Arnold W, Häusler R (eds): Otosclerosis and Stapes Surgery.
Adv Otorhinolaryngol. Basel, Karger, 2007, vol 65, pp 17–24

Evidence of Increased Average Age of Patients with Otosclerosis

H.P. Niedermeyer[a], *R. Häusler*[c], *D. Schwub*[a], *N.T. Neuner*[c], *R. Busch*[b], *W. Arnold*[a]

[a]Department of Otorhinolaryngology, Head and Neck Surgery, [b]Department of Medical Statistics and Epidemiology, Klinikum r.d. Isar, Technical University Munich, Munich, Germany; [c]Department of Otorhinolaryngology, Head and Neck Surgery, Inselspital, University of Bern, Bern, Switzerland

Abstract

Otosclerosis is an inflammatory disease of the human temporal bone which was assumed to affect up to 10% of the Caucasians. Histologic otosclerosis has an incidence of 3.4%. It is considered as a major cause of hearing loss in Western countries while a low incidence is observed among Africans. Many hypotheses about its origin had been formulated in the past. Otosclerosis genes (*OTSC1–5*) and collagen 1 genes are mutated in some familial cases of otosclerosis. On this genetic background, a common environmental factor such as a measles virus infection might be the triggering factor. Studies in the past indicated a distribution of otosclerosis among men and women of 1:1.4. Our study was designed to analyze the age of patients with otosclerosis at the time of surgery in the eighties and the nineties of the last century. Patients suffering from clinical otosclerosis who underwent stapedectomy between 1978 and 1999 with complete clinical data available (n = 1,351) were included in the study. Age and gender distribution, the age difference between men and women and the influence of gender and the year of recruitment were evaluated. Statistical analyses demonstrated an increase in the average age of patients with clinical otosclerosis from the eighties to the nineties ($p = 0.012$). The gender distribution showed no statistically significant variation ($p = 0.398$). These data might reflect an improved health consciousness among the elder population or could be the result of increased health awareness in the seventies and eighties. Finally, in the early seventies, measles virus vaccination was introduced in Germany and the shift of age could be the result of the measles virus immunization campaign.

Otosclerosis is considered among the major causes of hearing loss in the Western world [1–3]. The incidence of histologic otosclerosis is assumed at 10% of temporal bones, but Declau et al. [4], in their study of unselected temporal bones,

found otosclerotic foci in 3.4%. This disease restricted only to the human temporal bone develops with foci of bone resorption and reactive bone formation in the ontogenetically weak border region between bone and cartilage. Epidemiologic investigations in the past confirmed a higher incidence of otosclerosis in women than in men and in about 50% of cases familial inheritance has been described, suggesting a role of hereditary and genetic factors [1]. The age of onset of hearing loss due to otosclerotic fixation of the stapes has been considered to be between 15 and 40 years with a 1.4–2.0 times higher incidence in women [1, 2].

The incidence in Caucasians and South Indians is higher than in Europeans, while people from China and Indonesia suffer less frequently from otosclerosis. About otosclerosis in Africa, there are only rare reports in the literature [2]. Early epidemiologic data suggested low frequency of otosclerosis among the Japanese population, but recent investigations showed an incidence similar to that in Europeans [5, 6]. In the United States, 15 million people suffer from otosclerosis and it is considered to be among the most common causes of acquired deafness. In the last 30 years, a clear decrease in surgical otosclerosis occurred [3].

Histologic investigations of otosclerotic foci gave evidence of a chronic inflammatory process within the temporal bone. Many etiopathogenetic reasons such as mechanical distress, enzymatic imbalance, particular localization of Paget's disease, disease of the collagen tissue and others have been formulated. In some patients with otosclerosis, a particular genetic background could be detected. Mutations in otosclerosis genes (*OTSC1–5*) and collagen 1A1 were found in few families but no candidate genes have been sequenced up to now [7–9]. As a triggering factor, a measles virus (MeV) persistence was considered. Investigations by electron microscopy [10] and immunohistochemistry [11, 12] have shown the presence of MeV structures and proteins. Biochemical investigations have confirmed the strong MeV association with otosclerosis [13–15]. We and others observed MeV RNA within the otosclerotic tissue [13, 14, 16], but Grayeli et al. [17] failed to detect MeV RNA in otosclerotic tissue and cell culture. However, up to now no real proof has been found that MeV causes otosclerosis.

Since we felt that the average age of our patients increased over the years, we attempted to reevaluate the age of clinical onset of otosclerosis and the gender distribution considering the increased consciousness of health.

Patients and Methods

We included all patients with clinical otosclerosis who had undergone stapedectomy or stapedotomy in our Department of ENT, Head and Neck Surgery, Munich, Germany, between 1978 and 1999 (n = 1,351). Clinical diagnosis of otosclerosis was based on ear microscopy, air and bone conduction audiogram and speech data for Freiburger monosyllabic words, tympanogram, stapedial reflex and radiography of the mastoid. The footplate fragments were

Table 1. Average age of patients in the recruitment period from 1978 to 1999

Year of surgery	Patients n	Mean age ± SD years
1978	42	39.60 ± 10.83
1979	43	40.12 ± 9.93
1980	60	37.88 ± 13.54
1981	51	42.22 ± 11.47
1982	61	42.16 ± 11.28
1983	60	40.17 ± 13.69
1984	43	44.12 ± 12.40
1985	34	43.82 ± 12.76
1986	48	45.67 ± 11.32
1987	43	41.16 ± 12.06
1988	43	42.84 ± 11.93
1989	46	38.93 ± 13.31
1990	58	40.74 ± 13.13
1991	44	43.95 ± 13.04
1992	67	43.03 ± 12.63
1993	83	45.70 ± 11.27
1994	94	45.36 ± 12.26
1995	102	47.50 ± 13.32
1996	114	45.69 ± 11.97
1997	136	46.05 ± 13.27
1998	41	44.29 ± 12.68
1999	38	45.05 ± 10.88
Total	1,351	43.57 ± 12.5

fixed, decalcified and paraffin embedded. Histologic examination of the hematoxylin/eosin-stained fragments confirmed sclerosis of the ligamentum annulare in all cases. All patients had spent the major part of their lives in Germany. The study group consisted of 798 (59%) women and 553 (41%) men and all clinical data were available. The distribution of age was analyzed for normal distribution. The gender distribution over the recruitment period was tested with the χ^2 test. The differences of age between women and men were evaluated with Student's t test. A multivariate analysis of variance was performed to determine the influence of gender and year of recruitment. The level of significance was fixed at 5%. SPSS version 10 was used.

Results

Univariate analysis of the age of patients showed a statistically significant increase in the period examined ($p = 0.012$; table 1, fig. 1). An increase in the proportion of women at the limit of significance ($p = 0.054$) was observed in the

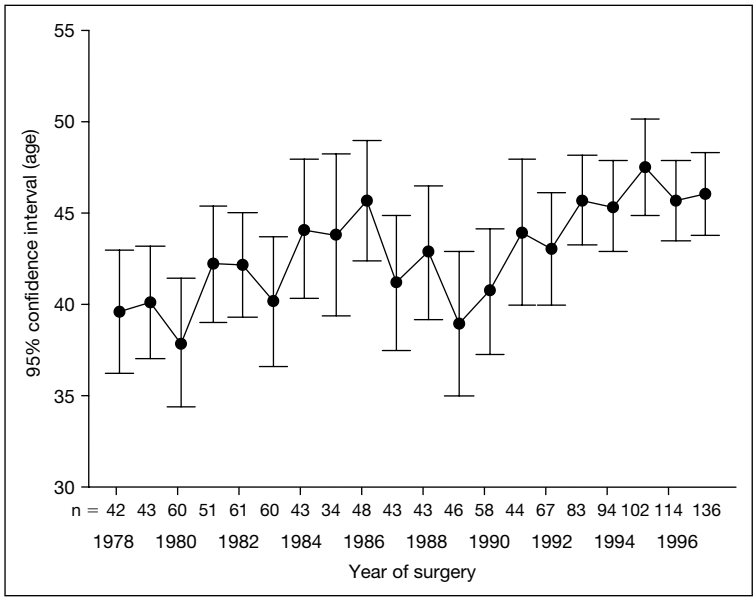

Fig. 1. Statistical analysis of the patients' average age over the period of recruitment.

univariate analysis of the distribution of gender. The difference of age between women and men ($p = 0.398$) (figs. 2, 3) was not statistically significant. The multivariate analysis confirmed that there is a significant increase in the patients' age over the period of recruitment ($p = 0.012$) while the increase in the incidence of otosclerosis in women in comparison with men from 1978 to 1999 was not statistically significant ($p = 0.418$; fig. 4).

Discussion

The statistical analysis of the available data gave evidence of an increase in the average age of patients with clinical otosclerosis in the recruitment period from 1978 through 1999, while no change in the distribution among gender and incidence in women and men occurred. The prevalence of otosclerosis in women is well known and our results are in good agreement with data published in the past. Various reasons were discussed: estrogens induce the proliferation of osteoblasts and calcification. The fact that otosclerosis occurs in women in particular after pregnancy supports this hypothesis. Furthermore, the administration of estrogens as contraceptives could explain the higher incidence of otosclerosis in women, whereas the low dose of hormones in the new generation of

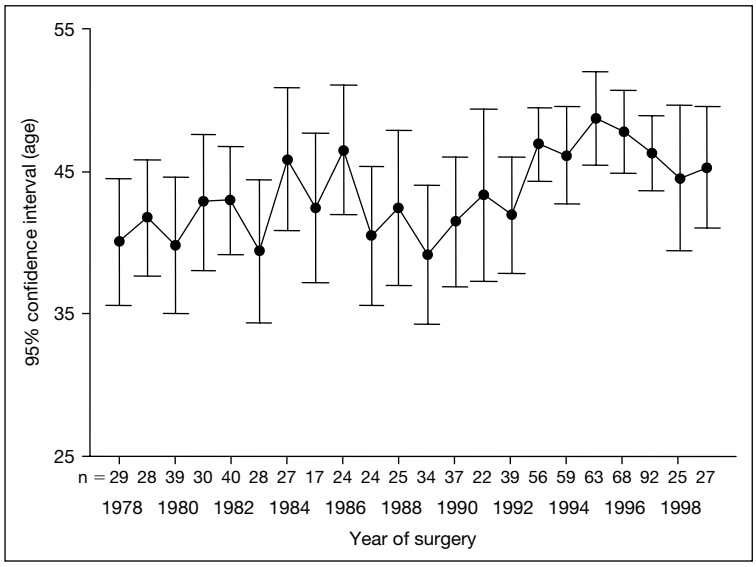

Fig. 2. Distribution of females in the years from 1978 to 1999.

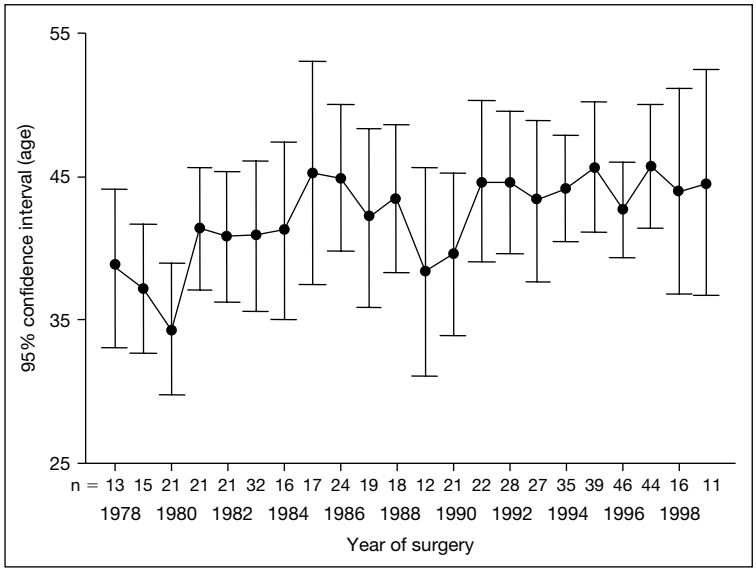

Fig. 3. Distribution of males in the years from 1978 to 1999.

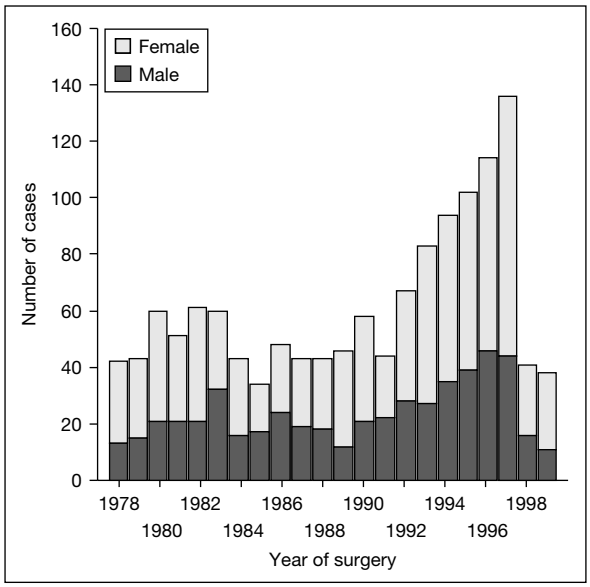

Fig. 4. Increase in age of women in comparison with men in the period of recruitment.

contraceptives may prevent the development of otosclerosis in early years. Administration of estrogens in the postmenopausal phase could explain the cases of otosclerosis in advanced age. However, in a large study, the influence of estrogens on the development of otosclerosis could not be confirmed [18].

The increase in the average age of onset of otosclerosis was clearly demonstrated in this study, considering some socioeconomic factors. The disattention of young patients regarding a progressive hearing loss because of social problems such as unemployment may play a role. This is confirmed by the fact that otosclerosis seems to be more frequent among people of higher social classes with minor social problems. However, in the last few years, concern about a high quality of life has increased and today patients do not put up with even small hearing problems. Another explanation for the increase in the age of patients with otosclerosis could be that large numbers of young patients with even a small air bone gap were operated in the seventies and eighties because of increased health awareness.

An increase in the use of fluoridated water was discussed as a reason for the decrease in otosclerosis. However, in a large study, this hypothesis could not be confirmed [19].

Finally, we have noted that the decrease in the incidence of otosclerosis in younger people coincides with the introduction of MeV vaccination in Germany.

The distribution of otosclerosis among women and men showed no significant change in the period of recruitment (women:men = 1.4–1.6:1). Our data

confirm the results from previous reports [1, 2]. Garenne [20] has reported a statistically significantly increased measles mortality for women during the reproductive period which is 1.4 times higher. One explanation discussed by Garenne is an immunologic weakness in the defense against MeV in women. However, our findings are in good agreement with investigations reported in the past.

Morphological and biochemical investigations in the past have shown a strong association between MeV and otosclerosis [15]. Since 1965, MeV vaccination with attenuated live Edmonston-strain-derived virus has been employed [21]. The administration of MeV vaccines has dramatically decreased the incidence of measles in all countries in which it has been effectively delivered (data from Centers of Disease Control and Prevention). In 1979, the USA identified as a goal the elimination of measles. Vaccination in the USA has led to a statistically significant reduction of MeV-related diseases, MeV inclusion body encephalitis and subacute sclerosing panencephalitis [22]. Otosclerosis has also decreased in the USA over the past 30 years. The authors state that the widespread immunization against MeV is a plausible reason [3].

However, the mechanisms of immunity are not completely understood. The duration of vaccine-induced immunity appears to be variable and the secondary vaccine failure rates have been estimated to be approximately 5% at 10 years after immunization [23]. Recently, we have genotyped MeV within the otosclerotic tissue of patients born in the sixties to group A which circulated in Europe before 1970 [unpubl. data]. This result confirms that MeV persists over several decades within the otosclerotic tissue. Studies on tissue from young patients immunized in the past could clarify which genotype – even the vaccination strain – can persist in the human temporal bone. We do not have any data which ascertain MeV persistence as the true cause of otosclerosis. MeV affects only humans and the genetic background certainly plays an important role. Thus, animal studies do not seem to be helpful to elucidate the causal role of MeV; however, epidemiologic data may contribute to answer this question.

In conclusion, there is evidence of a decrease in otosclerosis in patients aged between 20 and 40 years; however, the gender distribution did not change. The use of low-dose contraceptives, socioeconomic factors and vaccination strategies may partly explain these data. Further studies should be undertaken in the future to reevaluate the incidence and age of onset of otosclerosis.

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PD Dr. H.P. Niedermeyer
HNO Klinik und Poliklinik, Klinikum r.d. Isar, Technische Universität München
Ismaningerstrasse 22
DE–81675 Munich (Germany)
Tel. +49 89 4140 2371, Fax +49 89 41404853, E-Mail h.p.niedermeyer@lrz.tum.de