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Effect of day-case unilateral cochlear implantation in adults on general and disease-specific quality of life, postoperative complications and hearing results, tinnitus, vertigo and cost-effectiveness: protocol for a randomised controlled trial

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ABSTRACT

Introduction: Cochlear implantation is an increasingly common procedure in the treatment of severe to profound sensorineural hearing loss (SNHL) in children and adults. It is often performed as a day-case procedure. The major drive towards day-case surgery has been from a logistical, economical and societal perspective, but we also speculate that the patient's quality of life (QoL) is at least equal to inpatient surgery if not increased as a result of rapid discharge and rehabilitation. Even though cochlear implantation seems well suited to a day-case approach and this even seems to be common practice in some countries, evidence is scarce and of low quality to guide us towards the preferred treatment option.

Methods and analysis: A single-centre, non-blinded, randomised, controlled trial was designed to (primarily) investigate the effect on general QoL of day-case cochlear implantation compared to inpatient cochlear implantation and (secondarily) the effect of both methods on (subjective) hearing improvement, disease-specific QoL, tinnitus, vertigo and cost-effectiveness. 30 adult patients with severe to profound bilateral postlingual SNHL who are eligible for unilateral cochlear implantation will be randomly assigned to either the day-case or inpatient treatment group. The outcome measures will be assessed using auditory evaluations, questionnaires (preoperatively, at 1-week, 3-week, 3-month and 1-year follow-up) and costs diaries (weekly during the first month postoperatively, after which once in a month until 1-year follow-up). Preoperative and postoperative outcomes will be compared. The difference in costs and benefit will be represented using the incremental cost utility/effectiveness ratio. The analyses will be carried out on an intention-to-treat basis.

Strengths and limitations of this study

- This study allows for a comparison between day-case and inpatient cochlear implantation to investigate the hypothesis that day-case cochlear implantation is associated with a higher quality of life and higher cost-effectiveness, while maintaining an equal hearing outcome and complication rate, compared to inpatient cochlear implantation.
- This study is the first trial of high epidemiological quality evaluating and quantifying the benefits of day-case cochlear implantation for patients with severe to profound bilateral postlingual sensorineural hearing loss.
- The findings of this trial will give evidence-based proof of the feasibility of cochlear implantation in day-case setting, with great consequences for the postoperative management strategies of cochlear implantation.
- A limitation of this trial is that inclusion was possible only for patients with good understanding of the Dutch language and had quick access to communication and transportation in case of any complications.
- Another disadvantage is that due to logistic reasons some of the patients will be admitted 1 day before the surgery and others on the day of surgery.

Ethics and dissemination: This research protocol was approved by the Institutional Review Board of the UMC Utrecht (NL45590.041.13; V.5, November 2015). The trial results will be disseminated through peer-reviewed medical journals and presented at scientific conferences.

Trial registration number: NTR4464; Pre-results.

BACKGROUND

Cochlear implantation is an increasingly common procedure in the treatment of severe to profound sensorineural hearing loss (SNHL) in children and adults.[1–4] For patients in whom amplification with hearing aids does not suffice, cochlear implantation can be considered. Several studies have shown that cochlear implantation significantly improves the quality of life (QoL) of patients.[1 2] Cochlear implantation is associated with low complication rates: 1–9% for (transient) vertigo, 1–3% for tinnitus, 1–3% for postoperative bleeding or haematoma, 1–9% for wound infection, <1% for facial nerve injury and 4% for explantation.[5–8]

Currently, in our university medical centre, cochlear implantation involves overnight hospital stay. Many other otologic procedures that involved overnight hospital stay in the past are presently being performed, with good result, on an outpatient basis.[9–11] Ear, nose and throat (ENT) surgery is well suited to a day-case approach as many of the disease entities are benign and procedures are associated with low complication rates.[10] Even though one of the major drives towards day-case surgery has been financial from a societal perspective, other non-financial benefits are of major importance. Day-case surgery is associated with shorter waiting time for surgery and reduced risk of infection.[12] Moreover, as a result of a more rapid social and emotional rehabilitation compared to overnight stay, patients might prefer day-case surgery.

Cochlear implantation is increasingly being performed as a day-case procedure in several Western countries. However, reports on day-case cochlear implantation are scarce and mostly describe paediatric day-cases.[13 14] None of these studies compare the effects of day-case surgery to inpatient surgery. Liu *et al*[13] were the only ones to send out a patient satisfaction survey addressing parental and child satisfaction following outpatient cochlear implantation. Overall satisfaction with day-case surgery was 91%. Preoperative anxiety was diminished in 47% of families by planning the operation as day surgery, whereas preoperative anxiety was increased in 34%. Of the latter group, 44% would schedule the surgery as day surgery if they had to undergo the operation again. A total of 19% of parents would have preferred to let their children spend the night in the hospital. In the same study, two children (4%) had to be admitted for 23-hour observation as a result of postoperative nausea with vomiting and fever. In both studies, none of the participants had to be readmitted as a result of adverse events arising in the home situation.

The lack of (high-quality) studies precludes firm evidence-based recommendations and demonstrates the need for high-quality studies quantifying the benefits of day-case surgery, clinical and financial. To accommodate this need, in the proposed study we shall compare day-case cochlear implantation to inpatient cochlear implantation. The study will be conducted as a randomised controlled trial.

METHODS AND DESIGN

This protocol is reported according to the SPIRIT Statement, an international guideline on reporting protocols.[15]

Study objectives

The primary objective of this study is to evaluate the effect on general QoL of day-case cochlear implantation compared to inpatient cochlear implantation. In addition, subjective participants' perception on hearing improvement, auditory evaluations, disease-specific QoL, tinnitus, vertigo and cost-effectiveness will be assessed.

Study design

The study design will be a single-centre, non-blinded, randomised controlled trial. Participants will be assigned to one of the two groups: day-case cochlear implantation under general anaesthesia or inpatient cochlear implantation under general anaesthesia followed by 1-day to 2-day hospital admittance (figure 1).

Study population

The study population consists of adults with severe to profound bilateral postlingual SNHL, eligible for unilateral cochlear implantation. Participants will be recruited from the outpatient clinic of the ENT department at the University Medical Center Utrecht (UMC Utrecht), the Netherlands. To be eligible to participate in this study, a participant must meet all of the following criteria:

- Age ≥18 years;
- Severe to profound bilateral postlingual SNHL defined as ≥70 dB above-normal adult hearing level on pure-tone audiometry in the range of 500, 1000 and 2000 Hz;
- Willingness and ability to participate in all scheduled procedures outlined in the research protocol;
- General health allowing general anaesthesia in an outpatient setting as assessed by an anaesthesiologist;
- Quick access to communication and transportation in case of any complications;
- Good understanding of the Dutch language.

A potential participant who meets any of the following criteria will be excluded from participation in this study.

- Severe to profound pre-lingual or unilateral SNHL;
- Previous cochlear implantation;
- Aberrant (cochlear) anatomy on CT scan or chronic ear infection;
- Disability that could interfere with questionnaire fulfilment;
- Other medical considerations (eg, comorbidity) requiring inpatient care.

Sample size calculation and recruitment

To establish equivalence in general QoL of 0.15 points (SD 0.15) on the Health Utilities Index—Mark 3 between the day-case and the inpatient group with an α of 0.05 and a power of 80%, 14 participants per group

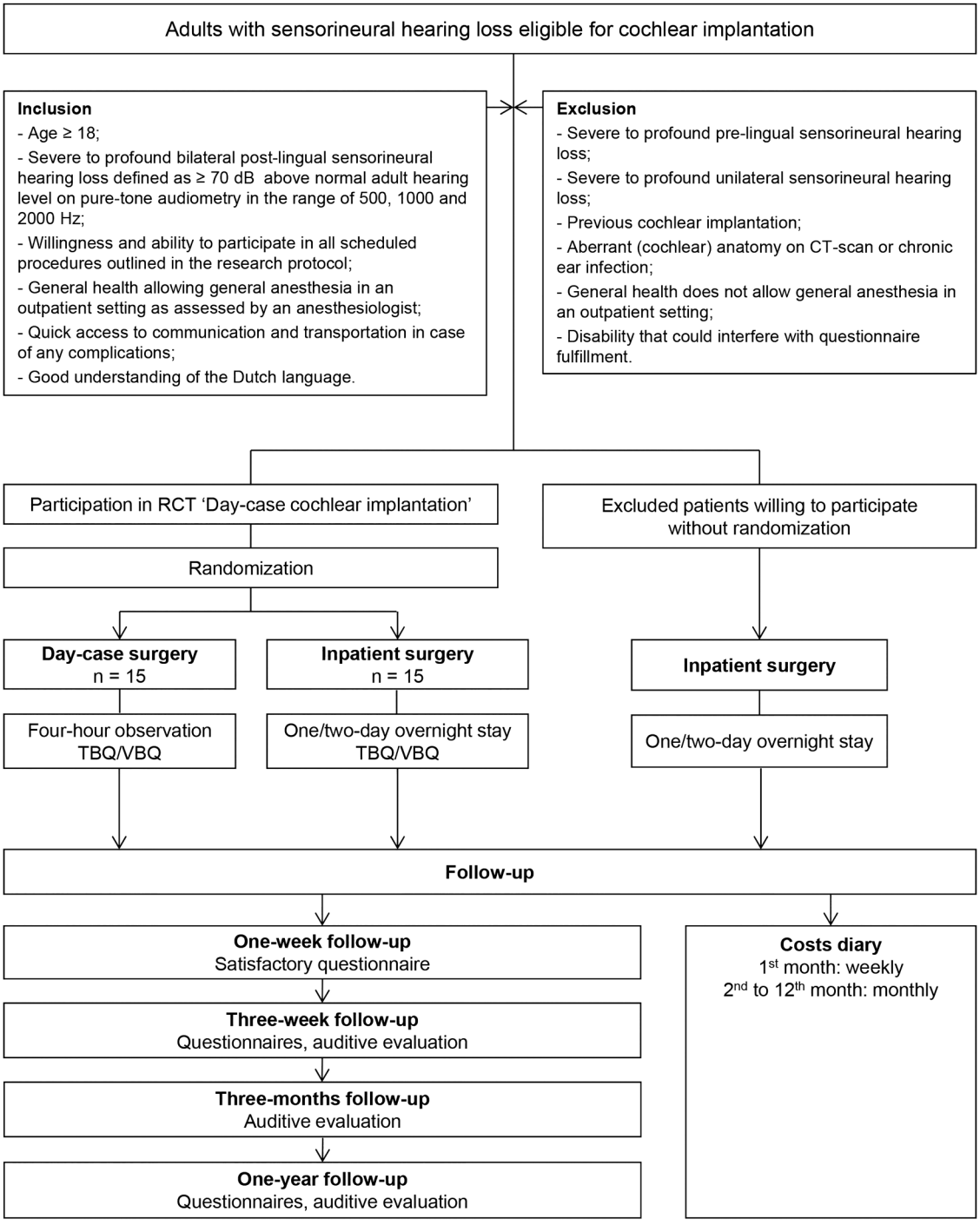

Figure 1 Flow diagram of day-case cochlear implantation study. RCT, randomised controlled trial; TBQ, Tinnitus Burden Questionnaire; VBQ, Vertigo Burden Questionnaire.

are needed.[1 4] To anticipate withdrawal of 10% of participants, one more participant than needed will be recruited per group. At the ENT department at the UMC Utrecht, we perform an average of 25 unilateral cochlear implantations per year in patients with bilateral, postlingual SNHL. Assuming a participation rate of 80%, we will be able to include the necessary number of 30 patients in 1.5 years. If participants wish to leave the study or the investigators decide to withdraw a participant from the study for urgent medical reasons, these participants will not be replaced unless these account for more than 10%.

Patients will be recruited from the outpatient ENT department at the UMC Utrecht. If a patient meets the criteria for cochlear implantation and the inclusion criteria for this study, one of the researchers will explain the content of the study and provide the patient with written patient information and an informed consent form. Patients consent to the use of their data for the research purposes outlined in this protocol, which

includes publication of the results once the trial has been completed. Further details can be found in online supplementary appendix 1 (informed consent form; translated to English, original in Dutch). Patients who do not want to be included in the study because they want to undergo cochlear implantation in a clinical setting will be asked whether they would like to fulfil the study procedures anyway and whether their data can be used for analysis. Furthermore, these patients will be asked to motivate their preference for inpatient surgery.

Randomisation, blinding and treatment allocation

A web-based randomisation programme (Julius Center, UMC Utrecht, Utrecht, the Netherlands) shall be used to allocate participants randomly into two groups with stratification for age. Block randomisation will be used with an allocation ratio of 1:1. The randomisation chart, including block size, is established before the start of the study by an independent data manager and will not be available to any of the people involved with enrolment or treatment of participants. Consequently, treatment allocation sequence is concealed for participants, care providers and researchers. Blinding of participants and care providers is not possible, because participants and care providers will be aware of the surgical setting and hospital stay.

Intervention

The surgical procedures, as well as hospitalisation in the inpatient group, will take place at the UMC Utrecht. Patients in both groups will undergo unilateral cochlear implantation under general anaesthesia.

Patients allocated to the conventional group will be admitted 1 day before or on the day of surgery and will be discharged 1 to 2 days after surgery. Patients allocated to the day-case group will be admitted into the outpatient unit 1 day before or on the day of surgery and will be discharged the day of surgery. Patients are not allowed to drive for 24 hours following day-case surgery and will be recommended 24 hours of relative bed rest. After a period of 24 hours, patients can return to their daily routine. Participants will be asked to contact the hospital in case of severe postoperative vertigo or pain. An ear compression bandage is applied to all patients during surgery. Patients allocated to the day-case group will either have to return to the hospital 2 days postoperatively to have the head dressings removed by the surgeon or will remove the head dressings themselves at home after being given proper instructions.

It is to be expected that patients who had surgery in day-case will sometimes stay overnight, for example due to postoperative nausea or dizziness. If patients are not physically capable of same-day discharge or if surgeons do not support same-day discharge, patients will stay overnight regardless of the group that they were allocated to. These patients will be asked to complete their follow-up, and analyses will be carried out on an intention-to-treat basis. Reasons for the overnight stay will be recorded and we will differentiate between anaesthesiological and otologic-related reasons for cross-over.

Outcome measures

Evaluation will take place preoperatively and at 1 week, ~3 weeks, 3 months and 1 year postoperatively by means of questionnaires and auditory evaluation of hearing results. Vertigo and tinnitus will also be evaluated directly postoperatively. In addition, participants will be asked to keep a costs diary for the duration of 1 year. Questionnaires and costs diaries can be filled digitally or on paper and will be sent via email or mail, respectively.

Primary outcome measure

Our primary outcome is the general QoL measured by the Health Utilities Index—Mark 3 at 3 weeks and 1 year postoperatively.

Secondary outcome measures

Our secondary outcome measures include (subjective) hearing improvement, disease-specific QoL, tinnitus and vertigo at 3 weeks and 1 year postoperatively, patient satisfaction with regard to day-case surgery at 1 week postoperatively and overall cost-effectiveness and occurrence of postoperative complications within 1 year postoperatively.

Auditory evaluation of hearing results

Auditory evaluation will be performed at 3 weeks, 3 and 12 months postoperatively. Speech perception tests will be performed in sound-treated booths at 65 dB sound pressure level. During the test recordings of a set of Dutch words with a consonant–vowel–consonant structure will be played in a free field setting and patients wearing the cochlear implant will be asked to repeat these. Besides this, patients will be asked to repeat Dutch sentences. The percentage of correctly repeated complete sentences, words and phonemes will be scored.

Patient satisfaction

Patient satisfaction will be evaluated at 1 week postoperatively using the Utrecht patient satisfaction survey (see online supplementary appendix 2; translated to English, original in Dutch). This seven-item questionnaire was developed in our centre and contains questions regarding hospital stay (day-case or overnight stay) and whether patients were satisfied with the intervention group that they were allocated to.

Quality of life

QoL and hearing benefit will be assessed preoperatively and at 3 weeks and 1 year postoperatively using the following four questionnaires:

- The *Glasgow Health Status Inventory Questionnaire*: an 18-item questionnaire that measures the effect of an otologic problem on QoL at the time the questionnaire is completed. Three domains (general, social support and physical health) are measured based on

a five-point Likert scale ranging from high health status to low health status. The total score ranges from 0 to +100.

- *Glasgow Benefit Inventory*: an 18-item questionnaire, which measures the change in health status as a result of a surgical intervention. A specific version of the Glasgow Benefit Inventory will be used that has been validated to measure changes in health status as a result of otorhinolaryngological procedures.[16] The same three domains as the Glasgow Health Status Inventory questionnaire are measured according to the five-point Likert scale. The total score ranges from −100 (maximal negative benefit), through 0 (no benefit), to +100 (maximum benefit);
- *EuroQoL-5D*: a five-item questionnaire on mobility, self-care, daily activities, pain and symptoms and anxiety or depression that assesses general health status.[17 18] In addition, the general health status is rated on a visual analogue scale than runs from 0 to 10. A score of 0 equals worst imaginable health state and a score of 10 equals best imaginable health state.
- *Health Utilities Index 3*: a 15-item questionnaire that measures general health status by evaluating eight domains: vision, hearing, speech, ambulation, dexterity, cognition, emotion and pain.[19]

Tinnitus and vertigo

Tinnitus and vertigo will be assessed preoperatively and at 3 weeks and 1 year postoperatively, if present, using the following four questionnaires. These questionnaires will assess tinnitus in the patients' daily life with the cochlear implant switched on. The Utrecht Burden Questionnaire for tinnitus and vertigo will also be administered directly postoperatively in case of direct postoperative tinnitus and/or vertigo:

- *Tinnitus Handicap Inventory:* a 25-item questionnaire evaluating three domains: a functional, emotional and catastrophic domain;[20 21]
- *Tinnitus Questionnaire*: a 52-item questionnaire evaluating five domains: tinnitus-related emotional and cognitive distress, intrusiveness, auditory perceptual difficulties, sleep disturbance and somatic symptoms. The response categories are 'true' (0/2 points), 'partly true' (1 point) and 'not true' (0/2 points), depending on the question. A validated Dutch version will be used;[22 23]
- *Dizziness Handicap Inventory*: a 25-item questionnaire evaluating three domains: functional, emotional and physical aspects of dizziness and unsteadiness. The response categories are 'yes' (4 points), 'sometimes' (2 points) and 'no' (0 points). The total score discriminates between a mild (16–34 points), moderate (36–52 points) and severe (54+ points) handicap. A validated Dutch version will be used;[24 25]
- *Utrecht Burden Questionnaire*: it measures severity and characteristics of tinnitus and vertigo by using visual analogue scales and numerical rating scales (see online supplementary appendix 3).

It needs to be noted that none of these questionnaires were validated for measuring treatment outcome.[26 27]

Postoperative complications

The severity of complications that can occur after cochlear implant surgery are classified according to Hoffman and Cohen's criteria.[28] Complications are considered major if hospitalisation or additional or revision surgery are required and minor if it resolves spontaneously or if only medication is required. Complications are prospectively registered in the patients' charts.

Cost-effectiveness/utility analysis

The difference in costs and benefit will be represented using the incremental cost utility/effectiveness ratio (ICUR/ICER). The ICUR/ICER is calculated by dividing the difference in costs by the difference in utility or effectiveness. Utility reflects the amounts of money that people are willing to pay to achieve a certain health status. Cost analysis will be performed from a health insurance and patient perspective. Utility scores derived from questionnaires such as the EuroQoL-5D and the Health Utilities Index 3 are used to calculate the ICUR.

Participants will be asked to keep a costs diary (see online supplementary appendix 4). They will fill this diary preoperatively and at regular intervals postoperatively. The first month the diary will be filled weekly followed by monthly for the duration of 1 year. Costs will be measured from a societal and healthcare perspective. Direct and indirect costs will be collected. Direct costs include hospitalisation, surgery, postoperative complications, doctor's visits and diagnostic tests. Indirect costs include travel expenses and sick leave. Published data of cumulative complications in large cohorts were used to determine weighted costs of complications.[29] Costs of medication such as antibiotics, outpatient clinic visits, hospitalisation, surgery, second implants, will be accounted for. The Dutch guidelines for costing research in health economic evaluations, issued by the National Healthcare Institute,[30] will be used to calculate unit prices of resources that were used.

Statistical analysis

Baseline characteristics per group will be described as means and SDs. Differences in the baseline will be analysed using the independent samples Student's t-test or non-parametric tests for continuous variables and the Fisher's exact test for categorical variables.

The primary and secondary outcome data are quantitative and will be presented continuous and categorical. Between-group mean differences, rate differences and rate ratios with 95% CIs will be calculated. For further analysis of between-group differences in primary and secondary outcomes, the independent samples Student's t-test or non-parametric tests will be used for continuous outcomes and the Fisher's exact test will be used for categorical outcomes. Within-subject comparisons will entail differences in mean values and percentages

before and after cochlear implantation. These will be analysed using paired t-tests for continuous measures and using the McNemar test for categorical outcomes.

Missing values will be handled using multiple imputation, and all analyses will be performed on an intention-to-treat basis. A sensitivity analysis will be performed using all of the data acquired from patients who opted not to be included in the study, but did fill out the questionnaires.

The data will be reported according to the CONSORT statement.[31 32]

Dissemination

All cases of serious adverse events will be reported to the local Institutional Review Board and adequately followed up. An independent monitor is appointed to check the trial quality (completeness of informed consent forms, validity of data etc) once a year. All data will be handled confidentially. The data will be coded by using a unique PIN and two of the investigators will safeguard the key to this code. The primary source of the data will be paper files, which will be stored in a locked room. The data will be stored on the investigators' computers as well, which are secured by a password and located in a locked room. The final trial data set will only be available to the research team.

The trial results will be disseminated through peer-reviewed medical journals and presented at scientific conferences.

Trial status

The trial is currently in recruitment phase.

CONCLUSION

Cochlear implantation seems to be a surgical procedure that is well suited for day-case treatment as it has proved to be a safe treatment with low complication rates. However, current literature lacks evidence-based recommendations supporting day-case cochlear implantation. This randomised controlled trial allows for a comparison between day-case and inpatient cochlear implantation to investigate the hypothesis that day-case cochlear implantation is associated with a higher QoL and higher cost-effectiveness, while maintaining an equal hearing outcome and complication rate, compared to inpatient cochlear implantation. This is the first trial of highest epidemiological quality evaluating and quantifying the benefits of day-case cochlear implantation for patients with severe to profound bilateral postlingual SNHL.

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Competing interests None declared.

Ethics approval The study will be conducted according to the principles of the Declaration of Helsinki (Fortaleza, 2013) and in accordance with the Medical Research Involving Human Subjects Act (WMO). The research protocol was approved by the Institutional Review Board of the UMC Utrecht (NL45590.041.13; V.5, November 2015), and protocol modifications will be presented to the Institutional Review Board of the UMC Utrecht for approval.

Provenance and peer review Not commissioned; externally peer reviewed.

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