The Influence of Cochlear Implantation on Tinnitus in Patients with Single-Sided Deafness: A Systematic Review

Nicole Peter, MD1,2*, Nuwan Liyanage, MSc1,2*, Flurin Pfiffner, PhD1,2, Alexander Huber, MD1,2, and Tobias Kleinjung, MD1,2

Abstract

Objectives. This systematic review provides an overview of the available studies (published by January 29, 2018) with descriptive data analysis about the influence of cochlear implantation on tinnitus in patients with single-sided deafness (SSD).

Data Sources. PubMed, EMBASE, Web of Science, Cochrane Library, and Google Scholar.

Review Methods. Original studies about the influence of cochlear implantation on tinnitus, measured with different tinnitus questionnaires or visual analog scale, in patients with SSD were included. The pre- and postimplantation tinnitus scores of the included studies were extracted for the further systematic review.

Results. The systematic search yielded 1028 studies. After evaluating titles, abstracts, and full texts, 1011 of these were dismissed. From the remaining 17 studies, 4 showed a low directness of evidence or high risk of bias and were therefore excluded. Due to the nature of cochlear implantation in SSD, only cohort studies and no randomized trials exist, which limits the evaluation in a systematic review. Generally, the mean tinnitus questionnaire scores decreased after cochlear implantation in these 13 studies with a total of 153 patients. The most widely used tinnitus questionnaire was the Tinnitus Handicap Inventory. In these studies, 34.2% of patients demonstrated complete suppression, 53.7% an improvement, 7.3% a stable value, and 4.9% an increase of tinnitus, and none of the patients reported an induction of tinnitus.

Conclusion. This review shows a clear improvement of tinnitus complaints after cochlear implantation in patients with SSD. Therefore, tinnitus might be considered as an additional indication for cochlear implantation in SSD.

Keywords
unilateral hearing loss, cochlear implant, CI, tinnitus, single-sided deafness, cochlear implantation, review

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Single-sided deafness (SSD) is defined as a severe to profound hearing loss in one ear and a preserved normal or near to normal hearing in the contralateral ear. In the consensus paper by Van de Heyning et al,1 SSD is specified as the mean thresholds at the pure-tone average (PTA) of 0.5, 1, 2, and 4 kHz being ≥70 dB hearing level (HL) in the poorer ear and ≤30 dB in the better ear. On the other hand, asymmetric hearing loss (AHL) includes patients with mean thresholds at the PTA of ≥30 dB HL and ≤55 dB HL in the better ear. The prevalence of SSD has been estimated to affect 3% to 6% of the population.2 Acquired postlingual SSD and AHL can be triggered by different diseases, from which sudden sensorineural hearing loss (SSNHL) is the most common cause.3,4 Other documented etiologies are Ménière’s disease, unilateral vestibular schwannoma, temporal bone fractures, unilateral noise damage, and infection (labyrinthitis, mumps, meningitis).5 SSD and AHL often lead to significant consequences in communication abilities with decreased speech perception in noise and in impaired sound localization. In addition, a significant proportion of patients with acquired SSD and AHL experience tinnitus.6 Chiossoine-Kerdel et al7 documented tinnitus in 67% of patients with SSNHL, with moderate to severe tinnitus handicap in 29% of the patients. The traditional hearing rehabilitation of this condition consists of the adjustment of hearing systems with routing of acoustic signals from the healthy ear to the deaf ear, for example, a

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bone-anchored hearing aid (BAHA) or contralateral routing of signal (CROS). These hearing aids can improve the head shadow effect but do usually not reduce the perception of tinnitus.

Tinnitus is defined as a perception of sound (usually, but not exclusively, a tone or buzzing) without any external sound source. The pathophysiology of tinnitus is not yet thoroughly understood. Different underlying theories assume that a peripheral lesion of the cochlear hair cells induces a suboptimal or maladaptive plasticity of the central nervous system, inducing reorganization and hyperactivity in central auditory and nonauditory structures. Consequently, restoring hearing by cochlear implantation may affect tinnitus perception. A recent systematic review of cochlear implantation in patients with bilateral hearing loss showed that most patients had a decrease in tinnitus perception after cochlear implantation with regard to the Tinnitus Handicap Inventory (THI), tinnitus loudness, and annoyance. As an attempt to treat severe to profound tinnitus in patients with postlingual SSD, Van de Heyning et al were the first to fit a group of patients with SSD with cochlear implants. This and following studies demonstrated that cochlear implantation represents an effective treatment option for tinnitus in patients with SSD. These results support the abovementioned theories about the pathophysiology of tinnitus. Furthermore, it was demonstrated that a cochlear implant (CI) improved the understanding of speech in noise and the ability to localize sound. However, in most countries, this rehabilitation technique is not reimbursed by the health authorities so far.

There are different studies reporting cochlear implantation as an effective treatment option for tinnitus in single-sided deaf patients. However, most studies investigated only small sample sizes, and for this reason, reviews are needed to pool data. Some reviews on this topic already exist, but the latest one is from 2015. Since then, 12 more studies related to the question of tinnitus suppression with CI in patients with SSD have been published, and so a current, systematic review of the literature following the principles of evidence-based medicine is still lacking.

Therefore, the objective of this study was to systematically review the effect of cochlear implantation on tinnitus in adults with SSD. A limitation to perform a systematic review is the fact that only cohort studies and no randomized trials exist due to the nature of cochlear implantation in SSD. To overcome this issue, the review is performed in a similar style of other ones investigating the effect of cochlear implantation on tinnitus.

**Methods**

The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement was used for this systematic review.

**Search Strategy**

A systematic search of published studies was performed in PubMed, EMBASE, Web of Science, Cochrane Library, and Google Scholar databases. The search was conducted on January 29, 2018, and all published studies available at this time in any language were included in the review process. The search terms included the combined expressions of *tinnitus*, *cochlear implants*, and *single-sided deafness* and all their synonyms. In **Table 1**, the comprehensive search syntax is presented for PubMed.

**Study Selection**

As a first step in the study selection process, all the duplicates of the collected studies were removed. Afterward, 2 authors (N.P. and T.K.) independently screened the studies, first based on title and abstract and second on full text. Studies were excluded from the reviewing process due to the following reasons: nonoriginal research studies (reviews), studies on animals, case reports and studies with fewer than 5 patients, studies of patients with bilateral deafness and bilateral cochlear implantation, only postimplantation scores mentioned with impossibility to compare to the preoperative tinnitus, studies by the same authors published on overlapping study populations, and full texts, which were not retrievable. In the case of overlapping patient populations, the latest study that reported relevant data for our analysis was included to ensure that the same population was included only once in our review. The 2 authors selected original studies performed on adult patients with tinnitus and SSD who underwent cochlear implantation. The complete selection process is shown in the PRISMA flowchart in **Figure 1**. In the case of a disagreement regarding the inclusion of a study between the authors at any stage, a consensus was reached after a discussion. Furthermore, we performed a manual search of the reference lists of the included studies to confirm that every related article was included in the review process.

**Quality Assessment of the Studies**

For the quality assessment of the selected full-text studies, directness of evidence and risk of bias were evaluated according to the GRADE approach outlined in the *Cochrane Handbook for Systematic Reviews of Interventions*. The criteria were adapted to suit the investigated question and followed a similar structure to the review by Ramakers et al about the effect of cochlear implantation on tinnitus with bilateral hearing loss. The quality assessment of the studies was performed through the use of predefined criteria, which resulted in the categories of satisfactory, unsatisfactory, or unclear if the information pertaining to these criteria was not reported.

Directness of evidence of the studies was evaluated in a similar way to the reported review of Ramakers et al and was based on the included patients, the type of therapy, the outcome assessment, and the follow-up period. A study with high directness of evidence indicated that all the 4 criteria were met. Studies that had only 3 of 4 criteria were considered to have moderate directness of evidence. Low directness of evidence was considered for studies with fewer than 3 criteria.
The risk of bias of every study was assessed according to "the Cochrane Collaboration’s tool for assessing risk of bias in randomized trials." The quality of the studies was evaluated using 5 criteria: selection, performance, detection, attrition, and reporting bias. Studies that reached 4 or 5 criteria were identified to have low risk of bias. A study with a score between 2 and 4 was considered to have moderate risk of bias. If the score was less than 2 out of 5, it was categorized as a study with a high risk of bias.

Studies that indicated low directness of evidence and/or high risk of bias were less likely to contribute toward the final analysis and were therefore removed from the study pool.

**Data Extraction and Evaluation**

We focused on the mean difference of tinnitus between pre- and postimplantation assessed with questionnaire scores as main outcome measures. The selected studies used different

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### Table 1. Search Strategies Used in Each Database.

<table>
<thead>
<tr>
<th>Database</th>
<th>Search</th>
<th>Keywords/Syntax</th>
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</tr>
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<td>73</td>
<td></td>
</tr>
<tr>
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<td>(((((((((((((cochlear[Title/Abstract]) AND implant[Title/Abstract]) OR cochlear[Title/Abstract]) AND prostheses[Title/Abstract]) OR cochlear[Title/Abstract]) AND prosthesis[Title/Abstract]) AND system[Title/Abstract]) OR cochlear[Title/Abstract]) AND prosthetic[Title/Abstract]) AND devices[Title/Abstract]) OR auditory[Title/Abstract]) AND prostheses[Title/Abstract]) OR CI[Title/Abstract]) OR implant[Title/Abstract]) OR prostheses[Title/Abstract]) OR &quot;cochlear implants&quot;[MeSH Terms]) OR &quot;cochlear implantation&quot;[MeSH Terms]</td>
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<td></td>
</tr>
<tr>
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<td>1 AND 2 AND 3</td>
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</tr>
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<td>Harzing’s Publish or Perish 6.21.6145.6594 software</td>
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</table>

*Default syntax was adapted where necessary.*
types of tinnitus evaluation questionnaires. In most cases, the data of interest for the analysis were clearly stated in the studies; if not, they were estimated from the graphs. This was performed independently by 2 authors (N.P. and N.L.). In case of disagreement of the extracted values, a consensus was reached after discussion.

In addition to the previous assessment, we also extracted the number of patients in each study who reported a complete recovery, an improvement, no change, a worsening, or a new induction of tinnitus.

**Questionnaires**

Different tinnitus evaluation questionnaires were used across these studies either exclusively or in combination. The most commonly used questionnaires were the THI\(^{49}\) and the visual analog scale (VAS).\(^{50}\) In the THI, tinnitus handicap was grouped according to the range of scores: slight (0-16), mild (18-36), moderate (38-56), severe (58-76), or catastrophic (78-100). The VAS was used to assess subjective tinnitus perception levels of each patient at each follow-up time point. Classically, patients were asked to make a mark representing their tinnitus on an analog (ie, continuous and unnumbered) line of about 10 cm with the description “quiet” on the left extreme and “very loud, cannot get any worse” on the right extreme. The measured distance from the left-hand side to the marked point reflects the tinnitus.\(^{35,51}\) Studies that used a numeric rating scale from 0 to 10 but also labeled this as VAS were treated like VAS. Furthermore, the VAS in tinnitus can be used to evaluate different qualities of tinnitus such as loudness, awareness, annoyance, degree of disability, stress, mood, and ability to influence the tinnitus.\(^{20,21,25,27,31,34,36}\)

Regardless of the type of the questionnaire, a higher reported value reflected more tinnitus burden while a lower value represented less disturbance from tinnitus.

**Meta-Analysis**

Due to the characteristics of the studies, we expected a high degree of heterogeneity. To investigate the heterogeneity of the included studies, we performed an \(I^2\) statistic. A further meta-analysis using Review Manager software (version 5.3; the Cochrane Collaboration, London, United Kingdom) would be performed in case of a probably not important or moderate heterogeneity, which, according to the Cochrane recommendation, should be a value of \(I^2 < 60\%\).\(^{47}\) Alternatively, in case of high \(I^2\) over 75\%, which implicates a considerable heterogeneity,\(^{47}\) we decided to proceed with a descriptive analysis. If the \(I^2\) has a value between 60\% and 75\%, the reasons for the heterogeneity will be evaluated and a meta-analysis or systematic review will be performed accordingly.

**Results**

**Search Strategy and Study Selection**

The complete selection process is shown in the PRISMA flowchart in Figure 1.\(^{46}\) During the exclusion process, 12 studies were identified that reported the outcomes of the same population over several years. In that case, the most recent article was selected by the reviewers. An exception was the study by Mertens et al\(^{35}\) which was replaced by that of Punte et al\(^{20}\) from the same research group. In the study by Mertens et al\(^{35}\) only the median was reported, whereas in Punte et al\(^{20}\) the mean and standard deviation could be extracted and then used in the further analysis. Finally, 17 studies remained for the quality assessment.

**Quality Assessment of the Studies**

A critical evaluation of the selected studies is described in Table 2. All studies were either prospective or retrospective cohort studies.

To include studies in our review, the following criteria had to be fulfilled: adults with SSD and tinnitus who received a cochlear implant. Nevertheless, some publications\(^{26,28,34,36}\) did not meet the criteria of SSD described in the consensus paper from Van de Heyning et al.\(^{1}\) In Macias et al\(^{34}\) in which a combination of patients with SSD and AHL was reported, only the SSD population data were considered in the analysis. In the studies by Arts et al\(^{26}\), Seo et al\(^{36}\) and Dillon et al\(^{28}\), the patients were not clearly separated into an SSD or an AHL group. This meant that the relevant details specific to patients with SSD could not be extracted despite the fact that the titles of these studies implied that most of the patients had SSD. Therefore, the patient selection for these studies was rated as unsatisfactory in the directness of evidence. The studies by Seo et al\(^{36}\) and Dillon et al\(^{28}\) could be included in the further analysis because the other factors for directness of evidence were satisfactory.

Due to the nature of cochlear implantation in SSD, there was a performance and selection bias because of the missing blinding and randomization.

For the final evaluation, 13 studies* with moderate or high directness of evidence and moderate risk of bias were selected for further data evaluation.

**Study Characteristics**

The characteristics of the studies are summarized in Table 3. The sample sizes vary from 5 to 28 patients. However, not all patients had tinnitus before cochlear implantation,\(^{25,31,34,38}\) so the sample size variation of patients with preoperative tinnitus varied from 5 to 26.

Seo et al\(^{36}\) evaluated tinnitus perception between 2 groups; one had middle ear implants and the other cochlear implants. Only the group with cochlear implants was included in the further evaluation.

The follow-up period over all studies ranged from 3 to 28 months. The longest follow-up period in each study is shown in Table 3. A decrease in the number of patients at the follow-up time point was observed in a few studies.\(^{5,27,31}\) The following data were considered for the calculation: the data with the longest follow-up period and fewest missing data.

*References 5, 20, 21, 24, 25, 27, 28, 30, 31, 33, 34, 36, 38.
<table>
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<tr>
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Abbreviations: H, high; L, low; M, moderate; PCS, prospective case series; RCS, retrospective case series; ● = Satisfactory; ○ = unsatisfactory; ? = unclear/not mentioned.

Directness of evidence: Patients: ● = patients with tinnitus and single-sided deafness (SSD); ○ = patients with tinnitus, SSD, and asymmetric hearing loss (AHL) can be separated; ? = patients with tinnitus and SSD or AHL. Therapy: ● = unilateral cochlear implantation; ○ = different therapy. Outcome: ● = evaluation of tinnitus after the cochlear implantation; ○ = no evaluation/information mentioned after the cochlear implantation. Follow-up: ● = ≥6 months; ○ = ≤6 months.

Risk of bias: Performance bias: ● = describe whether there was blinding among the parties involved; ○ = no blinding among the parties involved. Selection bias: ● = random or concealed treatment allocation; ○ = neither random nor concealed treatment allocation. Detection bias: ● = the same evaluation questionnaire(s) used in after cochlear implant evaluation of tinnitus; ○ = a different questionnaire was used or the evaluation is not reported. Reporting bias: ● = clearly defined inclusion/exclusion criteria of the patients; ○ = not clearly defined inclusion/exclusion criteria of the patients. Attrition bias: ● = completeness of reported data (≤10% missing data); ○ = ≥10% missing data.
<table>
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<tr>
<th>Study</th>
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<th>No. with Preoperative Tinnitus</th>
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<th>Age, Mean (SD), y</th>
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<td>50.0 (5.2)</td>
<td>Advanced Bionics</td>
<td>VAS</td>
</tr>
<tr>
<td>Macías et al</td>
<td>16</td>
<td>13</td>
<td>6</td>
<td>13 (10 SSD, 3 AHL)</td>
<td>8 8</td>
<td>52.8 (10.9)</td>
<td>Cochlear</td>
<td>THI (Spanish)/VAS</td>
</tr>
<tr>
<td>Arndt et al</td>
<td>11</td>
<td>10</td>
<td>6</td>
<td>11</td>
<td>NE NE</td>
<td>43.5 (11.9)</td>
<td>Cochlear</td>
<td>VAS</td>
</tr>
<tr>
<td>Dillon et al</td>
<td>20</td>
<td>20</td>
<td>12</td>
<td>20</td>
<td>NE NE</td>
<td>50.0 (11.5)</td>
<td>MED-EL</td>
<td>THI</td>
</tr>
<tr>
<td>Friedmann et al</td>
<td>12</td>
<td>12</td>
<td>?</td>
<td>10</td>
<td>6 6</td>
<td>50.5 (13.4)</td>
<td>Cochlear/Advanced Bionics</td>
<td>?</td>
</tr>
<tr>
<td>Härkönen et al</td>
<td>7</td>
<td>6</td>
<td>28</td>
<td>6</td>
<td>2 5</td>
<td>48.0 (NE)</td>
<td>Cochlear</td>
<td>VAS</td>
</tr>
<tr>
<td>Kitoh et al</td>
<td>5</td>
<td>5</td>
<td>12</td>
<td>5</td>
<td>1 4</td>
<td>52.2 (18.5)</td>
<td>MED-EL</td>
<td>THI</td>
</tr>
<tr>
<td>Ahmed and Khater</td>
<td>13</td>
<td>13</td>
<td>3</td>
<td>13</td>
<td>8 5</td>
<td>40.0 (10.0)</td>
<td>Cochlear/MED-EL/Advanced Bionics</td>
<td>THI/TRS</td>
</tr>
</tbody>
</table>

Abbreviations: AHL, asymmetric hearing loss; NE, not extractable; SSD, single-sided deafness; THI, Tinnitus Handicap Inventory; TQ, Tinnitus Questionnaire; TRQ, Tinnitus Reaction Questionnaire; TRS, Tinnitus Rating Scale; VAS, visual analog scale; ?, unclear.
The mean age of the patients ranged from 40 to 53.8 years, and 47% of patients were female and 53% male. To quantify the perception of tinnitus, the most commonly used rating instruments were the THI\(^5,21,24,26,28,33,34,36\) and the VAS.\(^21,25,27,31,34,36\) Several studies used a numerical rating scale, which ranged from 0 to 10 and presented this as the VAS.\(^25,31,34,36\) The VAS was also used to assess different qualities linked to tinnitus perception, such as loudness, awareness, annoyance, degree of disability, stress, mood, and ability to influence the tinnitus.\(^20,21,25,27,31,34,36\) Since the group of the different VAS qualities was too small for further analysis, all VAS questionnaires were pooled. Other questionnaires used were the Tinnitus Questionnaire (TQ),\(^30,52-54\) the Tinnitus Reaction Questionnaire (TRQ),\(^38,55\) the Tinnitus Test,\(^21\) and the Tinnitus Rating Scale (TRS).\(^24\)

**Meta-Analysis**

A visible heterogeneity was present among the studies due to differences in study design, reporting, evaluation and analysis method, inclusion criteria, sample size, follow-up periods, and outcome measurements. In addition, there were no studies with a low risk of bias that would have been desirable for our data pool (Table 2). To confirm this, we decided to pool the studies with the most commonly used outcome measurements, THI and VAS, and calculated the \(I^2\) statistic value of these studies for both questionnaires. When the required data for the \(I^2\) statistic were either not available or could not be extracted, the studies were not included in the \(I^2\) statistic.\(^30,38\) A substantial heterogeneity among the groups was confirmed in the pooled data of THI (\(I^2 = 92\%\)) and VAS (\(I^2 = 96\%\)), so no further meta-analysis could be performed.

**Descriptive Data Analysis of the Studies**

**Evaluation of tinnitus questionnaires.** The studies that were included in the further evaluation after quality assessment are listed in Table 4. The THI questionnaire found a reduction in postimplantation scores compared to the preimplantation scores.\(^5,21,24,26,28,33,34,36\) Each score mentioned here is followed by the SD in parentheses. The preimplantation scores varied from 25.4 (17.3) to 79.6 (7) and the postimplantation scores from 2.6 (4.8) to 35.2 (27.3). When comparing the scores, the highest reduction of THI was mentioned in the study by Ahmed and Karter\(^24\) and showed an improvement from 79.6 (7) to 12.0 (13.5).

For VAS, the mean (SD) preimplantation scores ranged from 5.0 (1.2) to 8.5 (1.1) and the postimplantation scores from 1.2 (SD was not extractable) to 5.7 (0.8). The mean (SD) maximum score reduction of VAS for tinnitus loudness/annoyance was from 8.1 (1.2) to 1.6 (2.9).\(^34\) Only 1 study reported a higher postimplantation value of VAS compared to the preimplantation value.\(^27\) However, this study documented a mean of different VAS scores, which accessed tinnitus loudness, tinnitus induced stress, mood, and ability to influence the tinnitus.

The differences in tinnitus scoring between pre- and post-implantation using THI and VAS are shown in Figures 2 and 3, respectively. Among the studies that used the THI, a noticeable improvement of tinnitus perception could be seen after the cochlear implantation, as shown in Figure 2. Figure 3 illustrates the same conclusion except in the study by Buechner et al.\(^27\) However, it is noteworthy that the difference between pre- and postimplantation in this latter study was relatively small and that it is 1 of 2 studies\(^27,33\) with the smallest patient populations of 5 patients.

The remaining studies that used different questionnaires also reported a significant reduction between pre- and postimplantation scores (Table 4).

Although it would have been interesting to find information about the effects of switching between on and off of the CI on tinnitus perception, only 3 studies reported this as a clinical outcome of the respective studies.\(^20,25,34\) These 3 studies showed that after switching off the CI, the tinnitus perception returned to a level approximately similar to their respective preimplantation stage (Table 4).

**Quantitative effects of tinnitus after cochlear implantation.** Ten of the included 13 studies either directly or by using graphics mentioned the number of patients who received complete recovery, improvement, stabilization, worsening, or induction of tinnitus by using the THI and/or VAS questionnaire.\(^5\) When shown in a graph, the data were extracted. These data were pooled for a descriptive analysis. Two studies\(^30,38\) did not perform the THI or VAS questionnaire, and 1 study using the VAS\(^27\) did not mention the numbers of patients with their postimplantation tinnitus perception status. These 3 studies were therefore excluded in the descriptive analysis. Figure 4 illustrates separately the number of patients in each postimplantation evaluated category for studies that used the THI or VAS. In studies using the THI (which included 82 subjects) as an outcome measurement, 28 patients (34.2%) demonstrated complete tinnitus suppression, 44 (53.7%) reported an improvement of tinnitus burden, 6 (7.3%) were stable, 4 (4.9%) experienced an increase of the tinnitus perception, and none of the patients reported a new induction of tinnitus. Similarly, considering the VAS scores (which included 79 subjects), 16 (20.3%) reported a complete suppression, 54 (68.4%) patients had a lesser tinnitus burden, 7 (8.9%) of the patients’ tinnitus perception was stable, 2 (2.5%) patients experienced worsening of the tinnitus, and none of the patients reported an induction of tinnitus. Neither of the questionnaires reported an induction of tinnitus in their patient cohorts.

**Discussion**

This systematic review describes the impact of cochlear implantation on tinnitus perception in patients with SSD and tinnitus. The major strength of our review is that it is characterized by a transparent search strategy and study

\(^{3}\)References 5, 20, 21, 24, 25, 28, 31, 33, 34, 36.
Table 4. Extracted and Processed Data from Each Study.

<table>
<thead>
<tr>
<th>Study</th>
<th>No. of Patients in Follow-up</th>
<th>Questionnaire Used</th>
<th>Preimplantation Score (CI On)</th>
<th>Postimplantation Score (CI Off)</th>
<th>P Value</th>
<th>Total Suppression</th>
<th>Improved (Tinnitus Decreased)</th>
<th>Stable (Tinnitus Stable)</th>
<th>Worsened (Tinnitus Increased)</th>
<th>Tinnitus Induced</th>
</tr>
</thead>
<tbody>
<tr>
<td>Távora-Vieira et al [38]</td>
<td>13</td>
<td>TRQ</td>
<td>48.8 (27.2)</td>
<td>1.8 (4.2)</td>
<td>NA</td>
<td>NA</td>
<td>NE</td>
<td>NE</td>
<td>NE</td>
<td>NA</td>
</tr>
<tr>
<td>Seo et al [36]</td>
<td>16</td>
<td>THI</td>
<td>46.5 (33.0)</td>
<td>34.6 (25.2)</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>56.0 (9)</td>
<td>25.0 (4)</td>
<td>19.0 (3)</td>
</tr>
<tr>
<td>Ramos et al [21a]</td>
<td>10</td>
<td>THI (Spanish)</td>
<td>72.1 (9.2)</td>
<td>14.3 (18.0)</td>
<td>NA</td>
<td>20.0 (2)</td>
<td>70.0 (7)</td>
<td>10.0 (1)</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Punke et al [20]</td>
<td>26</td>
<td>VAS</td>
<td>8.5 (1.1)</td>
<td>2.2 (1.4)</td>
<td>.001</td>
<td>15.4 (4)</td>
<td>84.6 (22)</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Holder et al [5]</td>
<td>8</td>
<td>THI</td>
<td>61.2 (27.5)</td>
<td>24.6 (28.2)</td>
<td>NA</td>
<td>45.0 (4)</td>
<td>37.5 (3)</td>
<td>12.5 (1)</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Buechner et al [27a]</td>
<td>5</td>
<td>VAS</td>
<td>4.96 (1.2)</td>
<td>5.7 (0.8)</td>
<td>NA</td>
<td>NE</td>
<td>NE</td>
<td>NE</td>
<td>NE</td>
<td>NE</td>
</tr>
<tr>
<td>Macias et al [34]</td>
<td>10</td>
<td>THI (Spanish)</td>
<td>71.2 (8.0)</td>
<td>35.2 (27.3)</td>
<td>NA</td>
<td>10.0 (1)</td>
<td>80.0 (8)</td>
<td>NA</td>
<td>10.0 (1)</td>
<td>NA</td>
</tr>
<tr>
<td>Arndt et al [25]</td>
<td>11</td>
<td>VAS</td>
<td>8.1 (1.2)</td>
<td>1.6 (2.9)</td>
<td>NA</td>
<td>60.0 (6)</td>
<td>40.0 (4)</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
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<tr>
<td>Dillon et al [28]</td>
<td>20</td>
<td>THI</td>
<td>25.4 (17.3)</td>
<td>2.6 (4.8)</td>
<td>&lt;.001</td>
<td>70.0 (14)</td>
<td>30.0 (6)</td>
<td>NA</td>
<td>NE</td>
<td>NE</td>
</tr>
<tr>
<td>Friedmann et al [30]</td>
<td>10</td>
<td>?</td>
<td>NE</td>
<td>NE</td>
<td>NA</td>
<td>NA</td>
<td>NE</td>
<td>NE</td>
<td>100.0 (12)</td>
<td>NA</td>
</tr>
<tr>
<td>Härkönen et al [31]</td>
<td>6</td>
<td>VAS</td>
<td>6.1 (NE)</td>
<td>1.2 (NE)</td>
<td>.027</td>
<td>NA</td>
<td>100.0 (6)</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Kitoh et al [33]</td>
<td>5</td>
<td>THI</td>
<td>63.2 (20.0)</td>
<td>14.0 (15.9)</td>
<td>NA</td>
<td>20.0 (1)</td>
<td>80.0 (4)</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Ahmed and Khater [24]</td>
<td>13</td>
<td>THI</td>
<td>79.6 (7.0)</td>
<td>12.0 (13.5)</td>
<td>&lt;.050</td>
<td>46.2 (6)</td>
<td>53.9 (7)</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td></td>
<td></td>
<td>TRS</td>
<td>4.5 (0.5)</td>
<td>1.5 (0.5)</td>
<td>&lt;.050</td>
<td>NA</td>
<td>100.0 (13)</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
</tr>
</tbody>
</table>

Abbreviations: CI, cochlear implant; NA, not applicable; NE, not extractable; THI, Tinnitus Handicap Inventory; TQ, Tinnitus Questionnaire; TRQ, Tinnitus Research Questionnaire; TRS, Tinnitus Rating Scale; VAS, visual analog scale; ?, unclear.

*Included the longest follow-up time.

Data extracted from graphs.

Calculated/approximated based on the data given.
Due to the nature of cochlear implantation in SSD, a performance and selection bias typically exists because of the impossibility of experimental blinding and randomization. For this reason, most of the included studies are cohort studies and not randomized controlled trials, as it would have been desirable for systematic reviews. This resulted in the fact that most of the included studies showed a high or moderate risk of bias. However, in most of the included studies, tinnitus was the major inclusion criterion for cochlear implantation in patients with SSD, whereas in studies with bilateral hearing loss, tinnitus was mostly evaluated as a side effect. Nevertheless, we were able to demonstrate in this systematic review that the mean tinnitus questionnaire scores were decreased after cochlear implantation in all included studies. The most frequently used tinnitus questionnaire was the THI, and these results were therefore pooled for further analysis. Because of a high degree of heterogeneity among the included studies and the abovementioned impossibility of blinding and randomization, no meta-analysis could have been performed. Overall, 34.2% of patients demonstrated complete tinnitus suppression, 53.7% reported an improvement of tinnitus burden, 7.3% were stable, 4.9% experienced an increase of the tinnitus perception, and none of the patients reported an induction of tinnitus in the descriptive THI analysis. Similar results were found by analyzing the VAS, although the effect was smaller than in the evaluation of the THI. A possible explanation is that the VAS represented different domains of tinnitus in the included studies like loudness, awareness, annoyance, degree of disability, stress, mood, and ability to influence the tinnitus, which could not be divided into the different tinnitus domains due to the resulting small group size.

Although the results of this review clearly indicate a positive effect on tinnitus perception in patients with SSD after cochlear implantation, we have to keep in mind that there were a few patients for whom the experience of tinnitus was worse after cochlear implantation. It is therefore important to inform possible CI candidates with SSD about this risk. Furthermore, the publication with the highest reduction of the THI showed a high mean (SD) preoperative THI value of 79.6 (7.0), indicating a catastrophic tinnitus handicap. This could suggest that patients with SSD and a high burden of tinnitus could have a better tinnitus improvement.

The pathophysiologic mechanisms of tinnitus suppression after cochlear implantation are not yet thoroughly understood. It is assumed that the CI induces a restoration of central auditory pathways and an induction of neuroplasticity, which may then affect the tinnitus perception. Some patients perceive a significant reduction of tinnitus directly after the first activation of the CI, which suggests a masking effect of the tinnitus due to the increased auditory information. However, the effect of tinnitus suppression could also be attributed to the effects of electrical stimulation. In this

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5References 5, 20, 21, 24, 28, 33, 34, 36, 38.
context, preliminary studies provide some evidence for the value of extracochlear electrical stimulation in humans with electrodes placed on the promontory, the external ear canal, or the round window. These techniques were tested in non-deaf subjects, which may suggest that a “tinnitus implant” could be developed for normal-hearing subjects in the future.\(^{57-59}\)

Typically, the tinnitus returns after removal of the speech processor but, in some cases, with some latency, which could be attributed to mechanisms of residual inhibition.\(^{60}\)

In addition, a reorganization of central auditory pathways has been demonstrated in the long term,\(^{61-63}\) and this could be the explanation in cases where late onset of tinnitus improvement after CI activation is reported. Furthermore, nonauditory areas of the brain belonging to different networks are also involved in tinnitus perception, like the perception, salience, distress, and memory networks.\(^{64-68}\)

Therefore, other effects after cochlear implantation like psychological health and increased quality of life could influence tinnitus perception in a positive way as well.\(^{69}\)

Among the studies, the differences in study design, sample size, follow-up durations, CI type, outcome measures, and measuring instruments gave rise to a notable heterogeneity. For example, the use of different questionnaires in each study made it difficult to pool all the studies and derive a collective outcome. When assessing the quality of the selected studies, some studies neglected to report important information such as follow-up duration or the analyzed group size. Therefore, at the data-analyzing stage, a few studies provided a weak impact on the overall outcome.\(^{30}\)

In addition to this, for some studies, the data extraction had to be done manually when the relevant data were not mentioned clearly or not illustrated in the figures. In the case of missing patient data toward the end of the trials, the maximum number of patients was included in the data extraction. Furthermore, the possibility to analyze the on or off conditions of CI on tinnitus perception was supported by only a few studies.

For this review, the inclusion criteria were adults with SSD and tinnitus who were eligible for cochlear implantation. Nevertheless, some publications\(^{26,28,34,36}\) did not meet the criteria of SSD described in the consensus paper by Van de Heyning et al.\(^1\) When the SSD population was separately listed in the publications, only this subgroup contributed to the further analysis.\(^{34}\)

In some studies, the AHL and SSD groups could not be separated, which led to a rating of unsatisfactory in the patient section of directness of evidence.\(^{26,28,34}\) If other subscales of the directness of evidence were insufficient, the studies were excluded.\(^{26}\)

The most commonly used tinnitus questionnaire was the THI by Newman et al.\(^{49}\) which is an internationally validated questionnaire. This questionnaire is used to measure treatment-related changes, although it was not designed for this purpose.\(^{70,71}\) To solve this problem the Tinnitus Functional Index (TFI) has been established.\(^{72}\) This questionnaire is highly responsive to treatment-related change and promises to be the new gold standard in tinnitus evaluation.\(^{72}\) To date, it has been validated in several different languages and should be used in further studies.\(^{71,73-77}\)

To enable the comparison of future studies with the existing studies, it is recommended to also assess tinnitus using the THI.

To overcome the limited methodological quality of the studies published so far, future investigations might consider a crossover study design for a more structured evaluation of different stimulation parameters within 1 subject (eg, implant on or off, different situation paradigms).

To sum up, further prospective cohort studies with the abovementioned definition of SSD and validated tinnitus questionnaires are needed to provide a higher level of evidence for the influence of cochlear implantation on tinnitus in patients with SSD. In addition, the improvement of tinnitus after cochlear implantation in SSD might represent an important factor in counseling patients in their respective situation. This review should help professionals to express realistic expectations when dealing with the affected persons. According to Van de Heyning (personal communication, March 20, 2018), this is extremely important in counseling situations with subjects who may have an additional mood disorder.

### Conclusion

This systematic review provides a descriptive analysis of the current literature about the influence of cochlear implantation on tinnitus in patients with SSD. These analyses showed a clear improvement of tinnitus after cochlear implantation, which indicates that tinnitus is a good indication for cochlear implantation in SSD. Patients with SSD and disturbing tinnitus can be counseled with regard to the prognosis of tinnitus improvement after cochlear implantation, with nearly 90% of the patients reporting a tinnitus suppression or improvement.

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### Author Contributions

Nicole Peter, conception and design of the work; interpretation of data; drafting the work, Nuwan Liyanage, acquisition, analysis, and interpretation of data; drafting the work; Flurin Pfiffner, interpretation of data; revising the work for important intellectual content; Alexander Huber, interpretation of data; revising the work for important intellectual content; Tobias Kleinjung, conception and design of the work; interpretation of data; revising the work for important intellectual content.

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