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Vidgad vestibularakvedukt hos patienter med cochleaimplantat

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Sammanfattning
Vidgad vestibularakvedukt (EVA) är en inneröremissbildning och en vanlig orsak till ärftlig hörselnedsättning. Hörselnedsättningen är ofta av kombinerad typ och orsaken till den konduktiva komponenten antas ligga i innerörat. EVA diagnostiseras med hjälp av radiologiska metoder, till exempel innan operation med cochleaimplantat (CI).

Syftet var att beskriva prevalens, demografi och hörselnedsättning hos EVA-patienter som fått CI.

Metoden var en retrospektiv journalstudie på CI-patienter konsekutivt opererade från år 2000 till 2008 på Sahlgrenska Universitetssjukhuset. CT-, audiometriska resultat, demografiska uppgifter och genetiska testresultat användes.

Fem procent av patienterna hade EVA. Av dessa hade 79 procent bilaterala EVA. EVA-patienterna fick en grav till mycket grav hörselnedsättning tidigare och blev opererade vid en yngre ålder jämfört med patienter utan EVA. Resultaten stödjer rådande teorier om att mekanismer i innerörat orsakar den konduktiva komponenten.

Nyckelord
Vidgad vestibularakvedukt, cochleaimplantat, ärftlig hörselnedsättning

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Enlarged vestibular aqueduct in cochlear implant patients

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Abstract
Enlarged vestibular aqueduct (EVA) is a malformation in the inner ear and a common cause of hereditary hearing loss. The aqueduct is usually considered enlarged when it is wider than 1.5 mm at midpoint. The hearing loss is often mixed and the cause of the conductive component is assumed to lie in the inner ear. EVA is diagnosed by radiologic methods, for example before cochlear implant (CI) surgery.

The aim was to describe prevalence, demography and hearing loss of EVA patients operated with a CI.

The study was conducted retrospectively on journals of patients consecutively operated with a CI from the year 2000 to 2008 at Sahlgrenska University Hospital. CT and MRI scans, audiometric results, demographics and genetic test results were consulted.

Five percent of the CI patients had EVA. Of these, 79 percent had bilateral EVA. The EVA patients developed a severe to profound hearing loss earlier in life and were operated at a younger age compared to the patients without EVA. The results support contemporary theories on the fact that inner ear mechanisms are the cause of the conductive component.

Key words
Enlarged vestibular aqueduct, cochlear implants, hereditary hearing loss

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Table of contents

Introduction

The vestibular aqueduct is a thin bony canal that is located between the inner ear and the endolymphatic sac, which is embedded in a separate cavity in the temporal bone. Within the vestibular aqueduct runs a fluid-filled tube, the endolymphatic duct, which transports water and ions between the endolymphatic sac and the inner ear fluid. The endolymphatic sac and duct are assumed to help to maintain a steady concentration of ions and pressure in the endolymph in the inner ear. Water and ion channels in the endolymphatic sac are assumed to be essential for the homeostasis of the inner ear fluid and for maintaining the endocochlear potential. The endocochlear potential is a requirement for the sensory cells in the inner ear to function properly (1). Other functions of the endolymphatic sac are regulation of the immune response of the inner ear and removal of waste products from the inner ear fluid by phagocytosis (2).

When the vestibular aqueduct is larger than 1.5 mm in diameter at midpoint it is usually considered an enlarged vestibular aqueduct (EVA) (3). Other studies question the usefulness of this somewhat arbitrarily set diameter as a criterion for EVA and argue for a wider range of diameters for EVA so as to include even somewhat smaller diameters as a criterion. However, > 1.5 mm is still a widely accepted measure of EVA (4). Synonyms to EVA are large vestibular aqueduct (LVA) and large vestibular aqueduct syndrome (LVAS). A possible cause of EVA is arrested development in the embryo, but the enlargement could also be due to maldevelopment in early childhood (5). An EVA is usually combined with an enlarged endolymphatic duct and sac. Approximately five to fifteen percent of children with sensorineural hearing loss have EVA (1). EVA can be diagnosed with computed tomography (CT) or magnetic resonance imaging (MRI). It is the most frequently found temporal bone anomaly in children with hearing loss (1). In different studies a slight female majority of between 59 and 65 % was found among EVA patients (3, 5, 6).

The onset of hearing loss in persons with EVA is sudden in about half of the patients and often occurs in childhood. Often an event such as a minor head trauma triggers the hearing loss (7 - 9). EVA is reported to be bilateral in 55 to 94 % (10 - 13). An overview study on 310 ears of children diagnosed with EVA demonstrated that 67 % of the ears had stable hearing over a period of several years, of which 34 % demonstrated fluctuations within this period. The remaining 33 % had a progressive hearing loss, of which 50 % demonstrated fluctuations (13).

One study found a conductive component in 59 percent of patients with EVA and hearing loss (14). There have been several theories regarding the air-bone gap typically seen in patients with EVA and hearing loss. Since the mobility of the ossicular chain has been found to be normal in patients with EVA, it is presumed that the air-bone gap is caused by a change in cochlear mechanics (8, 15). One theory suggests that an elevated pressure in the inner ear fluids could lead to decreased mobility of the stapes (15). According to different theories an abnormally large vestibular aqueduct functions as a third mobile window in the inner ear. This third mobile window would improve the thresholds for bone-conduction by changing the mechanisms of hearing by bone conduction (16). A recent theory hypothesizes that the third mobile window can produce an air-bone gap by diverting air-conducted sound that is conducted through the ossicular chain into the cochlea, away from the cochlea. This would lead to elevated air conduction thresholds (17).

About one-third of the patients with EVA have Pendred syndrome (PS) (1). PS symptoms are bilateral hearing loss, EVA and goiter with or without hypotyroidism. The gene SLC26A4 codes for the protein pendrin that functions as a chloride and iodide transporter, which is necessary for the endocochlear potential. Different mutations in SLC26A4 can lead to a congenital anomaly of the temporal bone, an increased pressure in the endolymph and a loss of the endocochlear potential, which could be the cause of the hearing loss in PS (18). The hearing loss can be purely sensorineural or mixed, stable, progressive or fluctuating. The goiter is due to an iodide organification defect in the thyroid (i.e. a defect in the production of thyroid hormone). PS is the most common form of syndromic deafness and up to 10 percent of the cases of hereditary deafness are caused by this syndrome (19). In the 1920s it was hypothesized that a recessive inheritance was responsible for deafness and an error in thyroid metabolism, described together as PS (20). Before more modern methods of diagnosis were available, PS was often described and diagnosed through hearing loss and goiter. A study in the 1960s of six PS patients described the diagnosis of hereditary congenital bilateral deafness at the age of 3 to 5 years and the age of onset of goiter at ages between 12 and 17 years (21).

EVA can also be found in other syndromes such as branchio-oto-renal syndrome, Waardenburg syndrome, CHARGE syndrome, distal renal tubular acidosis, oto-facio-cervical syndrome and in combination with cholesteatoma in children (22, 23 - 26).

One treatment option for persons with severe and profound bilateral sensorineural hearing losses (i.e. hearing losses of 70 dB HL or more) is a cochlear implant (CI). An example of a criterion used in Sweden is worse hearing thresholds than 50 to 60 dB at 2 and 4 kHz in the best-aided condition (27). A CI is an electronic device that directly

stimulates the neurons in the spiral ganglion and bypasses the hair cells' function. CIs can improve hearing and the ability of oral communication of people who have a severe to profound hearing loss. In the year 1975 the first CI was operated into a human and since then over 100 000 persons have been implanted. Over the years the youngest age at which patients can be operated has been lowered. For example, in 1995 surgery was not recommended for patients younger than two years (28). Nowadays many children under the age of one are being operated.

Before CI surgery all patients undergo CT or MRI scans. CT scanning uses radio magnetic waves and can give a good representation of temporal bone anatomy. MRI scans can give a high-quality representation of soft tissues, neural anatomy and fluid filled spaces of the inner ear and uses powerful magnets and radio waves. In a study on MRI scans before CI surgery, 4 % of 170 children were found to have EVA (29). Another study investigated CT scans of 242 ears of children who had CI surgery and found that 16 % of these had an enlarged vestibular aqueduct (30). In a study on 570 ears of cochlear implantees 9 % were found to have an EVA (31). All of these studies used the criterion that states that an EVA is larger than 1.5 mm in diameter.

Aim of the study

Relevance of the study

It is important for audiologists and other clinicians to gain knowledge about persons with EVA and their hearing loss pattern because the hearing loss often progresses to a severe to profound at a relatively young age. Hence these persons often are candidates for receiving a CI.

Aim and specific issues

The aim of this study was to describe prevalence, demography and hearing of CI recipients with EVA in the years 2000-2008 at Sahlgrenska University Hospital in Göteborg, Sweden.

The specific issues addressed were:

- What is the prevalence of EVA among CI recipients according to the medical investigation prior to surgery?
- How common is bilateral compared to unilateral EVA among CI recipients?
- Is there a significant gender difference in prevalence of EVA in CI recipients?

- At what age does the air-conduction pure tone average for 0.5, 1, 2 and 4 kHz ($ACPTA_4$) exceed 70 dB HL in CI recipients with EVA?
- How many of the CI recipients with EVA have a mixed hearing loss and could this be explained by a possible immobility of the ossicular chain?
- At what age are these persons with EVA operated with a CI for the first time compared to the age of the persons without EVA?

Material and methods

Data collection

The material of 262 cases undergoing CI surgery between the years 2000 and 2008 was studied retrospectively regarding the size of the vestibular aqueduct on CT scans. The CT scans of the temporal bone were performed as part of the presurgical evaluations by neuroradiologists. In doubtful cases a second opinion was performed. In this material 14 cases were found to have a vestibular aqueduct larger than the diagnosis criterion of 1.5 mm and were included in the study.

All persons' gender was noted. Audiometric data of CI recipients with EVA were analysed. The age at which the $ACPTA_4$ exceeded 70 dB HL for the first time, in the best ear of persons with bilateral EVA and in the EVA ear of persons with a unilateral EVA, was noted.

A conductive component of the hearing loss was defined as a gap of 15 dB or more between air and true (masked) bone thresholds at one or more frequencies and noted in at least one ear in persons with bilateral EVA and in the affected ear in persons with unilateral EVA. CI surgery journals were consulted according to the mobility of the ossicular chain. The mobility of the ossicular chain was performed by gently touching the chain while looking for a movement in the round window. If the ossicular chain and the stapes are mobile it is accompanied by a movement of the oval window.

Age of surgery was defined as the whole number of years of age for each patient at the date of the primary CI surgery, which in some cases took place before January 2000. For example, if a person was one year and eleven months at the day of operation, the person was considered to be one year of age. All persons were classified as either child (i.e. < 18 years) or adult at primary surgery.

Data processing and statistics

SPSS 14.0, 15.0, 16.0 and SPSS / PASW 17.0 was used to organise and process the collected data.

The number of persons with no EVA, unilateral EVA and bilateral EVA were studied in relation to the group of all CI recipients.

A z-test was performed to find a possible gender difference in the prevalence of EVA.

The mean age at which the $ACPTA_4$ surpassed 70 dB HL was calculated.

For each person available data on the type of hearing loss and ossicular chain mobility were compared to see if the cause of a possible gap could be explained by immobility of the ossicular chain.

Mean ages at primary surgery were calculated for all persons collectively as well as for adults and children separately. Possible statistically significant differences in these ages between the persons with EVA and persons without EVA were explored both for persons of all ages collectively and for adults and children separately. For both the adults and children a t-test was used to investigate a possible difference in age at primary surgery between the EVA group and the non-EVA group.

Results

Out of the 262 persons who had CI surgery, 14 (5,3 %) were diagnosed with EVA in one or both ears by CT scans of the temporal bone during the pre-surgical evaluation process. See Fig 1. Of the 14 EVA patients, 11 (79 %) had bilateral and 3 (21 %) unilateral EVA. See Fig 2.

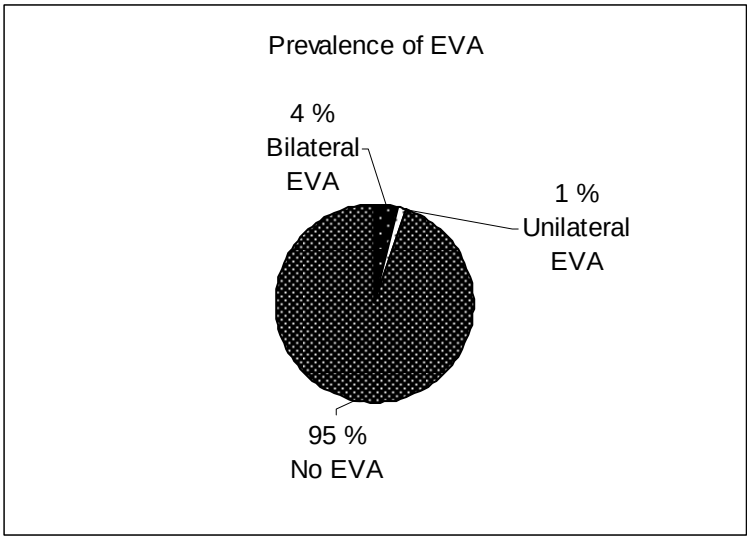

Fig 1. Prevalence of EVA among CI recipients. Of the 262 CI recipients, 11 (4 %) had bilateral EVA, 3 (1%) had a unilateral EVA and 248 (95%) had no EVA.

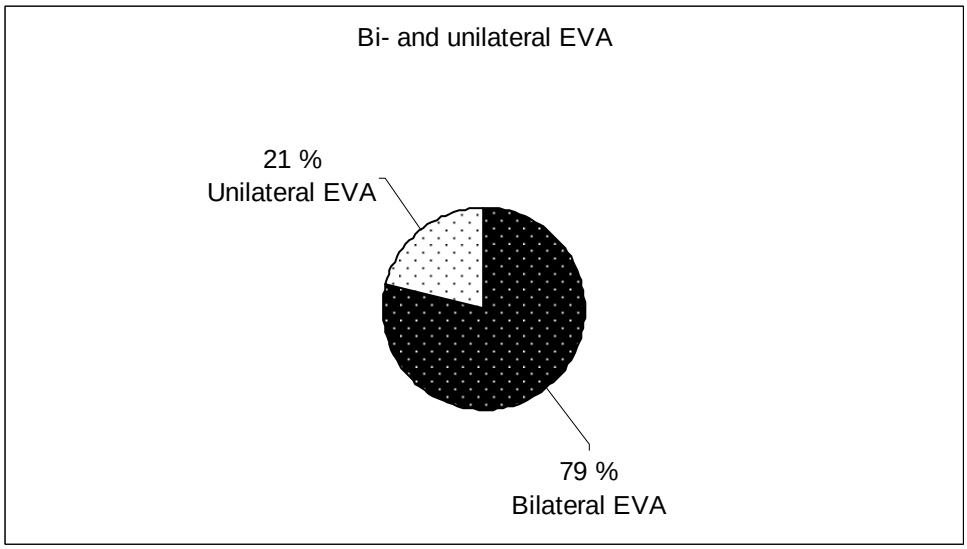

Fig 2. Prevalence of unilateral and bilateral EVA among the EVA patients. Of the 14 EVA patients 11 (79 %) had bilateral EVAs and 3 (21 %) had a unilateral EVA.

Among children who received a CI (n = 70), 6 (9 %) were diagnosed with EVA. Among adults who received a CI (n = 192), 8 (4 %) were diagnosed with EVA.

The prevalence of EVA among female and male CI recipients is shown in table 1. An equal number (n = 7) of women and men were found to have EVA. Of the patients without EVA (n = 248) slightly more were women (n = 134) than men (n = 114). The z-test showed no significant gender difference in the prevalence of EVA among CI recipients at the

α-level of 0.05. All of the three persons with unilateral EVA were women. Of the 11 persons with bilateral EVA, 7 were men and 4 women. It was not possible to determine if these latter differences were significant, due to the limited number of persons.

Table 1. Prevalence of EVA listed by gender and number of persons with cochlear implants.

		No EVA	EVA	Total
Gender	Female	134	7	141
	Male	114	7	121
Total		248	14	262

Not all audiograms on each person were available because many were referred to Sahlgrenska University Hospital by other hospitals that had patient journal systems to which access was not received for this study.

Data on 12 out of the 14 persons with EVA on the age at which the $ACPTA_4$ exceeded 70 dB HL for the first time were available for the best ear in persons with bilateral EVA and for the affected ear in persons with unilateral EVA. For 4 of these 14 persons the *exact* age, at which the $ACPTA_4$ exceeded 70 dB HL for the first time, could be established. These ages were 2, 6, 6 and 19 years. The mean age at which the $ACPTA_4$ passed 70 dB in this group was 8 years. The person with unilateral EVA was 6 years. For the remaining 8 persons only the highest theoretically possible age at which the $ACPTA_4$ exceeded 70 dB could be established, due to the lack of available audiograms taken before the persons' $ACPTA_4$ exceeded 70 dB. The mean highest possible age at which the $ACPTA_4$ surpassed 70 dB for the 12 persons with available data was 11 years.

Many audiograms of the persons with EVA lacked bone-conduction thresholds, which was a limiting factor in collecting audiometric data. For 9 of the 14 persons with EVA, data were available on bone-conduction thresholds. The hearing loss of all of these nine had a conductive component (at least 15 dB on one frequency) in an EVA ear.

Mobility of the ossicular chain in the operated ear was evaluated in 13 of the 14 EVA patients during surgery. 12 of these had a mobile ossicular chain. The remaining patient had ossicular chain immobility and an inner ear malformation. No data was available on bone-conduction thresholds of this person.

For 8 persons with EVA data were available on both the air-bone gap and mobility of the ossicular chain. All of these 8 had a conductive component in at least one EVA ear and all had a mobile ossicular chain.

Among the persons without EVA (n = 248) the mean age of primary CI surgery was 46 years (s.d. = 28 years). Among the EVA patients (n = 14) the mean age of primary surgery was 29 years (s.d. = 23 years). The difference between the mean age at surgery was 17 years. A t-test to examine the significance of this difference could not be carried out because the ages were not normally distributed.

In the group of adult persons without EVA (n = 184) the mean age of primary CI surgery was 60 years (s.d. = 15 years). Among the adult persons with EVA (n = 8) the mean age of primary surgery was 46 years (s.d. = 13 years). This difference is statistically significant ($p < 0.05$).

Fig 3 illustrates the difference in age distribution at primary CI surgery between adults with and without EVA. The oldest person with EVA was aged 67 at primary surgery, whereas the oldest person without EVA was 89 years at primary surgery.

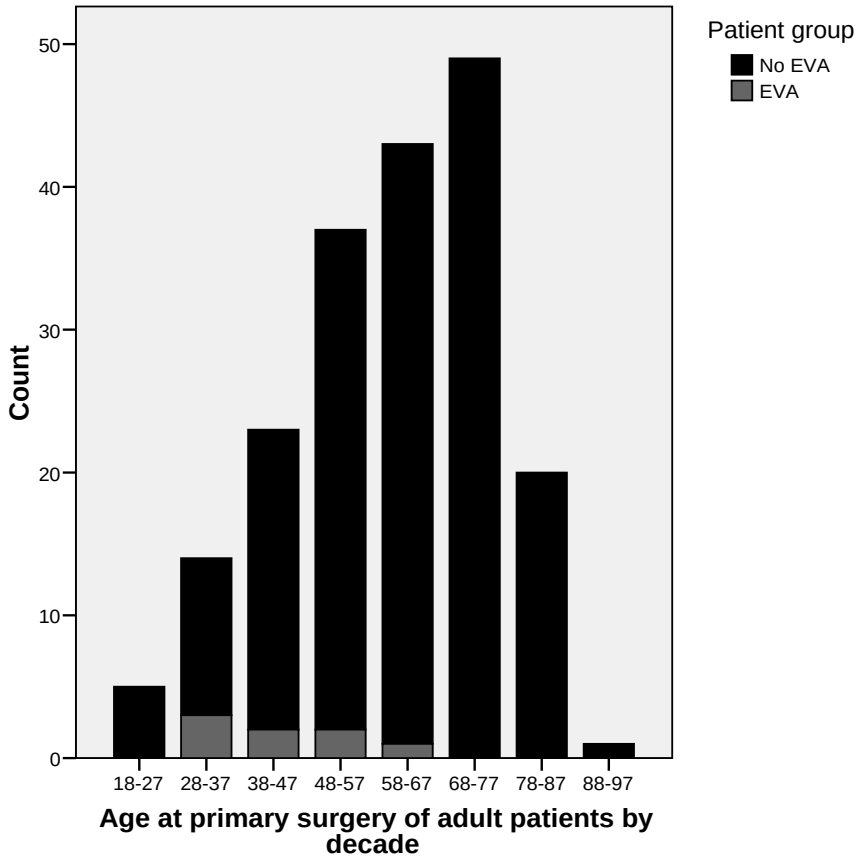

Fig 3. Number of adults with and without EVA divided into groups of 10 years by age at primary CI surgery. The histogram shows the distribution of adult patients' age at primary surgery. The grey areas denote persons with EVA. The black areas indicate persons without EVA.

Among children without EVA (n = 64) the mean age of primary CI surgery was 4 years (s.d. = 4 years). Among children with EVA (n = 6) the mean age of primary surgery was 6 years (s.d. = 5 years). This difference was not statistically significant at the α-level of 0.05.

Discussion

Method discussion

In this study 262 consecutive CI recipients were analyzed regarding the size of the vestibular aqueduct on CT scans. Of these, 14 persons had a vestibular aqueduct that was larger than 1.5 mm in diameter, which is the criterion for diagnosis with EVA, and were include in the study. The CT scans were analyzed by a neuroradiologist as part of the presurgical evaluation.

The strength of this study is that consecutive CI recipients of all ages over a period of nine years were analyzed. Therefore, data on both children and adults could be analyzed. The method, a retrospective patient journal study, was suitable for the purposes of this study, because many useful data, collected over the course of half a century, were accessible. CI recipients are an interesting group to study in itself. In the early days of cochlear implantation, EVAs were considered a contraindication of CI.

This study was not performed on a general patient group with hearing impairment due to EVA. Instead, a subgroup was studied, i.e. patients who had received a CI and thus had a severe to profound hearing loss.

A weakness of this study is the that the criterion of > 1.5 mm can be assumed to be a limiting factor in recognising all persons with a vestibular aqueduct that is somewhat larger than normal. Especially among those operated in the early 2000s, who were often evaluated in the late 1990's, some EVAs might have been left undetected because at the time not all radiologists investigated the size of the aqueducts on CT scans of the temporal bone area. The judgement of which vestibular aqueducts are either larger or smaller than 1.5 mm is a subjective process, which can also be considered a weakness.

The data collection could also have included information on air- and bone-conduction audiometric results as well as on ossicular mobility for *all* of the CI patients instead of just the EVA patients. More audiograms of CI recipients referred to Sahlgrenska University Hospital by other hospitals could have been accessed to collect more data on the $ACPTA_4$ and a possible conductive component. A permission to get this access would have

been needed, though. The available time for this project was limited so choices had to be made on which data we wanted to collect.

Discussion of results

In earlier studies, the prevalence of EVA in CI operated children varied between 4 % of the individuals and 16 % of the ears (29, 30). In a study on CI recipients of all ages it was found that 9 % of the ears had EVA (31). The result of this study was that 5 % of CI recipients were diagnosed with EVA. Among children this prevalence was 9 % and among adults 4 %. The results of this study are in line with previous studies on prevalence of EVA among CI recipients.

Further research is needed to compare this prevalence of EVA with that among a larger group of persons with severe to profound sensorineural hearing loss, by including persons who are not implanted with a CI.

In earlier research EVA was found to be bilateral in 55 to 94 % of the cases (10 - 13). In this study, EVA was bilateral in 79 % of the persons with EVA which is in line with the previous studies. More research is needed to describe the etiology and clinical significance of bilateral differences.

A female predominance for EVA was found in earlier studies (3, 5, 6). This study did not find a significant gender difference, which can be explained by the limited number of patients in the material. It could be important to be aware of gender differences within audiological research. Gender should be a topic of future research on a larger patient material to gain more knowledge about possible differences, their eventual causes and pathophysiological background.

Data on the age at which EVA patients' hearing loss becomes more severe than 70 dB HL could not be found in the literature. In this study, the $ACPTA_4$ of CI recipients with EVA surpassed 70 dB HL at a mean highest possible age of 11 years. This could be considered an early age compared to the age at which non-EVA CI recipients' $ACPTA_4$ exceeded 70 dB, though this figure was not compared to that of all CI patients. Therefore, further research is needed to make this comparison in a statistically significant manner by also evaluating CI recipients without EVA as well as additional earlier audiograms. This future research is possible within this patient material.

According to earlier studies more than half of the EVA patients have a combined hearing loss (14). This is due to a malfunction in the inner ear rather than the

middle ear according to different theories on a third mobile window in the cochlea (8, 15 - 17). These findings are confirmed by the results of this study: An air-bone gap was found in all persons with available bone-conduction thresholds. All of these persons, except one with a middle ear deformity, had a mobile ossicular chain. These results seem to confirm theories of the inner ear as the cause of the conductive component. The lack of available bone-conduction thresholds on many audiograms should be noticed by all audiologists working with diagnostics, because bone-conduction thresholds are an important tool in differential diagnostics of persons with severe to profound hearing losses.

In the literature, data on age at primary surgery of CI recipients with EVA compared to persons without EVA could not be found. The persons with EVA in this study were on average 17 years younger than the persons without EVA, although the statistical significance of this result could not be established due to the limited number of individuals in the EVA group. Among adults, the age of primary surgery was statistically significantly lower in persons with EVA compared to persons without EVA. Audiologists and other specialists can use this information to help to prepare patients and their significant others for surgery at a relatively early age. There was no significant difference in this respect among children. Research on a larger patient material is needed to find a possible statistically significant difference among persons of all ages collectively.

Conclusion

EVA is a frequently found anomaly among CI recipients, which was confirmed by this study. No gender difference in the prevalence of EVA among CI recipients was found in this study. A conductive component was found in the hearing of persons with EVA in this study. Among adult CI recipients, persons with EVA underwent surgery at a much younger age than persons without EVA.

Documented audiometric results in audiograms over time as well as a wider use of bone-conduction audiometry in persons with severe to profound presumed sensorineural hearing impairment can improve assessment, diagnosis and prognosis for this patient group.

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