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Models to Predict Positive and Negative Effects of Cochlear Implantation on Tinnitus

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Objectives: The effect of cochlear implantation on tinnitus is heterogeneous: implantation does not always reduce tinnitus and may even worsen tinnitus. Therefore, it is important to know which factors influence the consequences of cochlear implantation for tinnitus. To date, no consensus has been reached regarding the factors that influence tinnitus. This study aimed to create prognostic models, using binary logistic regression analyses to predict positive or negative changes in tinnitus after cochlear implantation.

Methods: For this study we retrospectively sent two questionnaire packages to 117 cochlear implant patients.

Results: In the binary logistic regression analyses of the responses to the questionnaires, it was not possible to create a significant model to predict a positive effect of cochlear implantation on tinnitus. However, a negative effect of cochlear implantation on tinnitus was predictable, using a backward stepwise selection method in a model including the Abbreviated Profile of Hearing Aid Benefit (APHAB) and Tinnitus Handicap Questionnaire (THQ) ($P < .001$, Nagelkerke $R^2 = 0.529$).

Conclusions: Our results suggest that the lower the preoperative tinnitus handicap and the preoperative hearing handicap, the higher the chance that cochlear implantation will worsen tinnitus. More research needs to be done, preferable in a big prospective study, to make this model instrumental for clinical decision making and preoperative patient counselling. However, our results might suggest that preoperative THQ and APHAB screening could be meaningful. Especially in patients who are afraid to develop tinnitus or tinnitus worsening as complication of cochlear implantation.

Level of Evidence: 4

Key Words: Sensorineural hearing loss, cochlear implants, audiology.

INTRODUCTION

Recently, some medical centers have started using cochlear implantation as a treatment for tinnitus in patients with single-sided deafness.[1] Since cochlear implantation does not always reduce tinnitus, and may even have deleterious effects, it is important to know which factors influence the outcome of cochlear implantation on tinnitus. Previous studies describing the factors influencing the outcome of cochlear implantation on tinnitus did not show consistent results, and in some even contrary outcomes were reported.

Some factors have been reported to predict a positive effect of cochlear implantation on tinnitus. These include: higher preoperative tinnitus handicap scores, especially higher scores on the emotional subscale of tinnitus handicap questionnaires,[2–5] a higher age at implantation, higher preoperative hearing handicap scores,[6] higher preoperative stress levels,[2,5] as well as fewer years of hearing loss.[2,5] However, a relationship between age at implantation, the number of years of tinnitus before implantation, and the level of hearing loss before implantation could not consistently be confirmed as exerting a positive effect of implantation on tinnitus.[7]

In cochlear implant candidates who receive their implant because of severe hearing loss, besides being able to predict a positive effect of cochlear implantation on tinnitus, it is also important to be able to predict a negative effect, ie, deterioration or the onset of tinnitus after implantation. Knowing negative predictive factors might help clinicians in their preoperative counselling on the risks of developing tinnitus after the operation. Previous studies suggest that a higher age at implantation, higher preoperative tinnitus handicap scores,[4] better hearing before implantation, a shorter period of hearing loss before implantation, higher additional hearing loss after implantation and worse phoneme scores after implantation correlate with a negative effect of implantation on tinnitus. However, most of these correlations lack statistical significance.[7]

Since there is no clear evidence concerning which factors reliably predict the effects of cochlear implantation, we created models predicting positive or negative changes in tinnitus after implantation.

MATERIALS AND METHODS

The present study describes logistic regression analyses of data that were reported in an earlier paper by Kloostra et al.[8] As that paper extensively described, patients who received a cochlear implant between 2000 and 2009 in the University

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Medical Center Groningen in the Netherlands were recruited for the study. All surgeries were performed by two neuro-otological surgeons who were experienced in a wide range of ear surgeries, including in particular cochlear implantation. A majority of patients (n = 86) were implanted with a cochlear implant of the firm "Cochlear" (implant type CI24RE or CI422), the other 31 patients were implanted with the cochlear implant of the firm "Advanced Bionics". There was full insertion of the electrode in all patients and all electrodes were inserted by a round window insertion. Only with the CI24RE and the Advanced Bionics implants the round window was enlarged using a small drill. The patients with an implant of the firm Cochlear used the following speech processors: Esprit 3G, N = 13; Freedom, N = 45; CP810, N = 28. The patients with an implant of the firm Advanced Bionics used the Harmony speech processor (N = 31) All patients older than 18 years of age who had used their cochlear implant for at least 6 months were approached for inclusion. A few months to several years after they were implanted, a total of 117 patients retrospectively and simultaneously filled in two questionnaire booklets. Booklet one contained a number of questionnaires concerning the situation before implantation and booklet two the situation after implantation. Patients who did not experience tinnitus before and/or after implantation did not fill in the questionnaires concerning a tinnitus handicap.

The principal question of the questionnaire booklets was: "Were there any changes concerning your tinnitus after the cochlear implantation?" Possible responses were: A) No, I did not experience tinnitus before and after implantation; B) No, my already existing tinnitus remained the same after implantation; C) Yes, I started to experience tinnitus after implantation; D) Yes, my already existing tinnitus got worse after implantation; E) Yes, my already existing tinnitus got better after implantation; F) Yes, the tinnitus I experienced before implantation disappeared after implantation. In addition, the two booklets contained a number of standardized questionnaires: 1) The Abbreviated Profile of Hearing Aid Benefit (APHAB)[9]; 2) The Hospital Anxiety and Depression Scale (HADS)[10]; 3) UMCG tinnitus questionnaire; 4) The Tinnitus Handicap Inventory (THI)[11]; 5) The Tinnitus Handicap Questionnaire (THQ)[12,13]; 6) The type D-Scale (DS14)[14]; and 7) The Life Orientation Test (LOT).[15]

Apart from the questionnaire booklets, information about audiological tests and the date of implantation was gathered from the patients' clinical files.

The study was approved by the Medical Ethics Committee of the University Medical Hospital Groningen. Before participation, all patients gave their written informed consent.

Statistical Analysis

In order to create a prognostic model, we used the question about the presence of tinnitus pre- and post-surgery as the dependent outcome factor (Table I).

We classified patients as having a positive effect of cochlear implantation on tinnitus when they answered this question with E) "My already existing tinnitus got better after implantation" and F) "The tinnitus I experienced before implantation disappeared after implantation". The model to predict a positive effect of implantation can, of course, only be assessed in patients that experienced tinnitus prior to surgery. Hence, 61 out of 117 patients were included in the analyses of a positive effect of implantation on tinnitus. Within this group of patients, we compared the subgroup who experienced a positive effect of implantation on their tinnitus with the subgroup who did not experience a positive effect of the implantation.

TABLE I.
Regrouping Dependent Outcome Factor

Patients with positive effect	Patients without positive effect
Answers E+F (23 + 11=34)	Answers B+D (22 + 5=27)
Patients with negative effect	Patients without negative effect
Answers C+D (11 + 5=16)	Answers A+B+E+F (45 + 22+23 + 11=101)

Of the 61 patients included with preoperative tinnitus, 34 patients experienced a positive effect of implantation on their tinnitus, ie, suppression or cessation of tinnitus after cochlear implantation.

We classified patients as having a negative effect of cochlear implantation on tinnitus when they answered the question with C) "I started to experience tinnitus after implantation" and D) 'my already existing tinnitus got worse after implantation'. In order to predict which cochlear implant candidates had more chance of a negative effect of implantation on tinnitus, we included all 117 patients that completed the questionnaires in the analyses, because we wanted to know from the whole group of operated patients which type of patient experienced a negative outcome of implantation on tinnitus. Of 117 patients, 16 experienced a negative effect on their tinnitus, ie, a worsening of tinnitus (n = 5) or onset (n = 11) of tinnitus after implantation.

Based on previous studies and our own expectations, we included the following continuous pre-operative predictors in our analysis: tinnitus handicap (THI and THQ), personality characteristics (social inhibition, negative affect (DS14), optimism (LOT)), anxiety and depression (HADS), hearing handicap (APHAB), pre-operative speech comprehension scores, mean pre-operative hearing loss in decibels, years of tinnitus before implantation, and the age at the time of inclusion. To test which factors could be relevant as predictors, we first analyzed the factors by means of t-tests (THI, PTA of 1000Hz/2000Hz/4000Hz, APHAB) or Mann Whitney U-tests (THQ, HADS-depression, HADS-anxiety, DS14-negative affectivity, DS14-social inhibition, LOT, phoneme scores, age at inclusion and years of preoperative tinnitus), dependent on whether the variables were normally distributed or not. With these t-tests and Mann Whitney U-tests, we tested whether there was a relevant difference in the scores for these factors between the positive effect group and the no effect + negative effect group. In addition, we tested if there was a relevant difference in the scores between the negative effect group and the no effect group + positive effect group, since this may identify this factor as a predictor of the postoperative effect. As a rule of thumb, we included variables in the subsequent logistic regression analysis if the corresponding difference was significant at $P < .25$.

For statistical analyses we used IBM SPSS Statistics 20.

RESULTS

Positive Effect of Cochlear Implantation on Tinnitus

A total of 61 of 117 patients were included in the logistic model for a positive effect of implantation on tinnitus. The initial analysis (Table II) revealed relevant differences ($P < .25$) in THI and DS-14 negative affectivity scores between patients with and without a positive effect of implantation on tinnitus. Therefore, we considered these variables to be potential predictors of a positive effect of implantation on tinnitus. Binary logistic analyses with these variables as predictors in the model identified neither THI-scores nor DS14-negative affectivity as a significant predictor of a positive effect of implantation on

TABLE II.
P-values of the Difference in Means of Patients With or Without a Positive Effect of CI on Tinnitus

	P-values	Mean patients with positive effect (N = 34)	Mean patients without positive effect (N = 27)
T-tests			
THI	.142	34.94	26.45
APHAB	.979	76.73	76.63
Mean dB hearing loss	.656	105.69	104.08
Mann-Whitney U tests			
THQ	.268	43.89	36.75
DS14 Negative affectivity	.082	13.00	10.12
DS14 Social inhibition	.844	12.88	12.84
LOT	.853	20.44	20.24
years of tinnitus	.429	25.38	21.89
Phonemescores	.358	7.93	9.30
Age at inclusion	.366	61.35	64.54
HADS-anxiety	.428	9.88	9.32
HADS-depression	.333	7.16	6.56

APHAB = abbreviated profile of hearing aid benefit; CI = cochlear implantation; DS14 = type D-scale; DS14-na = type D scale negative affectivity; DS14-si = type D-scale social inhibition; HADS = hospital anxiety and depression scale; HADS-a = hospital anxiety and depression scale-anxiety; HADS-d = hospital anxiety and depression scale-depression; THI = tinnitus handicap inventory; LOT = life orientation test; THQ = tinnitus handicap questionnaire

TABLE III.
P-values of the Difference in Means of Patients With or Without a Negative Effect of CI on Tinnitus

	P-values	Mean patients with negative effect (N = 16)	Mean patients without negative effect (N = 101)
T-tests			
THI	.000	8.34	31.87
APHAB	.001	58.82	73.95
Mean dB hearing loss	.981	105.83	105.74
Mann-Whitney U tests			
THQ	.000	10.60	41.15
DS14 Negative affectivity	.049	6.69	10.18
DS14 Social inhibition	.002	8.38	12.77
LOT	.871	20.69	20.34
years of tinnitus	.371	31.33	23.31
Phonemescores	.419	11.35	8.75
Age at inclusion	.739	59.00	62.87
HADS-anxiety	.173	8.06	9.24
HADS-depression	.030	4.94	6.52

APHAB = abbreviated profile of hearing aid benefit; CI = cochlear implantation; DS14 = type D-scale; DS14-na = type D scale negative affectivity; DS14-si = type D-scale social inhibition; HADS = hospital anxiety and depression scale; HADS-a = hospital anxiety and depression scale-anxiety; HADS-d = hospital anxiety and depression scale-depression; THI = tinnitus handicap inventory; LOT = life orientation test; THQ = tinnitus handicap questionnaire

tinnitus. The lack of significance was observed when including both THI and the DS14-negative affectivity in the model (THI + DS14-negative affectivity: $P = .239$, Nagelkerke $R^2 = 0.066$) and when these variables were included separately (THI: $P = .133$, Nagelkerke $R^2 = 0.051$; DS14-negative affectivity: $P = .096$, Nagelkerke $R^2 = 0.063$).

Negative Effect of Cochlear Implantation on Tinnitus

All 117 patients were included in the logistic model for a negative effect of implantation on tinnitus. The initial analysis (Table III) found relevant differences ($P < .25$) between patients with and without a negative effect of CI in tinnitus for the variables: THI, THQ, APHAB, DS14-negative affectivity, DS14-social inhibition, HADS-anxiety, and HADS-depression. Therefore, these variables were considered to be potential predictors of a negative effect of implantation. In a first binary logistic analysis, we included all of these variables and identified a significant model ($P < .001$, Nagelkerke $R^2 = 0.559$) (Table IV). However, not all individual variables in this model were significant predictors of a negative effect. We thus performed a backward stepwise selection method to create a more reliable model. We removed a variable from our model if the p-value on the Wald statistic and the significance of change of the likelihood ratio was >0.05. Based on this, we included only the APHAB and the THQ in our final model. With these variables, we created a model with a significance of $P < .001$ and a Nagelkerke R^2 of 0.529 (Table V). Both THQ ($P = .004$ Wald statistic, $P = .001$ THQ 0.89-0.977) and APHAB ($P = .031$ Wald statistic, $P = .026$ APHAB 0.899-0.995) were each significantly related to a negative effect of implantation on tinnitus. The relation of the THQ with a negative of implantation on tinnitus is only relevant for patients with tinnitus deterioration after implantation and not relevant for patients with tinnitus onset after implantation because these last patients did not fill in the preoperative THQ. Our model indicates that the lower the preoperative tinnitus handicap (B = -0.056) and the lower the preoperative hearing handicap (B = -0.070), the higher the chance a patient has of experiencing a negative effect of cochlear implantation on tinnitus.

Our model fulfilled all assumptions for logistic regression analysis. We tested the linearity of the logit of the model and found that none of the interaction terms were significant (THQ x LnTHQ $P = .305$, APHAB x LnAPHAB $P = .736$). This indicates that the assumption of linearity of the logit had been met. We tested multicollinearity by tolerance- and VIF-values. All tolerance values were larger than 0.1 and all VIF values were smaller than 10, which makes multicollinearity unlikely (see Table VI).

DISCUSSION

Because the predictors of the effect of cochlear implantation on tinnitus were unclear, in this study we

TABLE IV.
Binary Logistic Regression Analysis of Negative Effect of CI on Tinnitus (All Variables Included)

Variable	B	Standard error	Significance (Wald)	Exp (B)	95% Confidence interval
THI	−0.027	0.046	0.552	0.973	0.890–1.064
THQ	−0.027	0.038	0.488	0.974	0.903–1.050
DS14-na	0.029	0.096	0.761	1.030	0.854–1.242
DS14-si	−0.165	0.104	0.113	0.848	0.691–1.040
APHAB	−0.065	0.029	0.027	0.937	0.885–0.992
HADS-a	−0.094	0.203	0.644	0.911	0.612–1.355
HADS-d	−0.127	0.208	0.541	0.880	0.585–1.324

($P < .001$, Nagelkerke $R^2 = 0.559$)
APHAB = abbreviated profile of hearing aid benefit; CI = cochlear implantation; DS14 = type D-scale; DS14-na = type D scale negative affectivity; DS14-si = type D-scale social inhibition; HADS = hospital anxiety and depression scale; HADS-a = hospital anxiety and depression scale-anxiety; HADS-d = hospital anxiety and depression scale-depression; THI = tinnitus handicap inventory; THQ = tinnitus handicap questionnaire

created prognostic models for positive and negative changes in tinnitus after cochlear implantation.

Unfortunately, we could not create a well-fitted model to predict a positive effect on tinnitus in patients with preoperative tinnitus. In contrast, for the negative effects of cochlear implantation on tinnitus, predictors could be established. The strongest predictors for a negative effect of cochlear implantation were a low preoperative tinnitus handicap and a low preoperative hearing handicap.

With regard to a positive effect of cochlear implantation on tinnitus, we could not confirm the results from previous studies in which the years of hearing loss, higher preoperative hearing handicap scores, higher preoperative tinnitus handicap scores and a higher age at implantation predicted better effects of cochlear implantation on tinnitus.[2–7] Most likely this is due to there being other factors involved in the effect of cochlear implantation on tinnitus that we did not include in our models. Higher preoperative tinnitus handicap scores as a predictor in previous studies could also be explained by the "regression toward the mean" principle, ie, if the tinnitus handicap is extreme on its first measurement (before cochlear implantation), it will tend to be closer to the average on its second measurement (after cochlear implantation).

Concerning the negative effect of cochlear implantation on tinnitus, the strongest predictors in the binary logistic model were the preoperative tinnitus handicap and the preoperative hearing handicap.

A low preoperative tinnitus handicap (only relevant for patient with preoperative tinnitus) score as a predictor of a negative effect on tinnitus is consistent with our expectations. This outcome could be explained by the fact that the less handicap patients experience before the operation, the greater the chance that the postoperative outcome is disappointing. Besides, in patients with a high level of tinnitus handicap, the physiology of the brain can be changed due to the changed pattern of spontaneous activity of the neural system that occurs in tinnitus.[16] Possibly, this makes the brain of these patients less sensitive to (negative) changes in tinnitus after cochlear implantation, in contrast to patients with a low tinnitus handicap in whom these changes in the physiology of the brain have not (yet) occurred.

The result that a lower hearing handicap predicts a negative effect on tinnitus also confirms our expectations. This outcome could also be explained by same mechanisms as described above with a greater tinnitus handicap.

Our results concerning hearing handicap are in agreement with those described before by Kompis et al.[7] who describe that patients that develop tinnitus postoperatively had slightly better preoperative hearing thresholds in the implanted ear.

Also, some studies describe a positive relationship between the amount of hearing handicap and the amount of tinnitus distress a patient experiences.[6,17] Thus a hearing handicap as a predictor of a negative effect of cochlear implantation on tinnitus is possibly mediated by a tinnitus handicap.

Our results should be read with caution due to the retrospective design, which might cause bias in two areas.

First, the retrospective method is susceptible to recall bias. Since participants completed the questionnaires after the implant surgery, it is possible that they could not remember the situation before implantation. This could magnify the effects; for example patients with

TABLE V.
Binary Logistic Regression Analysis of Negative Effect of CI on Tinnitus (Reduced Model)

Standard error	Significance (Wald)	Exp (B)	95% Confidence interval
0.024	0.004	0.933	0.89–0.977
0.026	0.031	0.946	0.899–0.995

($P < .001$, Nagelkerke $R^2 = 0.529$)
CI = cochlear implantation

TABLE VI.
Collinearity Statistics

	Tolerance	VIF
THQ	0.888	1.126
APHAB	0.888	1.126

APHAB = abbreviated profile of hearing aid benefit; THQ = tinnitus handicap questionnaire; VIF = variance inflation factor

a negative effect of implantation on tinnitus may remember the situation before implantation better than it actually was. This could result in lower preoperative tinnitus handicap scores and lower hearing handicap scores. This would mean that in our analyses of the negative effect of cochlear implantation on tinnitus, the predictive power of low preoperative tinnitus and hearing handicap is overestimated.

Second, there is potential contamination in the data because of factors such as social desirability and effort justification. Consequently, our data could be more in favor of a positive effect of cochlear implantation on tinnitus, because patients want to fulfil our expectations.[18] Social desirability and effort justification may affect the data in two ways: First, not all patients with a negative effect of cochlear implantation on tinnitus might mention their negative effect in our questionnaires, which could bias our study populations. Second, patients might score their preoperative tinnitus and hearing handicap higher and again falsely make these factors predictors for a negative effect of cochlear implantation on tinnitus.

CONCLUSION

A regression analysis of possible predictive indicators of the effect of cochlear implantation on tinnitus did not reveal a good predictive model for a positive effect. In contrast, the negative effects of cochlear implantation on tinnitus could be modelled and were mainly related to low preoperative tinnitus and low hearing handicap scores. This predictive model needs to be viewed with caution due to the retrospective character of our study. More research needs to be done, preferable in a big prospective study, to make this model instrumental for clinical decision making and preoperative patient counselling. However, our results might suggest that preoperative THQ and APHAB screening could be meaningful. Especially in patients who are afraid to develop tinnitus or tinnitus worsening as complication of cochlear implantation.

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BIBLIOGRAPHY

1. Van de Heyning P, Vermeire K, Diebl M, Nopp P, Anderson I, De Ridder D. Incapacitating unilateral tinnitus in single-sided deafness treated by cochlear implantation. *Ann Otol Rhinol Laryngol* 2008;9: 645–652.
2. Olze H, Szczepek AJ, Haupt H, et al. Cochlear implantation has a positive influence on quality of life, tinnitus, and psychological comorbidity. *Laryngoscope* 2011;10:2220–2227.
3. Souliere CR Jr, Kileny PR, Zwolan TA, Kemink JL. Tinnitus suppression following cochlear implantation. A multifactorial investigation. *Arch Otolaryngol Head Neck Surg* 1992;12:1291–1297.
4. Pan T, Tyler RS, Ji H, Coelho C, Gehringer AK, Gogel SA. Changes in the tinnitus handicap questionnaire after cochlear implantation. *Am J Audiol* 2009;2:144–151.
5. Olze H, Szczepek AJ, Haupt H, Zirke N, Graebel S, Mazurek B. The impact of cochlear implantation on tinnitus, stress and quality of life in postlingually deafened patients. *Audiol Neurootol* 2011;1:2–11.
6. Amoodi HA, Mick PT, Shipp DB, et al. The effects of unilateral cochlear implantation on the tinnitus handicap inventory and the influence on quality of life. *Laryngoscope* 2011;7:1536–1540.
7. Kompis M, Pelizzone M, Dillier N, Allum J, Demin N, Senn P. Tinnitus before and 6 months after cochlear implantation. *Audiol Neurootol* 2012;3: 161–168.
8. Kloostra FJ, Arnold R, Hofman R, Van Dijk P. Changes in tinnitus after cochlear implantation and its relation with psychological functioning. *Audiol Neurootol* 2014;2,81–89.
9. Cox RM, Alexander GC. The abbreviated profile of hearing aid benefit. *Ear Hear* 1995;2:176–186.
10. Zigmond AS, Snaith RP. The hospital anxiety and depression scale. *Acta Psychiatr Scand* 1983;6,361–370.
11. Zeman F, Koller M, Figueiredo R, et al. Tinnitus handicap inventory for evaluating treatment effects: which changes are clinically relevant? *Otolaryngol Head Neck Surg* 2011;2:282–287.
12. Kuk FK, Tyler RS, Russell D, Jordan H. The psychometric properties of a tinnitus handicap questionnaire. *Ear Hear* 1990;6:434–445.
13. Vanneste S, To WT, De Ridder D. The psychometric properties of the Tinnitus Handicap Questionnaire in a Dutch-speaking population. *Clin Otolaryngol* 2011;1:9–16.
14. Denollet J. DS14: standard assessment of negative affectivity, social inhibition, and Type D personality. *Psychosom Med* 2005;1:89–97.
15. Scheier MF, Carver CS. Optimism, coping, and health: assessment and implications of generalized outcome expectancies. *Health Psychol* 1985;3: 219–247.
16. Eggermont JJ, Roberts LE. The neuroscience of tinnitus. *Trends Neurosci* 2004;11:676–682.
17. Andersson G, Freijd A, Baguley DM, Idrizbegovic E. Tinnitus distress, anxiety, depression, and hearing problems among cochlear implant patients with tinnitus. *J Am Acad Audiol* 2009;5:315–319.
18. Schwartz CE, Sprangers MA. Guidelines for improving the stringency of response shift research using the thentest. *Qual Life Res* 2010; 4,455–464.