before 4 years of age for both CP and CLP and a low rate of VT insertion at 2 years. Indeed, the rates of VT insertion noted in our report at 2 years of age was lower than in the literature and overall our cohort of children underwent VT insertion later than in the reported literature.[14,28] However, by promoting the restoration of a normal atmospheric pressure in middle ear, early VT insertion are suggested to play a role in the development of the mastoid air cell system in cleft children.[29]

The positive influence of ventilation tube insertion on hearing outcomes is observed not only at 4, 6 and 8 years of age, but also on long-term hearing outcomes. Alongside with previous study emphasizing the use of VT, we interpret this finding as confirming and strengthening the previous suggestion that an aerated and well ventilated middle ear cavity on hearing and thereby provide children with optimal auditory stimulation on language development. Another key point was the age of VT insertion. Herein, we observed the negative effect of an

early age of OME onset and of a lasting OME without VT insertion on short and long-term hearing. This emphasizes as previously suggested the need of early VT insertion to prevent adverse outcomes.[30,31] OME can disrupt the acoustic-mechanical properties of the middle ear system thereby causing a conductive hearing loss. [32,33] Impaired transmission of the acoustic signal may lead to impaired brainstem/cortical function,[34,35] abnormal development of speech and language development (*i.e.* articulatory issues) with related psychological, emotional and social problems.[36] It is also likely that the timing of deprivation plays a major role in the brain-based developmental impairments.[37] Therefore, when an OME is suspected, clinician should obtain an audiometry to better assess OME influence on hearing loss.

With regard to possible complications of VT insertion, several retrospective studies previously reported an increased rate of tympanic membrane scarring, tympanosclerosis, permanent TM perforations and otorrhea in cleft palate children secondary to VT insertion while conservative management had led to long term favorable audiometric outcomes.[14,38,39] However, the possible role of an active middle ear disease in the otologic complications was not evaluated neither mentioned. On the other hand, some studies suggested the use of hearing aids instead of VT insertion[16,20] but the long-lasting adverse effects of chronic effusion on middle ear was not mentioned. Caution should be taken regarding middle ear persistent effusion that lead to biofilm formation[40] and may damage both the middle ear and mastoid mucosa as well as the middle ear ossicles.[41] With regard to the question of possible biofilm formation on indwelling device, a wide range of VT have been considered as highly efficient to prevent biofilm formation (e.g. ionized, coated fluoroplastic grommets,[42] ion-bombarded silicone[43] or VT coated with albumin)[44] and to decrease the rate of post-VT insertion otorrhea.[45] In the present report, ear complications between VT and no VT insertion were no statistically different. We also noted that CLP children presented with a higher rate of OME and VT insertion than the children in the CP group. Such difference between the 2 groups may indicate more persistent OME or different adverse effect on the middle ear mucosa between CP and CLP children. These findings may support the CLP children to be a population at higher risk of sequelae from OME and hearing loss with long-lasting adverse hearing effects than CP children. These findings underscore the clinical need for close follow-up to provide children with early VT insertion, preventing from middle ear mucosa damages. We also observed that tympanosclerosis was the most reported VT insertion-related complication and unrelated in both groups in line with literature data (incidence 11-37%).[46] Eardrum retraction (with and without tympanosclerosis) was also observed but with an incidence lower than in the literature (26% for the CLP and 33% for the

CP group post VT insertion versus 11.5%-36.8%).[16,36,47] However methodological variation prevents specific comparison between studies.[46] As previously reported, tympanosclerosis had little influence on hearing.[14,48] Of note, tympanosclerosis plaques can be due whether to a prior history of VT placement or to a chronic OME. Its impact on hearing depends on the size of the tympanosclerotic plaque, its site and the involvement of the ossicular chain, leading to different hearing outcomes ranging from normal hearing to varying degrees of hearing loss. In line with such consideration, no significant relationship between tympanosclerosis and VT insertion on long-term follow-up were observed in the CLP group, nor the CP group.

Conclusion

Findings from the current study are noteworthy in several respects. First, the current findings reveal marked dissimilarity in the pattern of middle ear problems with influence of age and cleft type on incidence of OME and related hearing. Second, they provide a strong evidence yet that OME care strategy in childhood influence the child's development until transition from childhood to adulthood. The stronger predictor variables were the age of OME onset and the duration of OME without VT insertion. We will use the present findings to counsel patients and families and help in decision making that most children with cleft palate will experience middle ear effusion and thus related conductive hearing impairment during a critically period. VT insertion can be proposed as an effective option with relatively fewer and easier complications to handle.

Future is the development of prospective data base collection to provide a best possible individualized strategy in children with cleft palate since birth, and a global coordinated multidisciplinary approach.

FUNDING

There is no grant support for this research.

CONFLICT OF INTEREST/FINANCIAL DISCLOSURE

Thereby, the authors state that they do not have any financial or other relationships with other people or organizations that could inappropriately influence their work. No money or grant or other form of payment was given to anyone to produce the manuscript.

ACKNOWLEDGEMENTS

We would like to thank the clinicians and staff that permitted the completion this project. We would like also to thank the families that took part in this study. The authors are grateful to Laure Braconnier for reviewing the manuscript.

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Tables

		Boys (N, *%*)	**Girls (N, *%*)**
CLP (N=73)	Left	**26,** *36%*	**23,** *31.5%*
	Right	**17,** *23%*	**7,** *9.5%*
CP (N=73)	Split < half of the roof of the mouth	**28,** *38.5%*	**23,** *31.5%*
	Split > half of the roof of the mouth	**11,** *15%*	**11,** *15%*

Table I. Cleft type versus gender. CLP = Children with unilateral cleft lip palate. CP = Children with cleft palate.

a.

	Age (*year*)	2	4	6	8
Mean OME Duration without VT insertion (*day*)	**CP**	90	178	288	423
	CLP	60.9	106	205	357

b.

	At 8			At 10			At 15		
	OR	**95% CI**	***P***	**OR**	**95% CI**	***P***	**OR**	**95% CI**	***P***
OME Duration without VT insertion *(month)*	1.027	1.010-1.049	*0.005*	1.010	0.997-1.022	*0.119*	1.013	1.004-1.023	*0.004*
Pathology	2.080	0.784-5.748	*0.147*	2.777	1.037-7.948	*0.047*	5.346	1.490-26.136	*0.018*

Table II. Duration of OME without VT insertion.

a. Mean duration in the CP and CLP cohort at different ages.

b. Results of binary logistic regression analysis using the duration of middle ear effusion (MEE) without grommet insertion and the type of pathology (CP/CLP) as qualitative input variable and hearing at 8, 10 and 15 years of age as response variable.

		Age (year)											
		2 Number (%)		**4** Number (%)		**6** Number (%)		**8** Number (%)		**10** Number (%)		**15** Number (%)	
CP	Children with at least 1 OME since birth.	26	***36%***	45	***62%***	50	***68%***	52	***71%***	53	***73%***	53	***73%***
	with ≥ 1 grommet insertion	5	***7%***	19	***26%***	29	***40%***	32	***44%***	32	***44%***	32	***44%***
CLP	Children with at least 1 OME since birth.	27	***37%***	55	***75%***	60	***82%***	61	***84%***	61	***84%***	66	***90%***
	with ≥ 1 grommet insertion	7	***10%***	27	***36%***	41	***56%***	44	***60%***	49	***67%***	49	***67%***

Table III. Cumulative incidence of otitis media with effusion (OME) and grommet insertion in case of OME by cleft type and for different ages.

At 15 years of age	Grommet insertion			
	NO, n (%)		YES, n (%)	
	CLP	CP	CLP	CP
Normal TM	15	29	10	5
Chronic ear complications				
Tympanosclerosis	4 (16%)	7 (17%)	21 (42%)	8 (25%)
TM perforation	1 (4%)	0	0	3 (9%)
Tympanosclerosis and TM perforation	0	0	4 (8%)	5 (15%)
Tympanosclerosis and TM retraction	2 (8%)	2 (5%)	6 (12%)	6 (18%)
TM retraction	2 (8%)	3 (7%)	7 (14%)	5 (15%)
Cholesteatoma	0	0	1 (2%)	0
Total	**24**	**41**	**49**	**32**
Chronic ear complications And History of OME	9	5	39	27
Normal TM And History of OME	7	17	10	5

Table IV. Incidence of normal tympanic membrane (TM) and chronic middle ear disease related to type of cleft at 15 years of age. OME = Otitis Media with Effusion.

Figures

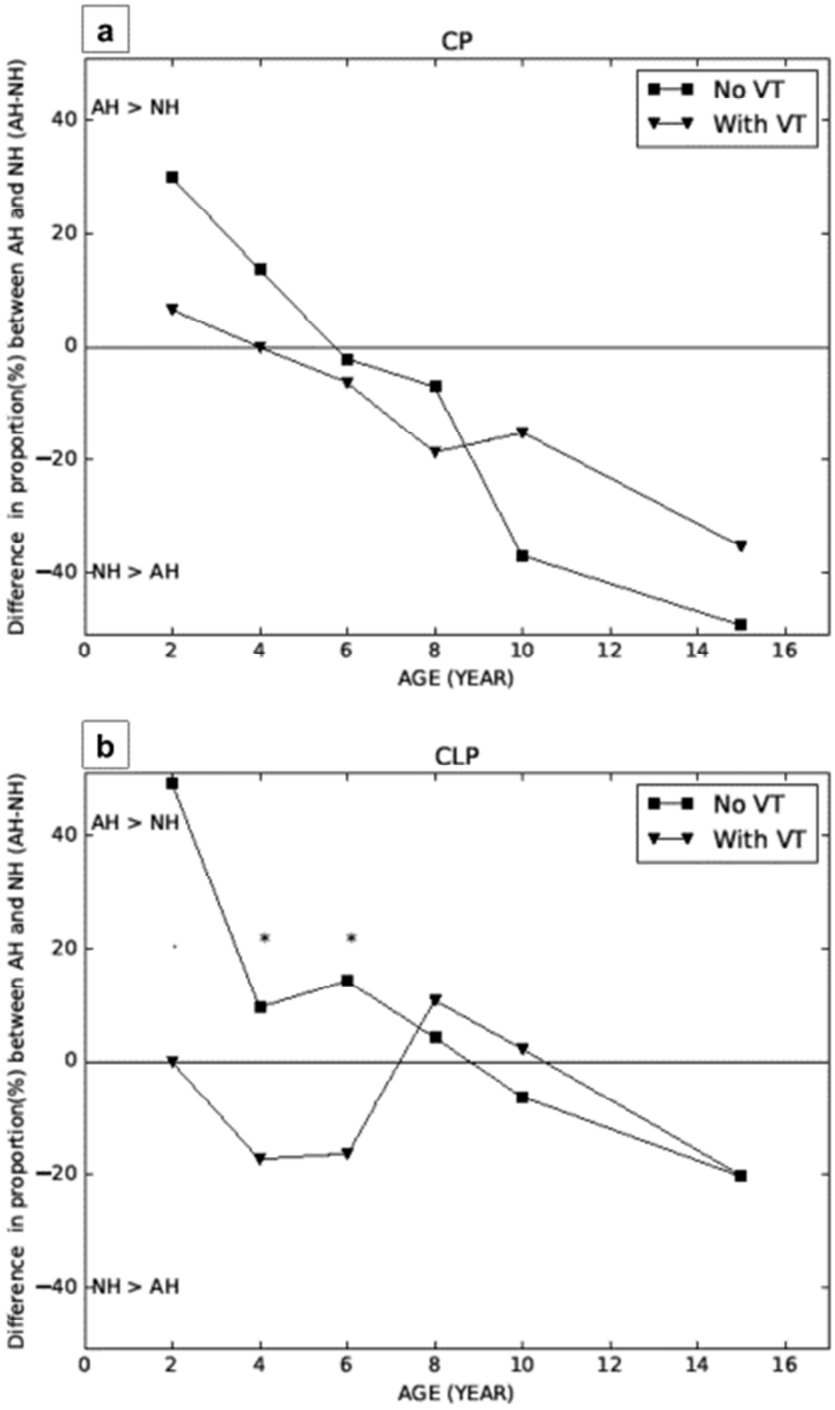

Figure 1. Difference between the proportion (%) of children with abnormal hearing (AH) and the proportion (%) of children with normal hearing (NH), with or without ventilation tube (VT) for the CP (left panel) and CLP groups at different ages. Results from the chi-square test with statistical significance are denoted as $P < 0.05$.*

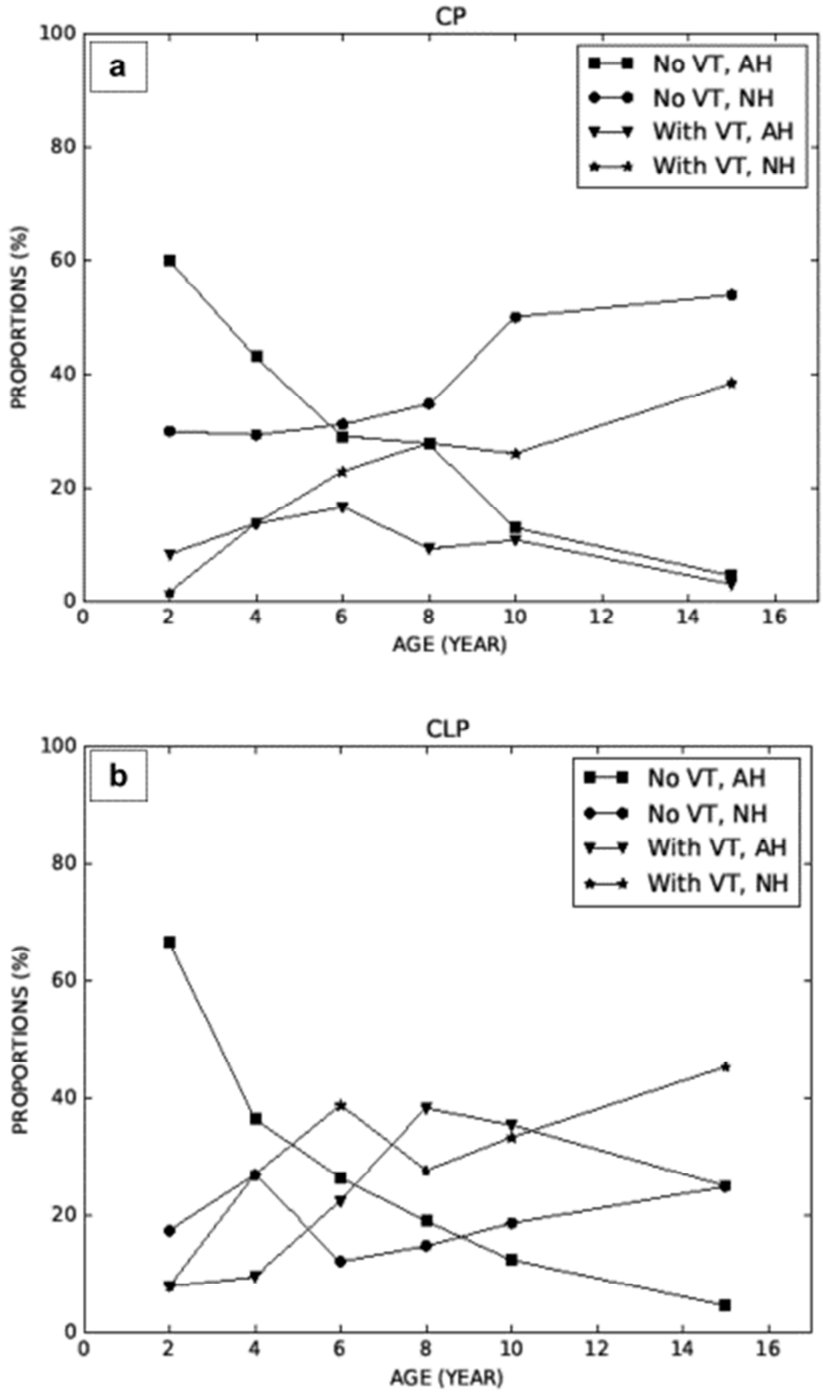

Figure 2. Percentage of children with normal (NH) and abnormal hearing (AH) related to ventilation tube (VT) insertion across ages. Children from the cleft palate group (CP) are presented in a, children born with cleft lip palate (CLP) are shown in b. Results from the chi-square test with statistical significance are denoted as $P < 0.05$.*