Original Study

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Performance Results and Timing of Cochlear Implantation in Patients With DFNA9 (p.Pro51Ser)

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Objective: To evaluate long-term outcomes of cochlear implantation (CI) in DFNA9 patients with the p.Pro51Ser COCH variant, compared with matched controls, and to identify clinical predictors of performance and quality of life (QoL).
Background: DFNA9, caused by pathogenic variants in the COCH gene, is a progressive hereditary hearing loss with variable vestibular dysfunction that often necessitates cochlear implantation.
Methods: In this retrospective cohort study, 56 DFNA9 patients were compared with case-matched postlingually deaf CI recipients without hereditary hearing loss. Speech perception, pure-tone thresholds, and QoL (Nijmegen Cochlear Implant Questionnaire, Glasgow Benefit Inventory) were assessed preimplantation and at 6 weeks, 1 year, and 5 years. Linear and mixed-effects models were applied to identify predictors and longitudinal changes.
Results: Cochlear implantation significantly improved speech perception and QoL in both groups, with no differences between DFNA9 and controls and stable performance up to 5 years. Postoperative residual hearing ($PTA_{0\cdot5}$–2 kHz) was a significant predictor of 1-year speech perception. In DFNA9, higher preoperative aided speech perception was more strongly associated with postoperative outcomes, underscoring the advantage of implantation before further decline. Speech perception scores predicted QoL, although the link with perceived social benefit was weaker in DFNA9 than in controls.
Conclusions: CI provides durable, noninferior outcomes in DFNA9 patients compared with controls. Although the study did not examine the impact of hearing loss severity or rate of decline, the excellent outcomes observed in this cohort may help clinicians to consider earlier implantation.

Keywords: COCH gene, Cochlear implantation, DFNA9, p.Pro51Ser mutation, Quality of life, Sensorineural hearing loss, Speech perception

Introduction

DFNA9 is a nonsyndromic, autosomal dominantly inherited, progressive type of sensorineural hearing loss (SNHL), accompanied by variable vestibular dysfunction with a mid-life onset[1]. It is caused by pathogenic variants in the *COCH* gene (coagulation factor C homology), located on chromosome 14q12–13[2]. Up to now, more than 30 pathogenic variants in *COCH* have been associated with DFNA9.

All currently known pathogenic variants lead to progressive SNHL; however, the rate of progression and degree of vestibular involvement vary[1,3]. The most common founder variant in the Netherlands and Belgium is p.Pro51Ser, which is associated with more progression of hearing loss and more pronounced vestibular involvement compared with other variants[1]. In patients with this variant, significant hearing loss generally begins between the fourth and sixth decade of life. However, recent studies show that subclinical hearing deterioration probably starts earlier, at well under 40 years of age[1,4]. In addition, DFNA9 shows a fast progression of 1.7 to 4.3 dB/year, on average 2.2 dB per year[1]. This rapid progression leads to severe or profound hearing loss within 20 to 25 years. Hearing rehabilitation usually starts with hearing aids (HA); however, over time, hearing loss worsens and causes increasing social inconvenience and communication problems. This eventually necessitates the need for cochlear implantation.

In general, cochlear implantation has a positive impact on the lives of numerous patients with severe to profound SNHL. The strong performance among CI recipients, along with marked improvements in quality of life and technological advancements, has substantially expanded implantation criteria[5]. As a result, cochlear implant selection criteria in the Netherlands have become more lenient in recent years. Dutch national guidelines advocate an individualized approach. Referral to a cochlear implant (CI) team is indicated for patients with severe hearing loss and insufficient speech recognition with a hearing aid[6]. However, since not all CI recipients perform equally well, and candidates differ in the rate of progression of their hearing loss, an individualized approach is both justifiable and necessary. Over the recent years, several factors have been identified that influence postoperative performance, such as duration of severe to profound hearing loss and age of implantation[7–10].

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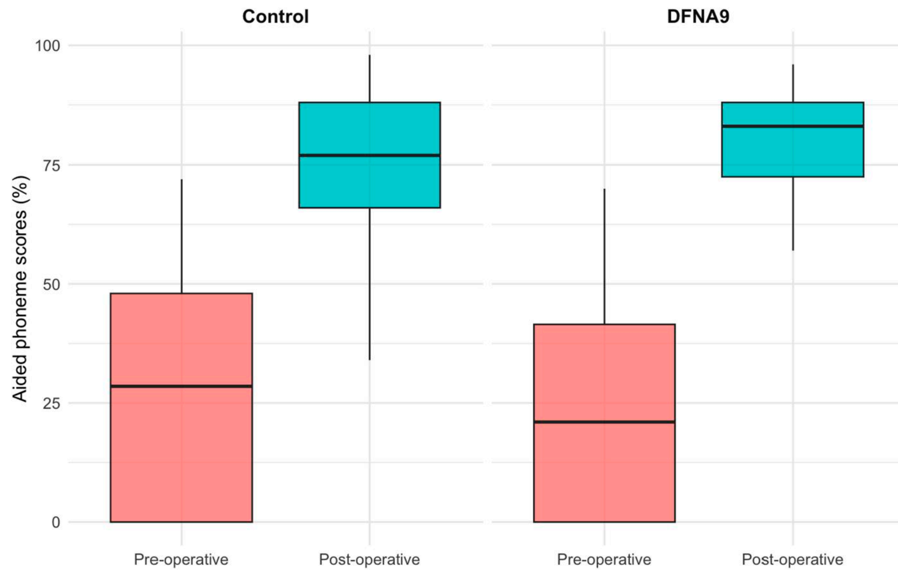

Figure 1. Boxplots showing pre- and postoperative aided phoneme scores (%) in the Control and DFNA9 groups. Both groups demonstrated improved scores postoperatively. Boxes represent the interquartile range, with medians indicated by horizontal lines.

One of the strongest predictors of postoperative performance is the pathophysiology of hearing loss[7–10]. The exact pathophysiology in DFNA9 remains unclear; it has been hypothesized that degeneration of the spiral ligament, the inadequate immune response[11–13], and deposition of eosinophilic acellular material[14,15], along with focal semicircular canal lesions observed in imaging studies[16,17], may contribute to secondary neural degeneration in the cochlea. It has been suggested that focal sclerosis may lead to underperformance in CI patients with DFNA9[18]. This hypothesis was further explored by Moyaert et al.[18], who observed higher electrode impedances in DFNA9 subjects than controls—possibly due to acellular deposits covering the electrode.

Both Fehrmann et al.[17] and Vermeire et al.[19] have previously examined cochlear implantation outcomes in individuals with DFNA9, demonstrating favorable effects on both functional hearing and quality of life. However, longitudinal data on functional hearing outcomes in this population have been evaluated only to a limited extent so far. Although cochlear implantation improves speech perception and patient-reported quality of life, the association between these two domains is often modest and variable across individuals[20]. The present study aims to evaluate both functional hearing and quality of life outcomes following cochlear implantation in the largest cohort of DFNA9 patients affected by the p.Pro51Ser variant to date. By doing so, it seeks to clarify the long-term efficacy of cochlear implantation for this specific genetic etiology and to enhance understanding of its impact on patient-centered outcomes.

Methods

Study design and population

A retrospective chart review was conducted on postlingually hearing-impaired adults with sensorineural hearing loss (SNHL) who underwent cochlear implantation. Two patient groups were retrospectively identified: a DFNA9 and a reference (control) group. The DFNA9 group included patients who underwent cochlear implantation at our center and had either a genetically confirmed p.Pro51Ser variant in *COCH* or a DFNA9 phenotype with a first-degree relative carrying this *COCH* variant and shared DFNA9 phenotype. No additional genetic testing was conducted for this study. The reference group included late-onset postlingual patients with severe to profound sensorineural hearing loss who were implanted between 2015 and 2020 and had no known or suspected hereditary cause of hearing impairment. Depending on case availability, subjects were matched case by case based on age at implantation and age of onset of hearing loss. Ideally, we also would have liked to match based on preoperative hearing criteria; however, limited availability prohibited that. Despite this, our analyses revealed no significant differences between the two groups (Fig. 1). The exclusion criteria for both groups were prelingual hearing loss, syndromic forms of hearing loss, inner ear malformations, severe comorbidities, cognitive impairment, acquired causes of hearing loss (eg, ototoxicity, cerebrovascular accident, acoustic trauma), re-implantation of the cochlear implant, or device failure.

Data collection

Demographic data and follow-up

Demographic data were collected through medical record review and included gender, self-reported age of hearing loss onset, age at implantation, and electrode type (peri-modiolar, mid-scalar, or lateral wall).

All adult, postlingual deaf patients undergoing cochlear implantation at Radboudumc follow a standardized testing and follow-up protocol. Tests are conducted at four standard time-points: preimplantation, 6 weeks, 1 year, and incidentally 5 years after implantation.

Pure tone audiometry (PTA) and speech perception performance

Audiologic testing consisted of speech perception *specific only* to the CI ear, both aided (with hearing aid on the CI ear, SPa) and unaided (without hearing aid on the CI ear, SPu), and pure tone audiometry (PTA). Subjects were, subsequently, subjected to evaluation preimplantation (SPa, SPu, and PTA), 6 weeks (SPa, PTA), 1 year (SPa), and incidentally at 5 years (SPa) after implantation. Missing values were allowed as long as either preoperative and postoperative speech perception scores could be compared, or speech perception scores could be related to quality-of-life data.

Pure tone audiometry was performed in a sound-attenuated booth, and thresholds were determined from 0.25 to 8 kHz, according to current standards. Out-of-range hearing thresholds were placed at 125 dB. Speech recognition was measured using a standard Dutch phonetically balanced word list (consonant-vocal-consonant [CVC] list)[21]. Data were only collected for the implanted ear. The SPu consisted of the maximum phoneme score regardless of a specific loudness level in the to be implanted ear. The SPa consisted of the phoneme score at 70 dB HL in the (to be) implanted ear.

Quality of life

NCIQ has become a standard validated questionnaire for assessing the QoL of patients with a CI[22–27]. This questionnaire is hearing loss specific and addresses three general domains with one or more subdomains: physical (basic sound perception, advanced sound perception, and speech production), social (activity limitation and social functioning), and psychological functioning (self esteem)[22]. Responses are given on a 5-point Likert scale, which can be transferred into scores. The scores range from 0 to 100, with 0 indicating extremely poor HRQoL and 100 excellent. Missing values and the “not applicable” response category were both considered incomplete. A maximum of three incomplete answers for each subdomain was allowed per patient; otherwise, the result was not used.

In addition, the Glasgow Benefit Inventory (GBI) was used to support the NCIQ further. The GBI consists of 3 domains (general health, social support, and physical health) and 18 questions using a 5-point Likert scale. The overall scores are scaled from −100 (maximum negative benefit) to +100 (maximum positive benefit). These tests questionnaires were taken preoperatively (NCIQ) and 1 year postoperatively (NCIQ and GBI).

Data analysis

Baseline characteristics were analyzed using IBM Statistical Package for the Social Sciences (SPSS version 29). A P-value of <0.05 was considered statistically significant. The Shapiro-Wilk test was used to assess normality. Normally distributed data were presented as mean with standard deviation, whereas non-normally distributed data were expressed as median with interquartile ranges (IQRs).

We adopted a hierarchical analytic framework to evaluate the pathway from clinical and audiological predictors to speech perception outcomes and, subsequently, from speech perception to patient-reported quality of life.

In the first stage, linear models were constructed to identify pre- and postoperative predictors of one-year speech perception. Candidate predictors included preoperative speech perception and pure tone averages (different averages were used for testing), onset and duration of hearing loss, and age at implantation and electrode type. To optimize model stability and interpretability, predictors with no significant associations, collinearity, or unstable estimates were excluded stepwise. Final models were evaluated using Type II ANOVA.

In the second stage, speech perception at 1 year was entered as the primary predictor of patient-reported benefit, assessed with the Nijmegen Cochlear Implant Questionnaire (NCIQ) and the Glasgow Benefit Inventory (GBI). This step tested whether speech outcomes served as a mediator linking auditory function to perceived quality of life.

Finally, longitudinal changes in speech perception were examined using linear mixed-effects models. Fixed effects included timepoint, group (DFNA9 vs. controls), and their interaction. Random intercepts and slopes for timepoints were specified at the subject level to account for within-subject correlation and individual variability. Post-hoc contrasts were performed using estimated marginal means with Tukey adjustment for multiple comparisons. These analyses and visualizations were performed using R (version 4.4.3), statistical programming language version 3.6.2[28], packages lme4[29] and ggplot2[30].

Results

Subjects

A total of 56 DFNA9 patients who underwent unilateral cochlear implantation were included in this study. An equal number of subjects were included in the control group. Additional baseline characteristics are presented in Table 1.

Audiological outcomes after cochlear implantation

The median preoperative unaided $PTA_{0.5-4 kHz}$ (dB HL) in the control group was 105 dB [IQR: 21.1], increasing to 118 dB [IQR: 14.4] postimplantation. In the DFNA9 group, it was 99.4 dB [IQR: 20.1] preoperatively and 125 dB [IQR: 6.9] postoperatively ($P<0.001$). Between-group comparisons

Table 1

Patient characteristics, there were no significant differences in baseline characteristics (*P* > .05)

Patient characteristics	DFNA9 (n = 56)	Controls (n = 56)
Male	29	27
Female	27	29
Mean age at implantation	66.14 ± 5.94 y	66.04 ± 6.07 y
Mean reported duration of hearing loss	20.39 ± 7.44 y	23.41 ± 10.27
Self-reported age of onset of hearing loss	45.75 ± 6.56 y	42.32 ± 11.8
Audiometric characteristics preimplantation		
$PTA_{0,25\text{-}1\ kHz}$ (dB HL)	90.3 (15.87)	85.21 (22.7)
$PTA_{0,5\text{-}2\ kHz}$ (dB HL)	93.69 (12.35)	97.44 (17.50)
$PTA_{0,5\text{-}4\ kHz}$ (dB HL)	100.45 (14.35)	104.21 (14.9)
Best-aided phoneme score at to be implanted ear	21 (IQR 43) %	28.50 (IQR48) %
Implant characteristics		
Modiolar	26	13
Mid-scalar	9	15
Lateral wall	19	27
Unkown	2	1

showed no significant difference in preoperative $PTA_{0.5-4kHz}$ (P = 0.220), but postoperative scores were significantly worse in the DFNA9 group (P = 0.026), indicating a greater loss of residual hearing. In the DFNA9 group, the preoperative best-aided speech perception score had a median of 21% [IQR: 41.5], improving to 83% postoperatively [IQR: 15.5]. In the control group, the preoperative best-aided speech perception was 28.5% [IQR: 48], increasing to 77% [IQR: 22] post-implantation. This reflects a significant improvement in speech perception scores across all participants in this study (P < 0.001). No significant group differences were found. Results are visualized in Figure 1. So, both groups demonstrated comparable and clinically meaningful improvements in speech perception despite greater postoperative hearing loss in the DFNA9 group.

Patient-reported outcome measures (NCIQ and GBI)

Table 2 presents the average changes (and standard deviations) in the NCIQ domain scores. After one year of cochlear implant use, a significant improvement was observed across all NCIQ domains and the total GBI score. No significant differences between the DFNA9 and control groups were detected in any of the domains.

Linear modeling

A series of linear models were constructed to evaluate the predictive value of several pre- and postoperative audiological and clinical variables on speech perception scores one year after cochlear implantation. Variables without significant associations, including onset of hearing loss, $PTA_{0.5}$–4kHz, and electrode type, were not included in the final model. The final model included preoperative $PTA_{0.25-1kHz}$ (dB HL), postoperative $PTA_{0.5-2kHz}$ (dB HL), preoperative aided speech perception, age at implantation, and duration of hearing loss. Together, these variables explained approximately 17.6% of the variance in speech perception outcomes one-year postimplantation (adjusted R^2 = 0.176, P = 0.0035). Among these, postoperative $PTA_{0.5-2kHz}$ was a significant independent predictor of speech perception at one year (P = 0.0029). Thus, better postoperative $PTA_{0.5-2kHz}$ (more residual hearing) scores predict better speech perception scores. Notably, a significant interaction was found between group (DFNA9 vs. controls) and preoperative aided speech perception (P = 0.0021), indicating that higher preoperative scores were more strongly associated with better postoperative outcomes in the DFNA9 group (Fig. 2). Age at implantation also showed significant interaction (P = 0.0320), suggesting better outcomes with younger implantation age.

To examine whether postoperative speech perception predicted patient-reported outcomes, additional linear models were fitted with one-year speech perception scores as the independent variable. Higher speech perception scores were significantly associated with greater perceived benefit on the Global Benefit Index (GBI) ($F(1,76)$ = 9.67, P = 0.003) and NCIQ subdomains, including speech production ($F(1,72)$ = 5.69, P = 0.020) and activity limitations ($F(1,72)$ = 4.71, P = 0.033).

For the NCIQ domain of social interactions, a significant interaction was observed between group and speech perception ($F(1,72)$ = 4.91, P = 0.030). Control participants demonstrated a stronger relationship between improved speech perception and perceived social benefit than DFNA9 patients. No other significant group interactions were identified. These findings are visualized in Figure 3.

Table 2

Changes in NCIQ domains and total GBI score

Patient-reported outcome measures (pre-post)	Group	Pre Mean (SD)	Post Mean (SD)
Sound perception basic	DFNA9	41.08 (13.11)	68.42 (15.75)
	Control	39.62 (12.82)	66.71 (13.77)
Sound perception advanced	DFNA9	68.27 (15.72)	79.92 (12.48)
	Control	70.55 (13.92)	81.01 (15.61)
Speech production	DFNA9	39.95 (9.25)	59.54 (12.67)
	Control	40.84 (11.92)	62.40 (16.69)
Self esteem	DFNA9	55.70 (13.00)	71.15 (14.37)
	Control	53.58 (18.47)	72.22 (16.92)
Activity limitations	DFNA9	49.47 (13.22)	72.90 (13.84)
	Control	49.77 (13.62)	73.28 (16.19)
Social interactions	DFNA9	51.33 (12.14)	71.38 (12.02)
	Control	50.99 (12.21)	73.09 (15.30)
GBI total	DFNA9		29.17 (14.45)
	Control		23.23 (19.42)

Higher scores indicate more benefit. Across all domains of the NCIQ, a significant improvement was shown. No significant differences were found between DFNA9 and the control group across any category.

Longitudinal analyses

The linear mixed-effects model included fixed effects for timepoint, group (DFNA9 vs. control), and their interaction, along with a random intercept for each participant to account for individual baseline differences in speech perception. The model explained a substantial proportion of the variance in outcomes, with a marginal R^2 of 0.61 (variance explained by fixed effects alone) and a conditional R^2 of 0.72 (variance explained by both fixed and random effects). This indicates that the combination of timepoint, group, and their interaction, along with subject-level baseline variation, accounted for most of the variability in speech perception scores over time. We tested whether allowing participants to have individual slopes over time improved the model, but the data were insufficient to support this added complexity, leading to unstable estimates.

The linear mixed-effects model revealed significant changes in speech perception over time. Relative to 6-week postimplantation scores, speech perception improved by 8.81 percentage points at 1 year (P = 0.034) and 12.75 percentage points at 5 years (P = 0.001). No significant difference was observed between the 1-year and 5-year scores, suggesting that performance plateaued following the initial postoperative improvement. There was no main effect of group (P = 0.894) and no significant interaction between timepoint and group (all P > 0.98), indicating that DFNA9 and control participants exhibited comparable patterns of improvement and long-term stability. These findings are illustrated in Figure 4, which depicts speech perception trajectories over time for both groups. Overall, the data support a sustained benefit of cochlear implantation, with no evidence of performance decline in the long term.

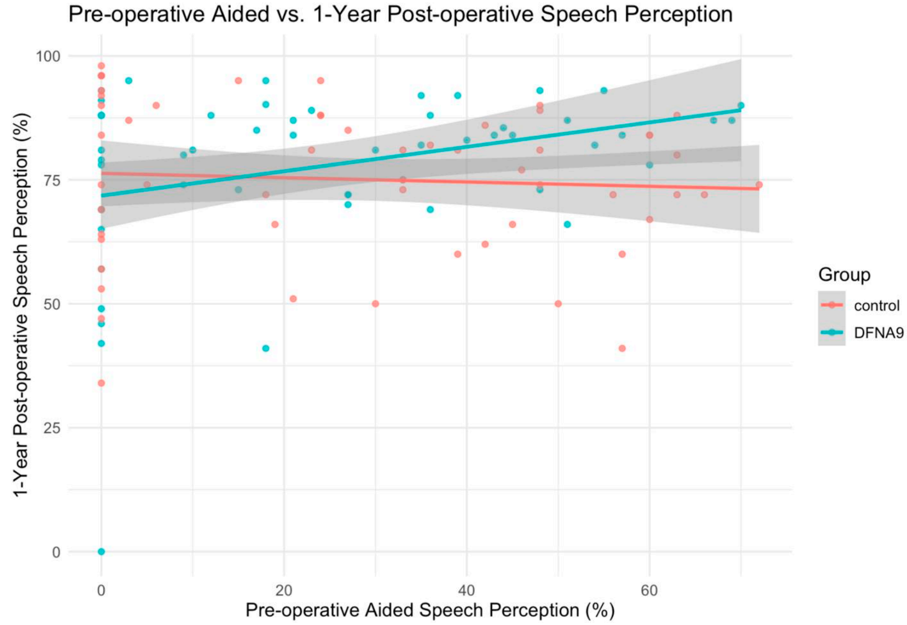

Figure 2. Relationship between preoperative aided speech scores and postoperative phoneme scores, for DFNA9 and control groups. A significant interaction was observed ($P = 0.010$), indicating that preoperative aided speech scores more strongly predict outcomes in DFNA9 patients than in controls.

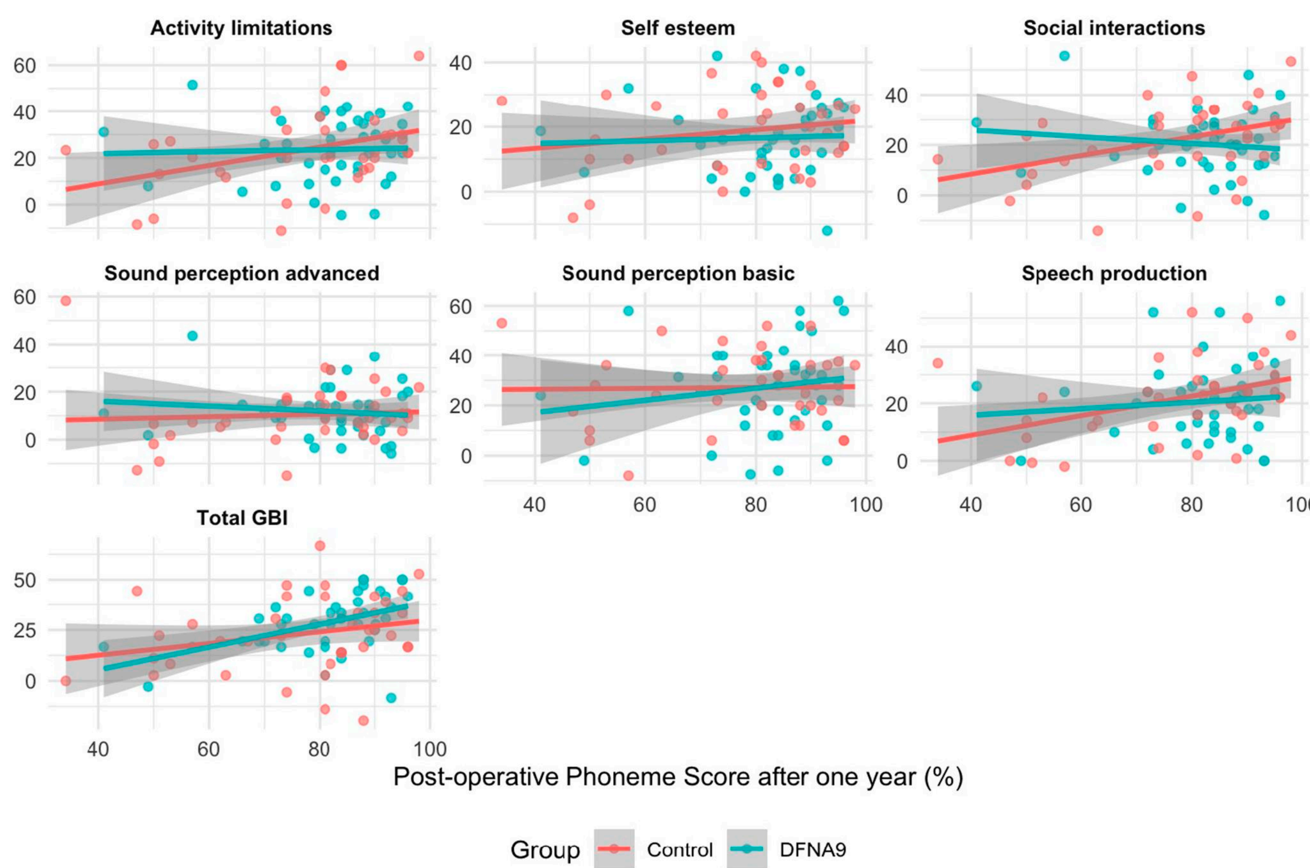

Figure 3. Associations between postoperative phoneme scores and patient-reported outcomes. Each panel shows a different outcome with separate regression lines for DFNA9 and control groups. NCIQ domains reflect change scores, while the GBI Total represents a final global rating. Y-axes are scaled individually.

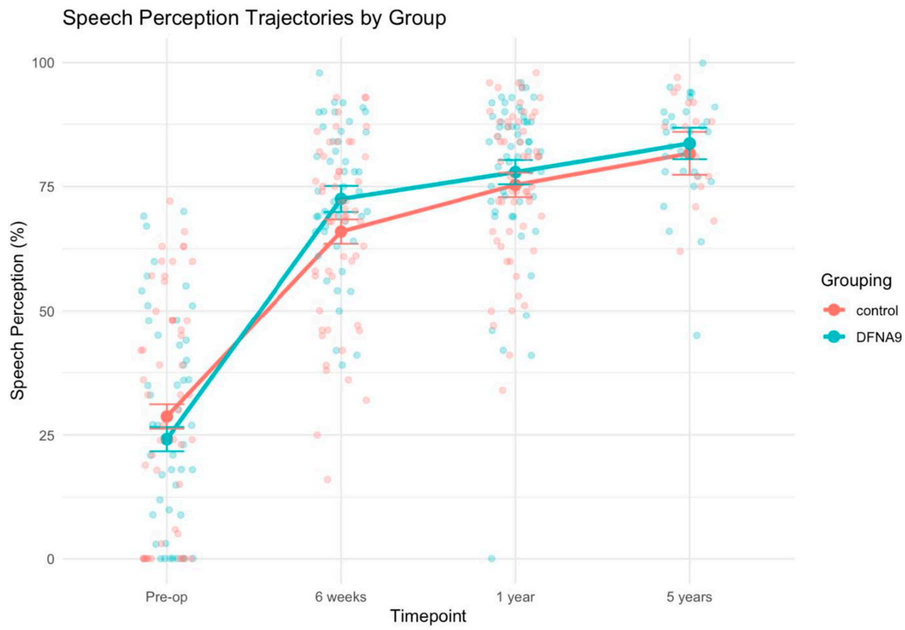

Figure 4. Estimated speech perception at 70 dB scores (± 95% CI) over time for DFNA9 and control groups, based on a mixed-effects model. Both groups show improvement postimplantation.

Discussion

This study demonstrates that cochlear implantation is an effective form of rehabilitation in DFNA9 patients, improving both hearing performance and patient-reported outcomes. When matched with a control group, DFNA9 participants showed noninferior outcomes, underscoring the suitability of cochlear implantation in this population, both in the short and long term. Some differences between the DFNA9 and control groups warrant closer examination.

First, participants in the control group showed a stronger association between improved speech perception and perceived social benefit, as measured by two NCIQ domains, compared with DFNA9 patients. This suggests that higher speech perception scores translated into greater perceived improvement in the control group. A hypothesis, but not assessed in this study, could be that the known progressive vestibular dysfunction, associated with carriers of pathologic variants in COCH (p.Pro51Ser), contributes to the attenuated perceived social benefit in relation with improved speech perception.

In addition, analysis of preoperative characteristics showed that better preoperative aided speech perception predicted greater postoperative benefit but only in DFNA9 participants. Given the retrospective design, this association should be interpreted with caution, and exact criteria for 'earlier implantation' could not be specified. Importantly, the absence of a similar association in the control group suggests that greater residual hearing does not necessarily confer additional benefit in this population. We hypothesize this may be explained by the greater heterogeneity of etiologies underlying nongenetic, postlingual sensorineural hearing loss, in which other underlying (etiological) factors may outweigh the contribution of residual hearing alone. In contrast, DFNA9 represents a genetically and clinically more homogeneous condition with a relatively predictable disease course[1], which may allow preoperative aided speech perception to function as a more reliable predictor of postoperative outcomes (as was shown by Huinck W. et al.[31]).

In motivated patients and considering the rapid progression of hearing loss in DFNA9, implantation at an earlier stage of functional decline may therefore be considered.

This study found that patients with DFNA9 had significantly less residual hearing after implantation than control participants while having similar or even better preoperative hearing (Table 1) although this did not translate into differences in postimplantation speech perception outcomes and most likely has limited clinical relevance, it may still be relevant from a surgical or pathophysiological perspective. We acknowledge that the present study did not include systematic intraoperative assessments or detailed preoperative imaging that would allow direct evaluation of cochlear sclerosis or insertion-related difficulties. Multiple studies have reported radiologic evidence of focal sclerosis in the semicircular canals of DFNA9 patients[17,32,33]. Histopathologic studies suggest that similar structural changes may occur in the cochlea[14,15,34]. If present, such alterations could, in theory, hinder atraumatic electrode insertion, thereby contributing to greater loss of residual hearing.

Finally, speech perception scores remained stable over a five-year follow-up, indicating that even if significant degeneration of spiral ganglion neurons is present in DFNA9 patients, as suggested by elevated eCAP impedances reported in previous studies[18], it does not seem to translate into a measurable decline in speech recognition over time.

Several methodological aspects warrant consideration. First, although control matching was performed with care, this process may still introduce selection bias—an inherent limitation of retrospective cohort designs. The retrospective nature of the study also led to some degree of missing data, which could not be entirely avoided. To mitigate the impact of incomplete data and maximize the use of available information, linear mixed-effects models were used alongside traditional linear models and ANOVA. These models are better suited for handling incomplete data and repeated measures, thereby strengthening the robustness of the longitudinal analyses[35]. Secondly, all DFNA9 patients in the present study carried the same COCH p.Pro51Ser mutation, resulting in a genetically homogeneous cohort. While this homogeneity strengthens internal validity by reducing biological variability, it might inhibit extrapolation to other pathologic mutations in COCH. Future studies including genetically diverse DFNA9 populations are needed to determine whether cochlear implant outcomes differ across mutation subtypes.

Our findings align with studies demonstrating the effectiveness of CI in improving speech recognition and quality of life for individuals with DFNA9. Fehrmann MLA and colleagues (2024), partially using the same dataset, found that most individuals with DFNA9 show improved speech recognition with CI. Specifically, speech perception scores significantly improved from 35% preimplantation to 84% one year postimplantation[17]. Moyaert and colleagues, while primarily looking at electrically evoked compound action potentials (eCAP), also evaluated speech perception thresholds postoperatively in 15 DFNA9 patients and 15 controls. No significant differences were found between the different groups regarding speech understanding. In their study, subjects with DFNA9 achieved a mean speech perception at 65 dB SPL of 85%, 89.5%, and 85% after 1, 6, and 12 months after implantation, respectively[18]. These speech perception thresholds closely resemble our outcomes of 83% (median), 12 months after implantation. Interestingly, while Moyaert and colleagues found statistically higher impedances during eCAP measurements for the DFNA9 subjects than the control subjects, this did not result in significantly worse speech understanding scores than controls. This is in line with our findings, which showed no group differences and, especially, no degeneration in speech recognition scores over time.

Conclusion and implications for future research

Patients with DFNA9 showed noninferior outcomes in both objective speech perception and patient-reported quality of life, supporting the suitability of cochlear implants in this genetically defined population. Importantly, speech perception remained stable up to five years after implantation, with no signs of clinical decline. This finding is especially relevant considering earlier hypotheses suggesting progressive sensorineural degeneration in DFNA9 due to cochlear fibrosis potentially limiting cochlear implant performance. Our results challenge the clinical relevance of such degeneration concerning cochlear implant performance and suggest sustained benefit over time.

As research advances toward genetic therapies for DFNA9, understanding the outcomes and limitations of current treatments is essential. Our findings help establish a clinical benchmark for comparison with future therapeutic strategies. Meanwhile, cochlear implantation remains a valuable and dependable form of rehabilitation for this progressive disease.

References

[1] Robijn SMM, Smits JJ, Sezer K, *et al.* Genotype-phenotype correlations of pathogenic COCH variants in DFNA9: a HuGE systematic review and audiometric meta-analysis. Biomolecules 2022;12:220.

[2] Robertson NG, Lu L, Heller S, *et al.* Mutations in a novel cochlear gene cause DFNA9, a human nonsyndromic deafness with vestibular dysfunction. Nat Genet 1998;20:299–303.

[3] JanssensdeVarebeke S, Topsakal V, Van Camp G, Van Rompaey V. A systematic review of hearing and vestibular function in carriers of the Pro51Ser mutation in the COCH gene. Eur Arch Otorhinolaryngol 2019;276:1251–62.

[4] JanssensdeVarebeke SPF, Moyaert J, Fransen E, *et al.* Genotype-phenotype correlation study in a large series of patients carrying the p. Pro51Ser (p.P51S) variant in COCH (DFNA9): part I—a cross-sectional study of hearing function in 111 carriers. Ear Hear 2021;42:1508–24.

[5] Arnoldner C, Lin VYW. Expanded selection criteria in adult cochlear implantation. Cochlear Implants Int 2013;14(suppl 4):S10–3.

[6] (NVKNO) NVvK-N-OeHvhH-H. Criteria doorverwijzing CI-team gehoorverlies National guideline. Federatie Medisch Specialisten. 2026. Accessed April 12, 2026. https://richtlijnendatabase.nl/richtlijn/perceptieve_slechthorendheid_bij_volwassenen/criteria_doorverwijzing_ci-team_gehoorverlies.html

[7] Blamey P, Arndt P, Bergeron F, *et al.* Factors affecting auditory performance of postlinguistically deaf adults using cochlear implants. Research Support, Non-U.S. Gov't Review. Audiol Neurootol 1996;1:293–306.

[8] Blamey P, Artieres F, Başkent D, *et al.* Factors affecting auditory performance of postlinguistically deaf adults using cochlear implants: an update with 2251 patients. Research Support, Non-U.S. Gov't. Audiol Neurootol 2013;18:36–47.

[9] Shearer AE, Eppsteiner RW, Frees K, *et al.* Genetic variants in the peripheral auditory system significantly affect adult cochlear implant performance. Hear Res 2017;348:138–42.

[10] Lazard DS, Vincent C, Venail F, *et al.* Pre-, per- and postoperative factors affecting performance of postlinguistically deaf adults using cochlear implants: a new conceptual model over time. PLoS One 2012;7:e48739.

[11] Boulassel M-R, Tomasi J-P, Deggouj N, Gersdorff M. COCH5B2 is a target antigen of anti-inner ear antibodies in autoimmune inner ear diseases. Otol Neurotol 2001;22:614–8.

[12] Jung J, Yoo JE, Choe YH, *et al.* Cleaved cochlin sequesters *Pseudomonas aeruginosa* and activates innate immunity in the inner ear. Cell Host Microbe 2019;25:513–525.e6.

[13] Rhyu HJ, Bae SH, Jung J, Hyun YM. Cochlin-cleaved LCCL is a dual-armed regulator of the innate immune response in the cochlea during inflammation. BMB Rep 2020;53:449–52.

[14] Burgess BJ, O''Malley JT, Kamakura T, *et al.* Histopathology of the human inner ear in the p.L114P COCH mutation (DFNA9). Audiol Neurootol 2016;21:88–97.

[15] Verdoodt D, Van Camp G, Ponsaerts P, Van Rompaey V. On the pathophysiology of DFNA9: Effect of pathogenic variants in the COCH gene on inner ear functioning in human and transgenic mice. Hear Res 2021;401:108162.

[16] de Varebeke SPJ, Termote B, Van Camp G, *et al.* Focal sclerosis of semicircular canals with severe DFNA9 hearing impairment caused by a P51S COCH-mutation: is there a link? Otol Neurotol 2014;35:1077–86.

[17] Fehrmann MLA, Meijer FJA, Mylanus EAM, Pennings RJE, Lanting CP, Huinck WJ. Evaluating cochlear implant outcomes in DFNA9 subjects: a comprehensive study on cerebral white matter lesions and vestibular abnormalities. Eur Arch Otorhinolaryngol 2025;282:183–91.

[18] Moyaert J, Gilles A, Ramekers D, *et al.* Cochlear health in a cohort of cochlear implant users carrying the p.Pro51Ser variant in the COCH gene (DFNA9): a cross-sectional study evaluating the changes in the electrically evoked compound action potential (eCAP). Hear Res 2025;460:109240.

[19] Vermeire K, Brokx JP, Wuyts FL, *et al.* Good speech recognition and quality-of-life scores after cochlear implantation in patients with DFNA9. Otol Neurotol 2006;27:44–9.

[20] Philpott N, Nijmeijer HGB, Philips B, *et al.* Beyond hearing: the impact of Cochlear implantation on the quality of life of users and their communication partners after 1 year. Int J Audiol 2025;27:32–43.

[21] Bosmana AJ, Smoorenburg GF. Intelligibility of Dutch CVC syllables and sentences for listeners with normal hearing and with three types of hearing impairment. Audiology Sep-Oct 1995;34:260–84.

[22] Hinderink JB, Krabbe PFM, Van Den Broek P. Development and application of a health-related quality-of-life instrument for adults with cochlear implants: the Nijmegen cochlear implant questionnaire. Clinical Trial Controlled Clinical Trial Validation Studies. Otolaryngol Head Neck Surg 2000;123:756–65.

[23] Krabbe PFM, Hinderink JB, Broek P. The effect of cochlear implant use in postlingually deaf adults. Int J Technol Assess Health Care 2000;16: 864–73.
[24] Cohen SM, Labadie RF, Dietrich MS, Haynes DS. Quality of life in hearing-impaired adults: the role of cochlear implants and hearing aids. Comparative Study. Otolaryngol Head Neck Surg 2004;131: 413–22.
[25] Damen GWJA, Beynon AJ, Krabbe PFM, Mulder JJS, Mylanus EAM. Cochlear implantation and quality of life in postlingually deaf adults: long-term follow-up. Otolaryngol Head Neck Surg 2007;136:597–604.
[26] Damen GWJA, Pennings RJE, Snik AFM, Mylanus EAM. Quality of life and cochlear implantation in Usher syndrome type I. Comparative Study Research Support, Non-U.S. Gov't. Laryngoscope 2006;116:723–8.
[27] Corrigendum. Otolaryngology–Head and Neck Surgery 2017;156:391.
[28] *R: A language and environment for statistical computing*. Version 3.6.2. R Foundation for Statistical Computing. 2019. Accessed March 2026. https://www.R-project.org/
[29] Bates D, Mächler M, Bolker B, Walker S. Fitting Linear Mixed-Effects Models Using lme4. J Stat Softw 2015;67:1–48.
[30] Wickham H. ggplot2: Elegant Graphics for Data Analysis. New York: Springer-Verlag, 2016.
[31] Huinck WJ, Mylanus EAM, Snik AFM. Expanding unilateral cochlear implantation criteria for adults with bilateral acquired severe sensorineural hearing loss. Eur Arch Otorhinolaryngol 2019;276:1313–20.
[32] Ihtijarevic B, Janssens de Varebeke S, Mertens G, Dekeyzer S, Van de Heyning P, Van Rompaey V. Correlations between vestibular function and imaging of the semicircular canals in DFNA9 patients. Front Neurol 2019;10:1341.
[33] Beerten A, Bosmans H, Lauwers M, Vermeulen H, Janssens de Varebeke SP. Radiologic features in cochlear implant candidates: a prospective study comparing candidates carrying the p.Pro51Ser mutation in coagulation factor C homology with noncarriers. Otol Neurotol 2022;43:e969–75.
[34] Geerardyn A, Zhu M, Klabbers T, *et al*. Human histology after structure preservation cochlear implantation via round window insertion. Laryngoscope 2024;134:945–53.
[35] Twisk JWR. Applied Longitudinal Data Analysis for Epidemiology: A Practical Guide, 2 ed. Cambridge University Press; 2013.