Hearing Loss after Cardiac Surgery in Infancy: An Unintended Consequence of Life-Saving Care

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Objectives To investigate the prevalence of hearing loss after cardiac surgery in infancy, patient and operative factors associated with hearing loss, and the relationship of hearing loss to neurodevelopmental outcomes.

Study design Audiologic and neurodevelopmental evaluations were conducted on 348 children who underwent repair of congenital heart disease at the Children's Hospital of Philadelphia as part of a prospective study evaluating neurodevelopmental outcomes at 4 years of age. A prevalence estimate was calculated based on presence and type of hearing loss. Potential risk factors and the impact of hearing loss on neurodevelopmental outcomes were evaluated.

Results The prevalence of hearing loss was 21.6% (95% CI, 17.2-25.9). The prevalence of conductive hearing loss, sensorineural hearing loss, and indeterminate hearing loss were 12.4% (95% CI, 8.8-16.0), 6.9% (95% CI, 4.1-9.7), and 2.3% (95% CI, 0.6-4.0), respectively. Only 18 of 348 subjects (5.2%) had screened positive for hearing loss before this study and 10 used a hearing aid. After adjusting for patient and operative covariates, younger gestational age, longer postoperative duration of stay, and a confirmed genetic anomaly were associated with hearing loss (all $P < .01$). The presence of hearing loss was associated with worse language, cognition and attention ($P < .01$).

Conclusions These findings suggest that the prevalence of hearing loss in preschool children after heart surgery in infancy may be 20-fold higher than in the 1% prevalence seen in the general population. Younger gestational age, presence of a genetic anomaly, and longer postoperative duration of stay were associated with hearing loss. Hearing loss was associated with worse neurodevelopmental outcomes. *(J Pediatr 2018;192:144-51).*

Congenital heart defects (CHDs) are the most common developmental defects and frequently require repair in infancy. As surgical techniques and procedures have improved over the last 25 years, mortality has declined. However, the recognition of neurodevelopmental disabilities as an adverse outcome has increased.[1-3] Understanding the causes of such morbidities is important in helping to mitigate them and improve long-term outcomes.

Hearing loss in childhood has the potential for life-long neurodevelopmental disability, poor language skills, and behavioral problems.[4] There is a paucity of population-based data regarding the prevalence of hearing loss in preschool age children, but the best estimates are a prevalence of around 1%.[5,6] Hearing is a prerequisite for learning spoken language and speech production. When these activities are impaired owing to hearing loss, language acquisition is impacted. The Joint Committee on Infant Hearing 2007 identified a series of risk factors associated with hearing loss in childhood.[7] Many of these also occur in children with CHDs, including prolonged intensive care, assisted ventilation, extracorporeal membrane oxygenation (ECMO), and exposure to ototoxic medications.[8-13] Hearing loss and its impact on neurodevelopmental indicators have not been studied explicitly in children with different types of CHDs, including those undergoing surgical repair.

The overall purposes of this study were to (1) estimate the prevalence of hearing loss after cardiac surgery in infancy, (2) evaluate potential risk factors for hearing loss, and (3) investigate the relationship between hearing loss and selected neurodevelopmental indicators.

CHD	Congenital heart defect
ECMO	Extracorporeal membrane oxygenation
GA	Gestational age
HFHL	High-frequency hearing loss
NEPSY	NEuro-PSYchology statue test
PSL-4	Preschool Language Scale-4
PTA	Pure tone average
SNHL	Sensorineural hearing loss
WPPSI-III	Wechsler Preschool and Primary Scale of Intelligence, Third Edition

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Methods

This study was a prospective observational study intended to evaluate the effects of apolipoprotein E polymorphisms on neurodevelopmental outcomes for preschool-aged patients 4-5 years of age after cardiac surgery in the neonatal and infant periods. Between September 1998 and April 2003, 675 eligible infants underwent cardiac surgery. Twenty-three infants died before consent, the parents of 102 patients declined participation, and 550 (81%) were enrolled.[14] Eligible patients were ≤6 months of age and undergoing surgical treatment of CHDs with cardiopulmonary bypass, with or without deep hypothermic circulatory arrest. Exclusion criteria included (1) multiple congenital anomalies, (2) recognizable genetic or phenotypic syndrome other than chromosome 22q11 microdeletion syndrome, and (3) language other than English spoken in the home. The current study evaluated those patients who completed a standard audiologic evaluation as part of a comprehensive neurodevelopmental evaluation at 4 years of age (2003-2008). The study was approved by the institutional review board at the Children's Hospital of Philadelphia. Informed consent was obtained from parents or guardians.

Audiologic evaluations were conducted using standard pediatric assessment methods based on developmental ability. Thresholds were obtained for pure tone air conduction stimuli at frequencies of 250-8000 Hz in an audiometric booth. Pure tone bone conduction thresholds were obtained when responses to pure tone air conduction signals were poorer than 15 dB hearing loss. Normal hearing sensitivity was defined as response thresholds of ≤15 dB hearing loss. Hearing loss was defined as average pure tone air conduction thresholds of ≥20 dB hearing loss at the following frequencies (500, 1000, 2000), or average pure tone air conduction thresholds of ≥25 dB hearing loss at 2 or more frequencies of >2000 Hz. Hearing loss was further classified as conductive or sensorineural (sensorineural hearing loss [SNHL]); conductive hearing loss was defined as pure tone bone conduction thresholds of ≤15 dB hearing loss and pure tone air conduction responses of ≥10 dB poorer than the pure tone bone conduction thresholds. SNHL occurred when both pure tone air conduction and pure tone bone conduction thresholds were >15 dB hearing loss, and the difference between the two was ≤10 dB. Hearing loss was classified as indeterminate hearing loss if the subject could not complete the pure tone bone conduction testing necessary (masked or unmasked) owing to immaturity or developmental delay, or could only be assessed in a sound field (responses obtained from the better hearing ear, if differences existed between the ears). Degree of hearing loss was determined based on the pure tone average (PTA). Normal hearing sensitivity was defined as PTA between 0 and 15 dB hearing loss. Hearing loss was defined as PTA of >20 dB hearing loss, using the following PTA ranges and descriptors: 21-39 dB hearing loss (mild); 40-54 dB hearing loss (moderate); 55-69 dB hearing loss (moderate to severe); 70-89 dB hearing loss (severe); and ≥90 dB hearing loss (profound). High-frequency hearing loss (HFHL) was defined as confined to the region at ≥2000 Hz, and using the same descriptors for the average of those responses (ie, "mild HFHL").

Patient-related variables (eg, age at testing, sex, race, anthropometric measures) and perioperative variables (eg, age at surgery, bypass support times, hematocrit, duration of stay) were collected from patient records and patient evaluations and laboratory testing. We were not able to quantify exposure to potentially ototoxic medications.

Patients were evaluated by a genetic dysmorphologist. Chromosome analysis and testing for microdeletion of 22q11 were performed as indicated. Results of the genetic evaluations were classified as normal if no genetic or chromosome abnormality was demonstrated, abnormal if a specific diagnosis was confirmed, and suspect if there was evidence of a genetic syndrome that could not be confirmed.

Language was assessed with the Preschool Language Scale-4 (PLS-4), Auditory Comprehension, Expressive Communication, and Total Language Score.[15] The Wechsler Preschool and Primary Scale of Intelligence, Third Edition (WPPSI-III) was used to assess cognition in children and provides a Full-Scale IQ score.[16] To examine executive functioning and attention the NEuro-PSYchology statue test (NEPSY) was used, targeting inhibition and motor persistence (2 components of executive function and attention).[17]

Statistical Analyses

Data analysis occurred in 3 distinct phases: a descriptive phase, a prevalence phase, and a risk modeling phase.

Measures of central tendency, variability, and association were computed for all relevant variables, for the group as a whole, and by hearing loss category. Cardiac diagnosis was coded according to a previously described classification incorporating anatomy and perioperative physiology that has been shown to be predictive of perioperative mortality. Class I is defined as 2 ventricles with no aortic arch obstruction, class II as 2 ventricles with aortic arch obstruction, class III as single ventricle with no arch obstruction, and class IV as single ventricle with arch obstruction.[18] Patients with tetralogy of Fallot and transposition of the great arteries are in class I, whereas patients with hypoplastic left heart syndrome or its variants are in class IV.

Prevalence estimates for the presence or absence of hearing loss and by each of 3 identified subtypes (conductive, SNHL, and indeterminate) were computed complete with 95% CIs.

Three different sets of risk models were specified and tested with presence or absence of hearing loss modeled as a dichotomous outcome. A total of 23 standard logistic regression models and 1 contingency table (ECMO/left ventricular assist device) were specified and tested, representing patient-related, perioperative, and postoperative factors. The single contingency table test for ECMO/left ventricular assist device was necessary owing to low cell counts in several cells. As a follow-up to these models, the percentage of patients with hearing loss who had ≥1 of these risk factors was calculated and compared with those without.