Review

Outcomes of Cochlear Implantation in Patients with Superficial Siderosis: A Systematic Review and Narrative Synthesis

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This study aimed to establish outcomes following cochlear implantation (CI) in patients with superficial siderosis (SS). MEDLINE, Embase, Web of Science, Cochrane, and ClinicalTrials.gov databases were searched for this systematic review. No limits were placed on the language or the year of publication. The review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement. Of a total of 46 studies, 19 studies met the inclusion criteria reporting outcomes in 38 patients. Of the 44 implants, 23 implants (52.27%) had good hearing outcomes at the last follow-up, 9 (20.45%) were initially beneficial for the patient, but then the performance deteriorated (4 of which were re-implanted), and 12 (27.27%) were not beneficial for the patient. All studies were classified as grade 4 studies using the Oxford Centre for Evidence-Based Medicine (OCEBM) grading system, being retrospective in nature and consisting of case reports and noncontrolled case series with a small number of patients. Of the 44 implants, 32 (72.73%) showed improved hearing outcomes following CI for SS at some point in time, of which 23 (52.2%) implants showed sustained benefit at the last follow-up (average follow-up time was 21.97 months). It is difficult to predict the longevity of benefit owing to the progressive nature of the disease or the patients in whom it may be beneficial, as the preoperative investigations inadequately predict benefit. Preimplantation and postimplantation counseling with the patient and their family regarding the potential limited benefit and eventual parallel decline with the neurological disease are crucial, along with thorough clinical investigations.

KEYWORDS: Cochlear implantation, superficial siderosis, hearing loss, systematic review

INTRODUCTION

Superficial siderosis (SS) was first described in 1908 by Hamill et al.[1] as a rare progressive disorder caused by recurrent hemorrhage in the subarachnoid space. The hemorrhaging leads to the spread of heme by circulating cerebrospinal fluid (CSF) and subsequent deposition of hemosiderin and other iron-containing pigments in the central nervous system (CNS). This accumulation occurs over several months, causing damage to the leptomeninges, brain surface, brainstem, cerebellum, cranial nerves, and spinal cord. These deposits propel lipid peroxidation, which ultimately leads to localized cell and tissue necrosis[2].

Iwanowski and Olszewski[3] were the first people to describe the mechanisms of SS, and they did this by successfully reproducing SS in dogs via repeated injections of blood or iron dextran into the subarachnoid space. With the emergence of magnetic resonance imaging (MRI), SS could be diagnosed *in vivo*, rather than only through postmortem examination. Through radiological advancements in the 1980s, the diagnosis of SS became more precise, and this rare condition could now be identified through the presence of a rim of hypointensity around the cerebellum, brainstem, cranial nerves, and spinal cord on T2-weighted and/or gradient echo sequence MRI scans[4]. Other diagnostic investigations that have emerged for SS include the presence of xanthochromia, increased blood cell count, and high protein levels in the CSF[5]. However, these findings are not universal as they can appear normal if the subarachnoid bleeding occurs intermittently[6].

The first two author contributed equally to this work.

SS is generally idiopathic in nature but can be associated with a history of neurosurgical procedures or CNS tumors and trauma[7,8]. If an identifiable source of hemorrhage has been located, then surgical correction may be possible; however, this is usually not a completely curative approach and SS can still continue to progress because of the already present hemosiderin deposits. Nonsurgical approaches so far have included utilization of steroids and iron-chelating medication. However, these management routes have seen limited success, and this could be attributed to their inability to cross the blood brain barrier[6]. Overall, in the absence of any clear management options, SS is typically treated symptomatically.

In many cases, decades pass before any symptoms emerge with the classic triad being progressive bilateral sensorineural hearing loss (SNHL), cerebellar ataxia, and myelopathy [6]. Other features include pyramidal signs (e.g., spastic paraparesis, quadriparesis), dementia, headache, and anosmia[9,10]. The vestibulocochlear nerve (VIII) is suspected to be more vulnerable to hemosiderin deposits when compared with other cranial nerves because of its long glial segment and by being subjected to a high level CSF flow as it passes through the pontine cistern[9,11]. Longitudinal analysis of hearing loss in patients with superficial siderosis suggests a progressive, predominantly high frequency hearing loss. Estimates for annual threshold deterioration rate range from 7–24 dB/year[2]. This hearing loss is the cardinal feature, present in 95% of the patients and generally commences early on in the course of disease, as described by Irving and Graham[12]. Temporal bone histopathology by Nadol et al.[11] in one patient with superficial siderosis showed severe bilateral degeneration associated with iron deposits in the organ of Corti, spiral ligament, stria vascularis, and spiral ganglion cells. A peripheral contribution to etiology is supported by Vanat et al.[13] who found brown fluid in the cochlea of a patient while performing cochlear implantation (CI) surgery.

In these patients, hearing rehabilitation is initially through hearing aids. However, because of the progressive retrocochlear nature of SS, amplification has minimal long-term benefit[2,5]. Once the patients have bilateral severe to profound hearing loss and exhibit poor

speech perception capacity, the next step in auditory rehabilitation in various studies includes vibrotactile stimulation, CI, and auditory brainstem implantation. The CI electrode array is placed within the scala tympani and directly stimulates the spiral ganglion cells that are innervated by the auditory nerve. The highly synchronous neural firing initiated by CI may overcome the limitations of a partly damaged auditory nerve. Even though the patients with SS are indistinguishable from the patients with standard CI based on pure-tone audiometry (PTA) alone and speech perception, CI should be considered with caution because of the predominantly retrocochlear nature of the damage, but potential iron deposited within the cochlea may also affect the spread of excitation within the cochlea[15].

In 2012, a systematic review (SR), by Tyler et al.[2] reported a clear sustained benefit in 7 of the 15 SS cases. They concluded that early implantation could be more beneficial, and outcomes were dependent on the site of lesion, neural deterioration, and the degree of cochlear nerve functionality. Three years later, Modest et al.[5] also published a SR concluding that CI is a viable option for auditory rehabilitation and that most patients received benefit from it. This SR aimed to pool all the available data via a rigorous SR methodology and to provide clinicians with the best evidence to date and advice on the use of CI in patients with confirmed SS.

Objectives
In this review, we looked at cochlear implant outcomes for patients with SS.

Population: Children or adults with SS.
Intervention: CI.
Comparison: No comparison group.
Outcomes: Preimplantation vs. postimplantation audiometric outcomes (where preimplantation outcomes were not available, we looked only at postimplantation audiometric outcomes).

MATERIALS AND METHODS
The study protocol was registered in the PROSPERO prospective database of systematic reviews (CRD42020191141).

Study Inclusion Criteria
Because of the limited number of reported cases, we placed no restriction on the types of studies and thus included all case-control studies, cohort studies, and case series/reports where outcomes of CI in patients with a confirmed diagnosis of SS were reported. Animal studies and human studies without the report of postoperative audiometric outcomes or where the abstract or full text were unavailable were excluded. The initial search yielded 95 articles and after removing duplicates, the total remaining number was 46 which then underwent title, abstract, and full-text screening leaving 19 studies for inclusion.

Search Strategy
A total of 2 reviewers (AC/DC) independently ran the searches and screened the abstracts. The following databases were searched: MEDLINE, Embase, Web of Science, Cochrane, and ClinicalTrials.gov. The search terms used were:
1) "Cochlear Implantion.mp. OR Cochlear Implantation/"
2) "Cochlear Implants.mp. OR Cochlear Implants/"

MAIN POINTS

- Hearing outcomes where generally good, of the 44 implants, 31 (70.45%) showed improved hearing outcomes following CI for SS at some point in time, and 22 implants (50%) had sustained benefit at the last follow-up.
- It is crucial that the patient and their family receives pre- and postimplantation counseling regarding the potential limited benefit and eventual parallel decline with the neurological disease to ensure realistic expectations, along with thorough audiometric investigations.
- The methodological quality of included studies was sufficient, consisting of case reports and small volume case series. All studies were OCEBM grade IV.
- Further research is required to more accurately understand SS pathophysiology, the role of CI in SS and develop pre-operative guidelines for an optimal testing schedule.

3) "Auditory Prosthesis.mp."
4) "Cochlear Prosthesis.mp."
5) "Siderosis/ OR Superficial Siderosis.mp."
6) "Hemosiderosis of the central nervous system.mp."
7) 1 OR 2 OR 3 OR 4
8) 5 OR 6
9) 7 AND 8

No limits were placed on language or the year of publication.

Selection of Studies

As mentioned above, 2 reviewers (AC/DC) independently screened all the records by title and abstract identified from searches retrieved from the database searches. Studies describing CI in patients with SS were assessed against the inclusion and exclusion criteria with any disagreement resolved by discussion with a third reviewer (JM). Studies without accessible abstract or full text after the title/abstract screening were followed up by attempting to contact the study authors. If they were unavailable, the study was excluded. Studies were also excluded if they did not report postintervention audiometric outcomes. Potentially relevant studies identified from the initial searches and abstract screening then underwent full-text screening by the 2 independent reviewers (AC/DC) before data extraction. Conflicts on the selection were resolved by discussion between the reviewers.

Data Extraction

The data was extracted by the first reviewer (AC) and then checked by the second reviewer (DC). The extracted data were arranged in a spreadsheet (Excel, Microsoft Corp, WA, USA).

Risk of Biased Quality Scoring

The risk of bias was evaluated by 2 independent reviewers using the Brazzelli risk of bias tool for nonrandomized studies[15]. The Oxford Centre for Evidence-Based Medicine (OCEBM) grading system [16] was utilized to grade the studies. Any discrepancies between the reviewers were resolved by discussion. Quality assessment of the studies is summarized in Table 1.

RESULTS

The searches were initially run on March 21, 2020. Figure 1 shows a flowsheet detailing the study selection according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.

Description of Studies

A total of 19 studies met the inclusion criteria with a total of 38 patients and 44 implants (2 bilateral, 13 right, 17 left-sided implants, and 4 re-implants). There were 11 case reports and 8 case series with the number of patients ranging from 2–7. All studies were published between 1999 and 2019. Since the last SR by Modest et al.[5], there have been 11 additional cases. All the patients were adults with the exception of one who was a child[5]. According to the available data, there were 25 men and 9 women. The average age at the time of CI was 50 years (ranging from 11–73). Of the studies include, 4 did not mention the type of implant used[5,17–19]. Alshehabi et al.[20] mentioned the type of implants used, however, failed to clarify who the recipients were. Grover et al.[21] reported the implant type in only 1 of the 2 patients. Only 2 studies measured quality of life as a postoperative outcome[20,22]. There was lack of data for 1 of the studies[18], and thus, we were not able to access the number of implants or other demographic data. The same patient was described in 2 papers; the first[23] discussing the implantation and follow-up of 5 years and the second[24] describing follow-up for an additional 3 years. From the reported data, the origin of SS can be credited to neurosurgical procedures in 11 cases (40.74%), history of head trauma in 11 cases (40.74%), and idiopathic causes in 5 cases (18.52%). The majority of SS diagnosis was based on MRI. Study characteristics are summarized in Table 2.

Quality of Studies

Our review contains 11 case reports and 8 case series that were non-controlled and consisted of a small number of patients. All the studies were retrospective in nature, and thus the level of evidence based on methodology was 4 using the OCEBM grading system[16]. A meta-analysis could not be conducted because of the heterogeneity of audiological and speech perception outcomes. Limitations were also seen in implants used, surgical technique, and rehabilitation details.

Audiological and Implant Outcomes

Of the 44 implants, 23 (52.27%) produced good hearing outcome at the last follow-up, 9 (20.45%) initially benefited but then regressed with time (4 of which were re-implants), and 12 (27.27%) did not benefit from them. The average follow-up period was 22 months (ranging from 3 months–84 months). The average duration of benefit per implant that reported benefit for any amount of time and follow-up is 22.5 months ranging from 4 months–84 months. Because of the heterogeneity of both pre- and postoperative tests, data, and time of reporting, an overall criterion for benefit could not be established, and was necessarily based on the individual criteria of each study.

Of the 4 re-implants, the first re-implanted patient initially showed promising results, however, soon exhibited a decreasing response
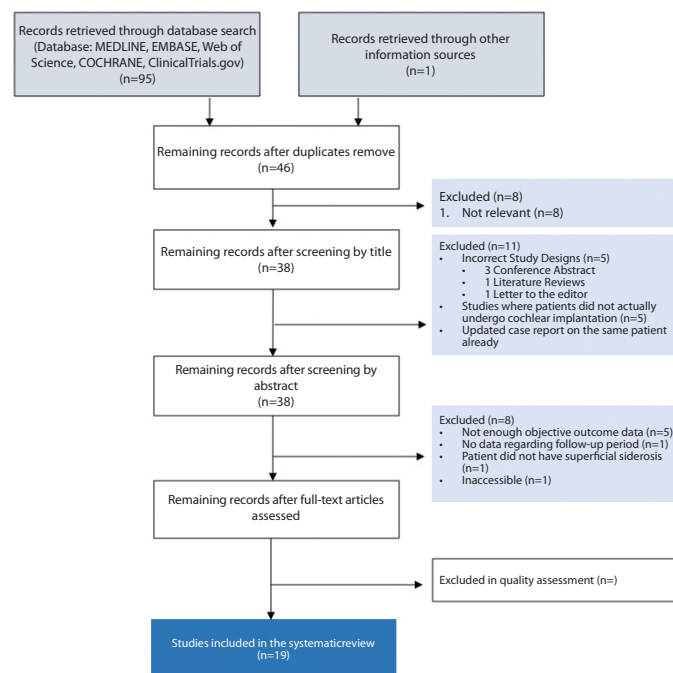

Figure 1. Flowsheet detailing study selection

Table 1. Brazzelli Risk of Bias Assessment

References	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18
Kim et al.[31]	R	R	G	N/A	R	R	G	Y	Y	G	G	R	R	R	G	N/A	G	R
Alshehabi et al.[20]	G	Y	R	Y	R	R	R	Y	Y	G	G	R	R	R	R	N/A	N/A	R
Irving and Graham[12]	R	R	G	N/A	R	R	G	Y	Y	G	G	R	G	R	N/A	N/A	G	R
Nogueira and Meehan[32]	R	R	G	N/A	R	R	G	Y	Y	G	G	R	G	R	N/A	N/A	G	R
Ryan et al.[17]	R	R	G	N/A	R	R	R	Y	Y	G	G	R	R	R	R	N/A	G	R
Grover et al.[21]	R	Y	G	Y	R	R	R	Y	Y	G	G	R	R	R	R	N/A	G	R
Wood et al.[9]	R	Y	R	Y	R	R	G	Y	Y	G	G	R	R	R	R	N/A	G	R
Berrettini et al.[28]	R	Y	R	Y	R	R	G	Y	Y	G	G	R	R	R	R	N/A	G	R
Hathaway et al. (updated in Yoshikawa and Hirsch)[23,24]	R	R	G	N/A	R	R	G	Y	Y	G	G	R	G	R	R	N/A	G	R
Sugimoto et al.[25]	R	R	G	N/A	R	R	R	Y	Y	G	G	R	R	R	R	N/A	G	R
Omichi et al.[22]	R	R	G	N/A	R	R	R	Y	Y	G	G	R	R	R	R	N/A	G	R
Nadol et al.[11]	R	R	R	N/A	R	R	G	Y	Y	G	G	R	R	R	R	N/A	G	R
Modest et al.[5]	G	Y	R	R	R	R	R	Y	Y	G	G	R	R	R	R	N/A	G	R
Sydlowski et al.[18]	G	G	R	Y	R	R	R	Y	Y	G	G	R	Y	R	R	N/A	G	R
Lee et al.[19]	R	Y	R	Y	R	R	R	Y	G	G	G	R	R	R	R	N/A	G	R
Bittencourt et al.[26]	R	Y	R	Y	R	R	G	Y	Y	G	G	R	R	R	R	N/A	G	R
Haferkamp et al.[27]	R	R	G	N/A	R	R	G	Y	Y	G	G	R	R	R	R	N/A	G	R
Vanat et al.[13]	R	R	G	N/A	R	R	G	Y	Y	G	G	R	R	R	R	N/A	G	R

Key

● = Yes (low risk of bias) [green]
● = No (high risk of bias) [red]
● = Unclear (unclear risk of bias) [yellow]
● = N/A [gray]

1) Were participants a representative sample selected from a relevant patient population?
2) Were the inclusion/exclusion criteria of participants clearly described?
3) Were participants entering the study at a similar point in their disease progression?
4) Was selection of patients consecutive?
5) Was data collection undertaken prospectively?
6) Were the groups comparable on demographic characteristics and clinical features?
7) Was the intervention (and comparison) clearly defined?
8) Was the intervention undertaken by someone experienced at performing the procedure?
9) Were the staff, place, and facilities where the patients were treated appropriate for performing the procedure?
10) Were any of the important outcomes considered (i.e. on clinical effectiveness, cost-effectiveness, or learning curves)?
11) Were objective outcome measures used, including satisfaction scale?
12) Was the assessment of main outcomes blind?
13) Was follow-up long enough (≥1 year) to detect important effects on outcomes of interest?
14) Was information provided on non-respondents, dropouts?
15) Were the characteristics of withdrawals/dropouts similar to those that completed the study and therefore unlikely to cause bias?
16) Was the length of follow-up similar between comparison groups?
17) Were the important prognostic factors identified?
18) Were the analyses adjusted for confounding factors?

which was owing to broken wires in the straight section of the electrode lead indicating mechanical fatigue [20]. He was successfully re-implanted in the ipsilateral ear a year after the original procedure without any compilations and benefited once again. The second patient that required re-implantation reported discharge from the surgical site 1 week postoperatively. Despite treatment with multiple courses of broad-spectrum antibiotics and multiple hospitalizations over the next 4 months, the device had to be explanted[20]. He was also successfully re-implanted in the ipsilateral ear a year after

the original procedure in spite of it being heavily sclerotic. The third patient with a re-implant suffered from device infection postoperatively and subsequently required re-implantation 4 months later[5]. Another re-implantation took place 3 years later when the device experienced hard failure. The third implant was successful and functioning at the 7-month follow-up.

All studies, except 1[24], presented preimplantation audiometric data, and all the patients had suffered from progressive SNHL.

Table 2. Study Characteristics

References	Year	Country	Study Type	Number of Patients	Number of Implants
Kim et al.[31]	2006	South Korea	Case report	1	1 (right)
Alshehabi et al.[20]	2019	Ireland	Case series	7	10 (2 right, 4 left, 1 bilateral, 2 re-implants)
Irving and Graham[12]	1996	USA	Case report	1	1 (right)
Nogueira and Meehan[32]	2012	UK	Case report	1	1 (left)
Ryan et al.[17]	2014	Canada	Case report	1	1 (left)
Grover et al.[21]	2011	UK	Case series	2	2 (1 right, 1 left)
Wood et al.[9]	2008	New Zealand	Case series	2	2 (1 right[9]
Berrettini et al.[28]	2012	Italy	Case series	3	3 (1 right, 2 left)
Hathaway et al. (updated in Yoshikawa and Hirsch)[23,24]	2006 (updated in 2010)	USA	Case report	1	1 (left)
Sugimoto et al.[25]	2011	Japan	Case report	1	1 (right)
Omichi et al.[22]	2016	Japan	Case report	1	1 (right)
Nadol et al.[11]	2011	USA	Case report	1	1 (right)
Modest et al.[5]	2015	USA	Case series	6	9 (2 right, 3 left, 1 bilateral, 2 re-implants)
Sydlowski et al.[18]	2009	USA	Case series	5	NR
Lee et al.[19]	2018	South Korea	Case series	1	NR
Bittencourt et al.[26]	2012	Brazil	Case series	2	2 (2 left)
Haferkamp et al.[27]	1999	Germany	Case report	1	1 (right)
Vanat et al.[13]	2010	UK	Case report	1	1 (left)

Table 3. Audiological Outcomes

Case	References	Age/Sex	SS Cause	Preoperative Hearing Evaluation	Implanted Device	Postoperative Hearing Evaluation	Follow-up
1	Kim et al.[31]	25/Male	Head trauma – white water rafting	PTA (R) = profound, PTA (L) = dead; ABR = bsent; eABR = aconsistent response present on right; OAE = absent; Speech = 0% in open set testing	Right, NucleusCI24 Contour Advance	Speech: = 76% open set sentence, 60% monosyllabic, 50% multisyllabic	NR
2	Alshehabi et al.[20]	48/Male	Head trauma – RTA aged 8	PTA (R) = dead, PTA (L) = profound; BKB = 8.6%	Left	6m: BKB = 96% (Q) 64.3% (N)	NR
3	Alshehabi et al.[20]	66/Female	None	PTA (R) = profound, PTA (L) = dead; BKB = 0%	Right	6m: BKB = 22% (Q) 0%(N)	6m
4	Alshehabi et al.[20]	48/Male	Head trauma – RTA aged 20	PTA (R) = dead, PTA (L) = dead; BKB = 0%	Left	6m: BKB = 0%	6m
5	Alshehabi et al.[20]	25/Male	Neurosurgical – shunt insertion aged 4 for cerebellar cyst; post-op pseudomeningocele	PTA (R) = profound, PTA (L) = profound; BKB = 13.5%	Left	6m: BKB = N/A	NR
6	Alshehabi et al.[20]	71/Male	None	PTA (R) = moderate-severe, PTA (L) = moderate-severe, Preoperative BKB = 0%	Left	6m: BKB = 0%	6m
7	Alshehabi et al.[20]	31/Female	Neurosurgical – ventriculoperitoneal shunt inserted aged 10	PTA (R) = profound, PTA (L) = profound, BKB = 0%	Right	6m: BKB = 100% (Q)	6m

Table 3. Audiological Outcomes (Continued)

Case	References	Age/Sex	SS Cause	Preoperative Hearing Evaluation	Implanted Device	Postoperative Hearing Evaluation	Follow-up
8 R	Alshehabi et al.[20]	55/Male	Neurosurgical – Excision of posterior fossa tumor plus adjuvant radiotherapy	PTA (R) = profound, PTA (L) = N/A, BKB = 0%	Right	6m: BKB = 0%	6m
8 L	Alshehabi et al.[20]	54/Male	Neurosurgical – Excision of posterior fossa tumor plus adjuvant radiotherapy	PTA (R) = profound, PTA (L) = profound, BKB = 0%	Left	6m: BKB = 0%	6m
9	Irving and Graham[12]	33/Female	Idiopathic	PTA (R) = profound (response to a 250 Hz tone at 70 dB HL but no response to frequencies higher than this), PTA (L) = dead; ABR = absent at 95 dB; OAE = absent; (R) Aided responses 50 dBA at 250 Hz, 100 dBA at 3 kHz; ECoG = absent at 100 db HL; Promontory = Right buzzing and ringing between 50-400 Hz, Left vibration then pain at 50 Hz; UCL-CUNY = no discrimination with her (R) ear aided	Right, Nucleus® multi-channel device	9m: Free field audiogram thresholds = 0.5 kHz-45 dB, 1.0 kHz-55 dB, 2.0 kHz-45 dB and 4 kHz-45 dB; UCL-CUNY = 0%; CID = 66% 24m: no indication of change	24m
10	Nogueira and Meehan[32]	57/Male	NR	PTA (R) = 110 dB HL, PTA (L) = 115 dB HL; ABR threshold (R) = 100 dB nHL, ABR threshold (L) = no response to 100 dB nHL; OAE = absent bilaterally; CUNY = 40%; BKB = 5%	Left, HiRes 90K device	24m: CUNY = 98%; BKB = 86%	24m
11	Ryan et al.[17]	60/Male	NR	PTA (R) = 92 dB HL, PTA (L) = 88 dB HL; ABR = no identifiable or replicable waveforms at 90 dB nHL for either ear; OAE = absent; CNC word = 4%, CNC Phoneme= 20%; AzBio Sentences = 5%; CID Sentences (Audio only) = 4%, CID Sentences (Audio + Visual) = 25%; ESP-pattern perception = 100%, ESP-spondee identification = 38%, ESP-monosyllabic identification = 38%	Left	11m: CNC word = 8%, CNC Phoneme = 36%; AZ Bio Sentences = 0%; CID Sentences (audio only) = 25%, CID Sentences (audio + visual) = 86%; ESP-pattern perception = 100%, ESP-spondee identification = 83%, ESP-monosyllabic identification= 83%	11m
12	Grover et al.[21]	56/Male	Head trauma – RTA in childhood	PTA = profound; Hearing Threshold (L) = 50 – 60 dB below 2 kHz and >90 dB in higher frequencies; BKB = 22%; Promontory (bilaterally) = 50 Hz at 1500 µA, 100 Hz at 1650 µA, 200 Hz at 1900 µA	Left, Clarion high-focus system	84m: Free Field Audiogram Thresholds = 30-40 dB from 0.25 – 4kHz, BKB = 84%	84m
13	Grover et al.[21]	54/Male	NR	Speech discrimination = 0%	Right	9m: No meaningful auditory stimulus, only whistling	9m
14	Wood et al.[9]	53/Male	Neurosurgical – aneurysm in the left	PTA = sloping mild to profound; ABR = absent; DP-OAE = absent;	NR, Nucleus Freedom Contour Advance	Switch on: HINT = AV 25% 3m: HINT = AA 14%,	12m

Table 3. Audiological Outcomes (Continued)

Case	References	Age/Sex	SS Cause	Preoperative Hearing Evaluation	Implanted Device	Postoperative Hearing Evaluation	Follow-up
			carotid artery	Speech: HINT AA 17%, AV 41%, VA 12%; CNC = AA 0%, AV 11%, VA 7%		AV 46% 4m: HINT = deterioration in hearing 12m: Speech discrimination = 0, nonauditory stimulation	
15	Wood et al.[9]	50/Male	Neurosurgical – radiotherapy aged 5 for midline cerebella astrocytoma	PTA = severe to profound; ABR = absent; Promontory (R) = 123 µA at 50 Hz	Right, Nucleus CI24 Contour Advance	Switch on: Aided thresholds = 25 – 40 dB across the range of frequencies; HINT = AA 19% , AV 77.3%; CNC = AA 0%, AV 60% 1w: no sound	9m
16	Berrettini et al.[28]	68/Male	Head trauma – head injury with a consequent subarachnoid hemorrhage	PTA = profound, ABR = absent; OAE = absent; Speech = aided 10% open set bisyllabic word; HINT = 0%	Right, Nucleus Contour Advanced	3m: Speech 70% open set AA disyllabic; HINT = 82% 24m: 90% open set AA disyllabic; HINT = 92%	24m
17	Berrettini et al.[28]	73/Male	Head trauma – temporal bone fracture	PTA (R) = dead, PTA (L) = 90 dB; ABR = absent; OAE = absent; Speech = Aided 5% open set bisyllabic word; HINT = 0%	Left, Nucleus Contour Advance	6m = 90% open set AA bisyllabic, HINT = 96% 36m: stable	36m
18	Berrettini et al.[28]	36/Male	Neurosurgical – left cerebella cystic astrocytoma aged 14	PTA (R) = ski slope, PTA (L) = dead; ABR = absent; OAE = absent; Speech = aided 10% open set bisyllabic word; HINT = 0%	Left, Nucleus Contour Advance	36m: Speech = 40% closed set disyllabic word	36m
19	Hathaway et al. (updated by Yoshikawa and Hirsch)[23,24]	54/Female	Head trauma – RTA aged 7; Hydrocephalus aged 41	PTA (R) = 98 dB, PTA (L) = 87 dB; Speech: HINT and live voice = 0%; Promontory = tactile response in right, elevated thresholds in left	Left, Nucleus CI24	15m — 60m: Speech Awareness Threshold = 24 dB; Speech Recognition Threshold = 34 dB, HINT = 71% 72m: Threshold = 26 dB; HINT = 25%	72m
20	Sugimoto et al.[25]	65/Female	Neurosurgical – V-P shunt for SAH aged 62	PTA (L) = 105 dB; ABR = absent; OAE = absent; Word recognition = 0% at 104 dB (monitored live voice)	Right, CI24RE (CA) implant	8m: Sentence scores = 96% AA	8m
21	Omichi et al.[22]	38/Male	Idiopathic	Audiogram (R) Hearing Level (dB):Frequency (Hz) for Bone Conduction= 60:250, 65:500, 75:1000, 75:1000, 65:4000, Hearing Level (dB):Frequency (Hz) for Air Conduction = 90:250, 110:500, 120:1000, 135:2000, 120:4000; ABR = absent; Speech discrimination using monosyllables = 0% at 80 dB HL; APHAB = 91% EC, 84.8% RV, 80.8% BN, 18.5% AV	Right, Nucleus®CI422	3m: Sound Field Threshold: Hearing Level (dB):Frequency (Hz) = 55:250, 45:500, 40:1000, 35:200 5m: APHAB =7 2.8% EC, 60.7% RV, 47.7% BN, 33.3% AV 0	5m
22	Nadol et al.[11]	51/Male	Neurosurgical – lumbar disk surgery	PTA (R) = profound, PTA (L) = dead ear; OAE = absent; Speech word discrimination = 0%	Right, Nucleus CI24	6m: CNC = 28%, Connected speech test sentences = 61%	6m

Table 3. Audiological Outcomes (Continued)

Case	References	Age/Sex	SS Cause	Preoperative Hearing Evaluation	Implanted Device	Postoperative Hearing Evaluation	Follow-up
23	Modest et al.[5]	42/Male	Neurosurgical	PTA = 75 dB; CNC = 44%; Speech discrimination (L) = 20%	Left	Threshold (mean, dB) = 16.25; CNC = 51%; AzBio = 70%	64m
24	Modest et al.[5]	53/Female	Head trauma	PTA = 87 dB; HINT = 30%; Speech discrimination (L) = 0%	Left	Threshold (mean, dB) = 32.5; CNC = 48%	11m
25	Modest et al.[5]	68/Male	Neurosurgical	PTA: 87 dB; HINT = 40%; CNC = 16%; AzBio = 24%	Left	Threshold (mean, dB) = 17.5; CNC = 64%; AzBio = 75%	13m
26	Modest et al.[5]	70/Female	Head trauma	PTA: 120 dB; HINT = 62%; CNC = 42%; AzBio = 25%; Speech Discrimination (L) = 70%	Right	Threshold (mean, dB) = 32.5; CNC = 8%	18m
27	Modest et al.[5]	70/Male	Head trauma	PTA: 95 dB; HINT = 10%; Speech discrimination = 0%	Right	Threshold (mean, dB) = 27.5; CNC = 48%	58m
28 L	Modest et al.[5]	11/Male	Idiopathic	PTA: 90 dB; CNC = 0%; Speech Discrimination = 4%	Left	Threshold (mean, dB) = 36.5; HINT = 92%; AzBio = 82%	3m
28 R	Modest et al.[5]	11/Male	Idiopathic	PTA: 90 dB; CNC = 0%' Speech Discrimination = 0%	Right	Threshold (mean, dB) = 35; HINT = 80%	64m
29	Sydlowski et al.[18]	NR	NR	NR	NR	CNC words = 8%, CNC phonemes = 16%; HINT = 11%	NR
30	Sydlowski et al.[18]	NR	NR	NR	NR	CNC words = 48%, CNC phonemes =74%; CID = 96%	NR
31	Sydlowski et al.[18]	NR	NR	NR	NR	CUNY = 39%	NR
32	Sydlowski et al.[18]	NR	NR	NR	NR	NR, Unable to complete speech testing	NR
33	Sydlowski et al.[18]	NR	NR	NR	NR	Overlearned Speech Randomization Test = 33%; Four-choice spondees = 75%; HINT = 2%	NR
34	Lee et al.[19]	52/Female	Neurosurgical – brain hemorrhage due to cavernous hemangioma	PTA (R) = 10 dB HL, PTA (L) = 60 dB HL; Audiograms: Frequency (Hz) : Air conduction thresholds (dB HL): Right = 250:8 , 500:8 , 1k:11 , 2k:17 , 3k:21 , 4k:21 , 8k: 42 – Left = 250:102 , 500:112 , 1k:115 , 2k:120 , 3k:120 , 4k:120 , 8k:110; Speech discrimination (R) = 100%, Speech discrimination (L) = 36%	NR	Open-set speech: sentence = 70%, mono-syllabic = 60%; multi-syllabic = 50%	NR
35	Bittencourt et al.[26]	62/Male	NR	PTA = severe-profound; Speech Perception (HA): Vowel recognition = 100%, Closed set sentence identification = 60%, Open set sentence recognition (in quiet) = 0%; ABR = absent; OAE = absent	Left, Nucleus 24 Contour device	4m: Speech Perception (HA): Vowel recognition = 67%, Closed set sentence identification = 40%, Open set sentence recognition (in quiet) = 0% 36m: Speech Perception (HA): Vowel recognition = 100%, Closed set sentence identification = 100%,	36m

Table 3. Audiological Outcomes (Continued)

Case	References	Age/Sex	SS Cause	Preoperative Hearing Evaluation	Implanted Device	Postoperative Hearing Evaluation	Follow-up
						Open set sentence recognition (in quiet) = 0%	
36	Bittencourt et al.[26]	39/Male	NR	PTA (L) = 70 dB; Speech Perception (HA): Vowel recognition = 60%, Closed set sentence identification = 30%, Open set sentence recognition (in quiet) = 0%; ABR = absent; OAE = absent	Left, Nucleus 24RE Contour Advance device	4m: Speech Perception (HA): Closed set sentence identification = 100%, Open set sentence recognition (in quiet) = 70%	6m
37	Haferkamp et al.[27]	44/Male	NR	ABR = absent; OAE = absent; communication with the patient was only possible via the wife or in writing	Right, Combi40 + type (Med-El)	2.5m = Freiburg language test without lip-reading: numbers = 90% understood, monosyllables = 60% understood; HSM sentence test: with lip reading = 88%, without lip reading = 65% 6m = reported subjectively about a further improvement in hearing, including communication on the phone, even with unknown persons	6m
38	Vanat et al.[13]	58/Male	Head trauma	eABR = absent	Left, Advanced Bionics HiRes 90K	6m = Aided Soundfield Thresholds: reverse sloping 60-75 dB between 0.25-6 kHz; Nonauditory stimulation	6m

PTA: Pure Tone Audiometry; ABR: Auditory Brainstem Response; eABR: Electrical Auditory Brainstem Response; OAE: Otoacoustic Emission; R: Right; L: Left; RTA: Road Traffic Accident; BKB: Bench-Kowal-Bamford Sentences; N/A: Not applicable/ Not available; NR: Not Reported/ Not specified; UCL-CUNY: University College London - City University of New York Sentences; CUNY: City University of New York Sentences; CID: Central Institute for the Deaf; CNC: Consonant-Nucleus-Consonant word lists; DP-OAE: Distortion product Otoacoustic Emissions; HINT: Hearing in Noise Testing; AV: Auditory-Visual; AA: Auditory Alone; VA: Visual Alone; APHAB: Abbreviated Profile of Hearing Aid Benefit; EC: Ease of communication; RV: Reverberation; BN: Background noise; AV: Aversiveness; m: months, ESP: Early Speech Perception.

Table 4. CI Benefits, complications and re-implantations

Case	References	Post-operative Initial Benefit	Complications	Re-implantation	Subjective Sustained Benefit from CI at last Follow-up [months]
1	Kim et al.[31]	Y	N	N	Y [NR]
2	Alshehabi et al.[20]	Y	Device Failure (mechanical fatigue)	Y (1y after original implantation, the patient was re-implanted on the ipsilateral side. The post-operative course was uncomplicated, and the patient once again enjoyed augmented audiological performance from his implant)	Y [NR]
3	Alshehabi et al.[20]	Y	N	N	Y [6m]
4	Alshehabi et al.[20]	N	N	N	N [6m]
5	Alshehabi et al.[20]	Y	Wound/device infection 1w post-op	Y (Just over 1y after original implantation, the patient was re-implanted on the ipsilateral side. At the time of re-implantation, the patient's cochlea was found to be heavily sclerotic. However, in spite of this a successful implantation was performed.)	Y [NR]
6	Alshehabi et al.[20]	N	N/A	N	N [6m]

Table 4. CI Benefits, complications and re-implantations (Continued)

Case	References	Post-operative Initial Benefit	Complications	Re-implantation	Subjective Sustained Benefit from CI at last Follow-up [months]
7	Alshehabi et al.[20]	Y	N	N	Y [6m]
8 R	Alshehabi et al.[20]	N/A	N	N	N [6m]
8 L	Alshehabi et al.[20]	N/A	N	N	N [6m]
9	Irving and Graham[12]	Y	N	N	Y [24m]
10	Nogueira and Meehan[32]	Y	N	N	Y [24m]
11	Ryan et al.[17]	Y	N	N	Y [11m]
12	Grover et al.[21]	Y	4m after implantation, he developed meningitis. Subsequent mapping sessions revealed a dysfunction of the four apical electrodes with a high current requirement for the remainder.	N	Y [84m]
13	Grover et al.[21]	N	Electrodes required extremely high currents	N	N [9m]
14	Wood et al.[9]	Y	N	N	N (progressive neural deterioration was the etiology of the hearing loss and ataxia) [12m]
15	Wood et al.[9]	Y	N	N	N (marked deterioration in his global functioning and cognitive abilities, dementia secondary to SS) [9m]
16	Berrettini et al.[28]	Y	N	N	Y [24m]
17	Berrettini et al.[28]	Y	N	N	Y [36m]
18	Berrettini et al.[28]	N	N	N	N [36m]
19	Hathaway et al. updated by Yoshikawa and Hirsch)[23,24]	Y	N	N	N (deterioration occurred at 6y after undergoing general decline) [72m]
20	Sugimoto et al.[25]	Y	N	N	Y [8m]
21	Omichi et al.[22]	Y	N	N	Y [5m]
22	Nadol et al.[11]	Y	N	N	Y [6m]
23	Modest et al.[5]	Y	0-4m: Device Infection 4m-36m = Hard failure	4m: Reimplantation 36m: Reimplantation	Y [64m]
24	Modest et al.[5]	Y	N	N	Y [11m]
25	Modest et al.[5]	Y	N	N	Y [13m]
26	Modest et al.[5]	Y	N	N	N (Advancement of initially stable mild dementia) [18m]
27	Modest et al.[5]	Y	N	N	N (New onset dementia at 18-24m) [58m]

Table 4. CI Benefits, complications and re-implantations (Continued)

Case	References	Post-operative Initial Benefit	Complications	Re-implantation	Subjective Sustained Benefit from CI at last Follow-up [months]
28 L	Modest et al.[5]	NR	N	N	N [3m]
28 R	Modest et al.[5]	Y	N	N	Y [64m]
29	Sydlowski et al.[18]	NR	NR	NR	NR [NR]
30	Sydlowski et al.[18]	NR	NR	NR	NR [NR]
31	Sydlowski et al.[18]	NR	NR	NR	NR [NR]
32	Sydlowski et al.[18]	N	NR	NR	N [NR]
33	Sydlowski et al.[18]	NR	NR	NR	NR [NR]
34	Lee et al.[19]	Y	N	N	Y [NR]
35	Bittencourt et al.[26]	N	N	N	Y [36m]
36	Bittencourt et al.[26]	Y	N	N	Y [6m]
37	Haferkamp et al.[27]	Y	N	N	Y [6m]
38	Vanat et al.[13]	N	N	N	N [6m]

Y: Yes; N: No; NR: Not Reported/ Not specified; N/A: Not applicable/ Not available; m: months; SS: Superficial Siderosis

Preimplantation speech perception scores were not available in 5 studies[12,13,19,20,27], and 2 studies did not report postimplant speech perception[13,22]. A range of speech measures were used including Bamford-Kowal-Bench (BKB) sentence testing, City University of New York (CUNY) sentences, Hearing in Noise Test (HINT), and Consonant-Nucleus-Consonant (CNC) word lists, combined with different follow-up times, and speech testing at different levels make comparison impossible. However, where recorded, the average maximum postop results compared with preop results are as follows: BKB average showed 39.16% improvement (ranging from 0% to 96%), CUNY average showed 39% improvement (ranging from 0%–98%), HINT average showed 66% improvement (ranging from 46%–96%), and CNC words showed 6.25% improvement (ranging from 8%–64%). Audiological outcomes are summarized in Table 3 and the benefits of CI, its complications, and re-implantations are summarized in Table 4.

DISCUSSION

Across the 19 studies included in our review, we identified 44 implants of which 22 (50%) showed sustained benefit at the last follow-up compared with 47% in Tyler et al.[2] and 59.26% in Modest et al.[5]. From the cases that reported benefit for any period of time (31 implants) and the follow-up period, the average time of benefit per implant in those who declined and those who did not was 22.5 months ranging from 4 months–84 months. The degree of hearing improvement is variable in this group of patients, and there are limited data about the long-term durability with the average follow-up being 21.97 months (range 3 months–84 months). Another interesting point raised by Nadol 2011 et al. [11] is that long-term follow-up may not always be possible because of the patient's ongoing health issues. This point is further amplified in Modest et al. [5], in which 2 cases died secondary to other causes at 11 months and 13 months postimplantation. Thus, along with monitoring the patient's audiological data, it is also imperative to measure disease progression as part of their ongoing multidisciplinary care as cognitive decline will affect their hearing performance.

Of the 44 implants, 9 (20.45%) showed initial benefit but then deteriorated with time (4 of which required re-implantation) compared with 13.33% in Tyler et al.[2] and 18.52% in Modest et al.[5] The rest of the 5 implants deteriorated because of the progressive nature of the disease. The patient in the study by Hathaway et al.[23] (updated in Yoshikawa and Hirsch[24]) had benefited for the first 6 years after implantation with a speech recognition threshold of 34 dB and 71% correct on HINT but then deteriorated to 26 dB and 25% after undergoing general decline. One of the patients in Wood et al.[9] reported a marked reduction in hearing after 4 months which coincided with a fall; however, it was ultimately due to progressive neural deterioration. The other patient in Wood et al.[9] reported deterioration to preimplantation levels just 1 week after implantation which was due to compromised adaptation to electrical stimulation, further investigation concluded that he had dementia secondary to SS. The other 2 patients reported in the study by Modest et al.[5] also had similar courses of decline after seeing initial benefit; the first had advancement of initially stable mild dementia, and the second had new onset dementia at 18–24 month postimplant.

Of the 44 implants, 13 (29.55%) failed to demonstrate improvement at any point in time compared with 40% implants in Tyler et al.[2] and 25.93% in Modest et al.[5] Of these implants, 4 were reported in a study by Alshehabi et al.[20] One case was reported in which the implant required extremely high currents for the electrodes and was still unable to produce any meaningful auditory stimulus[21]. In another patient, very high stimulation was need to reach adequate hearing sensation causing facial twitching; and therefore, the implant was deemed unsatisfactory[28]. Modest et al.[5] also reported an implant in the left ear that was not beneficial; however, the patient had a CI in the right ear which was successful and thus benefited overall. Sydlowski et al.[18] failed to provide preoperative data, and thus, we could not conclude which patient benefited. Using their descriptive analysis, we conclude that only 1 of the 5 patients was able to benefit,

achieving average speech recognition for both sentences and monosyllabic words. The last patient who did not benefit was reported by Vanat et al.[13] whose data were also very scarce.

Age, sex, and cause of SS can be predicting factors for the success of CI outcomes. Of the 31 implants that reported benefit for any period of time (from the data available), the average age of patients was 49.2 years, there were 23 men and 8 women, 10 were caused by head trauma and 12 were due to neurosurgical causes. Of the 13 implants that failed to demonstrate improvement at any point in time (from the data available), the average age of patients was 47 years, there were 8 men, 2 were caused by head trauma and 3 were due to neurosurgical causes. However, the dataset was too small to draw any conclusions; thus, these results should be seen as a correlation rather than a causation relationship.

The small number of cases identified may be explained by the low prevalence of SS cases. Another reason for the limited number of patients may be the progressive and ultimately fatal nature of SS, combined with the intensive rehabilitation program required for CI and variable success rates, many patients may choose not to proceed with implantation. Owing to the dominance of case reports and the small number of patients in the case series, there may be reporting bias with departments only publishing about patients on either end of the impact spectrum. Owing to the cohort of patients, the variation in preimplant and postimplant data, variable follow-up periods, and the lack of information on implant details make it difficult to draw a meaningful conclusion regarding the degree and duration of benefit of CI in patients with SS. These problems could be overcome through the mandatory implementation of an implantation recipients register. Hurdles such as funding, legal implications, and oversight are yet to be overcome; however, increase in digital records and interest in patient outcomes are positive signs into the advancement of such a database[29,30]. Likewise, a homogenous approach to publishing pre- and postimplantation data and follow-up period can help amalgamate a larger patient database and hence provide a more accurate reflection of CI in SS.

The site of the hearing pathway damage in the cochlear or retrocochlear area can be hard to define and will likely affect the hearing outcome following CI. One such tool that might help define this is the diagnostic auditory brainstem response (ABR) to look for delayed latencies or abnormal morphology. Of the 38 patients, 15 used ABR (all of which were recorded as absent) as a preoperative measure to determine auditory threshold, degree and type of hearing loss, and detect lesions in the auditory nerve and/or brainstem. Multiple studies support the use of ABR as a preoperative measure to confirm the integrity of the cochlear nerve and thus try to predict positive outcomes[13,28,31]. However, Dhooge et al.[8] reports a patient who despite having reproducible electrical ABR responses at elevated levels before the implant produced disappointing results. A total of 13 patients had otoacoustic emissions (OAE) as a preoperative investigation, all of whom showed absent results. Other recommended preoperative investigations that have not been utilized by any studies so far are electrocochleography (ECochG)[28] and MRI[32]. As 95% of the patients with SS suffer from hearing loss[12], we recommend periodic hearing assessments, such as PTA, speech perception tests, and tympanometry to enable hearing rehabilitation to be started as soon as possible. There may be a role for additional tests, such as ABR, OAE, ECochG, and MRI; however, given the material available in the published literature, it is not possible to advocate any one test or combination of tests, nor to suggest an optimal testing schedule.

Early diagnosis of SS with MRI and understanding the pathology behind SNHL is crucial for optimal management; however, as mentioned above, preimplant measures are imperfect prognostic factors, perhaps owing to the progressive and diverse course of the disease and lack of data. Therefore, education and having an open and honest communication with the patient is essential to establishing realistic expectations.

CONCLUSION

Of the 44 implants, 31 (70.45%) showed improved hearing outcomes following CI for SS at some point in time, and 22 implants (50%) had sustained benefit at the last follow-up. This supports previous numbers from Tyler et al.[2] and Modest et al.[5] It is difficult to predict the longevity of benefit because of the progressive nature of the disease or the patients in whom it might be beneficial as preoperative investigations are inadequate prognosticators. It is perhaps wise to teach potential candidates other useful communication skills such as lip reading, which will enable the patients to continue communicating, as visual communication methods before hearing is totally lost, understanding that there may be a cognitive decline as well as disease progression. Pre- and postimplantation counseling regarding the potential limited benefit and eventual parallel decline with the neurological disease are crucial with the patient and family to ensure realistic expectations, along with thorough audiometric investigations.

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