Original Investigation

Influence of Ossicular Chain Damage on Hearing After Chronic Otitis Media and Cholesteatoma Surgery
A Systematic Review and Meta-analysis

Erik F. Blom, Bsc; Marlise N. Gunning, Bsc; Nienke J. Kleinrensink, Bsc; Alexander S. H. J. Lokin, Bsc; Hanneke Bruijnzeel, MD; Adriana L. Smit, MD; Wilko Grolman, MD, PhD

IMPORTANCE Physicians should ideally be able to provide patients with chronic otitis media and/or cholesteatoma specific information about postoperative hearing outcome, based on their level of preoperative ossicular chain damage (OCD).

OBJECTIVE To identify the influence of preoperative OCD on hearing outcomes in patients after chronic otitis media and/or cholesteatoma surgery.

DATA SOURCES PubMed, EMBASE, and the Cochrane Library databases were systematically searched for available evidence, without any constraints, on December 13, 2014, for articles published between January 1, 1975, and December 13, 2014.

STUDY SELECTION We reviewed the literature for articles assessing the prognostic value of OCD on postoperative hearing outcome (air-bone gap [ABG] in decibels), using Austin-Kartush criteria or independent OCD classification systems. We assessed relevance and validity using a self-designed critical appraisal tool based on the Cochrane Collaboration's risk of bias tool.

DATA EXTRACTION Characteristics of study populations and postoperative ABGs in decibels were extracted from all included studies by 4 authors (E.F.B., M.N.G., N.J.K., A.S.H.J.L.).

RESULTS The tested hypothesis was formulated before data collection. Primary study outcome was defined as postoperative adult hearing outcomes after COM and/or cholesteatoma surgery defined as mean postoperative ABG. Our search yielded 5661 articles. Nine articles with high relevance were included. Pooled results of studies using the Austin-Kartush criteria showed a significant ($P < .001$) difference in mean ABG in favor of group B, when comparing group B (patients with malleus present, stapes absent; 11.1 [95% CI, 10.3-11.8] dB) to group C (patients with malleus absent, stapes present; 15.7 [95% CI, 14.6-16.7] dB) and group B to group D (patients with malleus absent, stapes absent; 16.5 [95% CI, 15.2-17.9] dB). Three studies using independent OCD classification criteria found no influence of stapes structure (intact stapes suprastructure, 13.5 [95% CI, 10.3-16.7], 15.1 [95% CI, 11.8-18.3], and 21.9 [95% CI, 15.0-28.8] dB vs absent stapes structure, 12.8 [95% CI, 9.5-16.1], 19.5 [95% CI, 14.9-24.1], and 30.2 [95% CI, 24.7-35.8] dB) on postoperative ABG. One study reported a significant ($P = .04$) difference in mean ABG between patients with present (18.9 [95% CI, 15.7-22.1] dB) and absent (24.4 [95% CI, 20.2-28.6] dB) malleus.

CONCLUSIONS AND RELEVANCE Pooled results of Austin-Kartush studies showed that in patients with COM, with or without cholesteatoma, the malleus status is a significant predictor of postoperative hearing outcome, independent of the stapes condition. Studies reporting on individual ossicle status supported this finding by showing that only malleus condition influenced postoperative hearing outcome. These findings are based on level IV evidence, which indicates the need for future high-level evidence studies.

JAMA Otolaryngol Head Neck Surg. 2015;141(11):974-982. doi:10.1001/jamaoto.2015.2269
Published online October 22, 2015.

Supplemental content at jamaotolaryngology.com

Author Affiliations: Department of Otorhinolaryngology–Head and Neck Surgery, University Medical Center Utrecht, Utrecht, the Netherlands (Blom, Gunning, Kleinrensink, Lokin, Bruijnzeel, Smit, Grolman); Brain Center Rudolf Magnus, Utrecht, the Netherlands (Bruijnzeel, Grolman).

Corresponding Author: Hanneke Bruijnzeel, MD, Department of Otolaryngology–Head and Neck Surgery, Utrecht Medical Center, Heidelberglaan 100, 3584 CX, Utrecht, the Netherlands (ent-research@umcutrecht.nl).

Chronic otitis media (COM) is a long-standing middle ear infection, with or without a tympanic membrane perforation.[1] Symptoms include painless otorrhea and conductive hearing loss.[2] Chronic otitis media can be divided into COM with and without cholesteatoma. Cholesteatomas consist of keratinizing squamous epithelium and can grow expansively in the middle ear, destroying surrounding middle ear structures.[3]

Both COM and cholesteatoma can cause ossicular chain damage (OCD). A COM study in Chinese patients showed OCD to occur in 54% of patients with cholesteatoma and in 11% of patients without cholesteatoma.[4] The incus is the ossicle most frequently affected by OCD.[5,6] The pathophysiological process of ossicular chain destruction is thought to be multifactorial and might result from a combination of ostitis, pressure necrosis, and enzyme-mediated lysis.[3-8]

Because of disruption of the ossicular chain, OCD can lead to conductive hearing loss. This is clinically reflected on the audiogram as a difference between bone and air conduction thresholds, termed an air-bone gap (ABG).[9] In 1971, Austin[6] defined OCD classification criteria to match the type of OCD with specific ossicular chain reconstruction techniques. Austin defined 4 groups (A-D) on the basis of presence or absence of the malleus handle and stapes arch.[6] Kartush extended the Austin[6] criteria by adding 3 groups: group 0 with intact malleus, incus, and stapes; group E, fixation of the malleus head; and group F, fixation of the stapes. The latter criteria were therefore renamed the Austin-Kartush criteria.[6,15] Since the development of the Austin-Kartush criteria,[6,15] other authors have applied their own classification systems. Damage to individual (parts of) ossicles is specified in these other systems; however, the status of the other ossicles is not specified.

The aim of this systematic review with meta-analysis was to identify the influence of the preoperative OCD level on postoperative hearing outcomes after COM and/or cholesteatoma surgery in adult patients. A larger postoperative ABG was expected in patients with extended preoperative OCD.

Methods

Search Strategy

A systematic search in the PubMed, EMBASE, and Cochrane Library databases was performed on December 13, 2014, for articles published between January 1, 1975, and December 13, 2014. Relevant synonyms for the search terms "chronic otitis media," "cholesteatoma," "hearing outcome," and "air-bone gap" were combined in 1 search syntax (eAppendix in the Supplement). Because of the prognostic nature of our search query, the determinant OCD was not included in the search syntax in order to avoid missing relevant studies.

Study Selection

Using ProQuest Refworks software, duplicates were removed. Four authors (E.F.B., M.N.G., N.J.K., A.S.H.J.L.) screened all retrieved articles individually on title and abstract, using predefined inclusion and exclusion criteria (**Figure**). Subsequently, full-text screening was performed by pairs of authors (E.F.B. and A.S.H.J.L., M.N.G. and N.J.K.). Studies evaluating the prognostic value of the preoperative OCD level in patients with COM with or without acquired cholesteatoma were included. Both studies using the Austin or Austin-Kartush criteria[6,15] and studies evaluating OCD using alternative classification systems were included. All authors who performed literature screening participated in the discussion leading to selection of articles for this systematic review. A cross-reference check was performed for all selected articles. Final inclusion of articles was decided with 1 additional independent author (H.B.).

The method of surgical ossicular chain reconstruction reported in studies can vary as a result of the type of identified OCD. Therefore, we did not select studies on the basis of the type of applied reconstruction and assumed all patients to have received optimal therapy. Only studies reporting original data were included.

Critical Appraisal

Four authors (E.F.B., M.N.G., N.J.K., A.S.H.J.L.) critically appraised the selected studies on relevance and validity (**Table 1**). Critical appraisal criteria were based on the Cochrane Collaboration tool for assessing risk of bias[36] (Table 1). To optimally select the available evidence, we allocated most value to the combination of the following relevance criteria: (1) exclusion of congenital cholesteatoma, (2) application of predefined OCD categories, and (3) outcome defined as mean postoperative ABG, preferably measured using the American Academy of Otolaryngology–Head and Neck Surgery (AAO-HNS) guidelines.[37] These criteria were used because congenital cholesteatomas are of different etiology, pathophysiologic characteristics, and behavior than acquired cholesteatomas.[38] Second, it was essential for OCD to be reported in a similar and categorical manner in order to compare results between studies. Finally, to pool hearing outcome data, postoperative ABGs had to be measured according to a similar protocol.

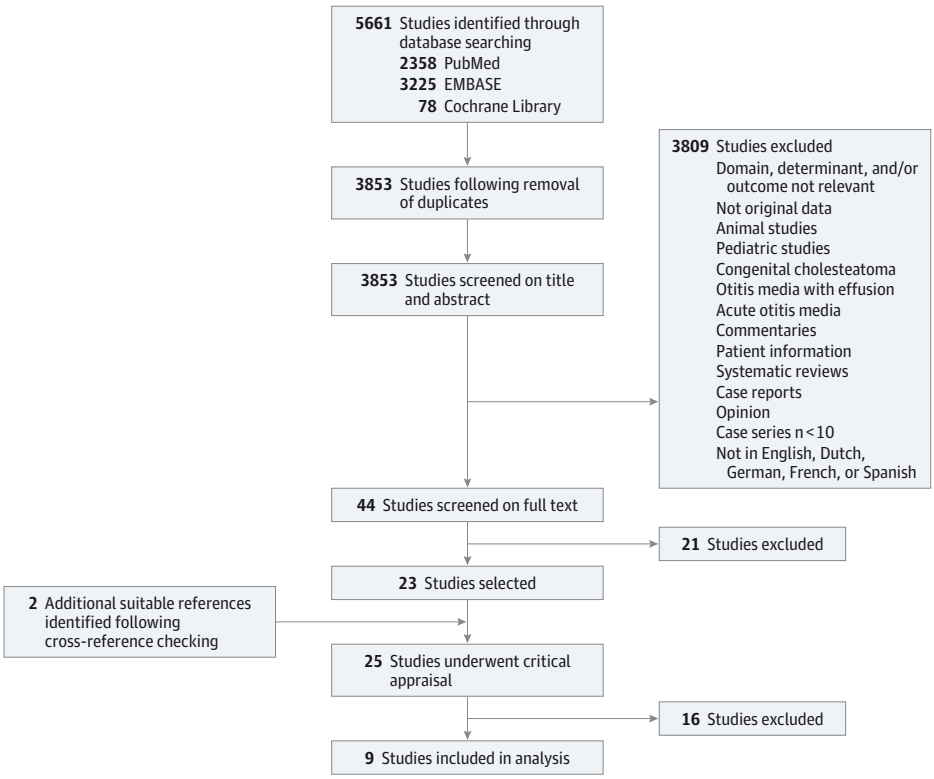
Each item of the critical appraisal was rated satisfactory, partly satisfactory, or unsatisfactory. In addition to rating individual relevance and validity criteria, we graded the overall relevance and validity using high, medium, and low ratings. High relevance represented 2 or more satisfactory ratings; medium, 1 satisfactory rating; and low relevance, no satisfactory rating. For the validity sections of the critical appraisal, at least 3 satisfactory ratings led to a high score, 2 satisfactory ratings represented a medium score, and 1 satisfactory rating, a low score (Table 1). We included studies that were graded as having high relevance.

Data Extraction

We compared results using mean postoperative ABGs in decibels as outcome measure. If studies did not report 95% confidence intervals (CIs), raw data were extracted from the original articles and 95% CIs were calculated using Graphpad Software 2015.[39] We assessed whether studies corrected for confounding variables in their analysis.

Data were pooled when hearing outcomes (ABGs) of patients with the same OCD subtype, after a comparable fol-

Figure. Flowchart of the Selection of Studies Reporting on the Prognostic Value of Ossicular Chain Damage on the Postoperative Hearing Outcome (Air-Bone Gap)



low-up period, were reported using standard deviations or 95% CIs. Heterogeneity tests between similar OCD subgroups from different studies were performed, both in Austin-Kartush groups[6,15] and study groups in which the status of individual ossicles was reported. Comprehensive Meta-analysis (Biostat; version 2.2.046) was used to perform heterogeneity analysis and pool results from studies when the I^2 was smaller than 50%.[40] To determine significance between reported data when no *P* values were provided within a study, we elected to calculate *P* values using an unpaired 2-tailed *t* test (Graphpad Software 2015).[39] Furthermore, we calculated *P* values to compare pooled results.

Results

Search Strategy and Study Selection

Our search yielded 5661 articles. After title and abstract screening, we considered 44 articles eligible for full-text assessment. Five authors were contacted to retrieve additional information; only one[41] replied. We identified 2 additional relevant articles by cross-reference checking of reference lists of selected articles (Figure).[11,25] We selected 25 articles for critical appraisal after full-text assessment (Figure). All selected studies were retrospective case series, except for 1 prospective case series[30] (Table 1).

Critical Appraisal

The relevance of evidence was high in 9 of 25 studies, so these were included in the present review (Table 1).[10-14,16-19] Sixteen articles were excluded because they had only a low to medium degree of relevance of evidence (Table 1).[20-35] Included studies carried a low to high risk of bias. Air-bone gaps were measured according to the frequencies recommended by the AAO-HNS.[37] Only 3 of 9 studies specified that patients with congenital cholesteatoma were excluded (Table 1).[10,12,14] One study included only older adolescent and adult patients (**Table 2**).[16] Six studies included both children and adults,[10,11,13,17-19] and the remaining 2 studies did not report the mean age of patients.[12,14] Dornhoffer and Gardner[11] and Stankovic[12] used the Austin criteria,[6] whereas Felek et al[13] used the Austin-Kartush criteria[15] (**Table 3**). The remaining 6 studies quantified OCD by applying individually developed classification systems (**Table 4**).[10,14,16-19] Vartiainen[10] did not report standard deviations of ABGs; therefore, outcome was scored as "not applicable." Although the study by Vartiainen[10] was included because of high domain relevance, we did refrain from including reported outcomes into our meta-analysis.

Seven included studies reported loss to follow-up.[10-14,16,17] Only 1 study reported the quantity and method of handling of missing data.[12] Blinding of the health care professional who performed determinant measurement was not reported in any of the included studies (Table 1). In none of the

Table 1. Critical Appraisal of Studies Reporting the Prognostic Value of Ossicular Chain Damage on Postoperative Air-Bone Gap

		Relevance							Validity						
			Domain									Standardization			
Source	Patients, No.	Study design	Disease[a]	Cholesteatoma[b]	Age[c]	Determinant[d]	Outcome[e]	Overall Relevance	Loss to Follow-up[f]	Missing Data[g]	Blinding of Audiologists	Determinant[h]	Outcome: Follow-up[i]	Outcome: Guidelines[j]	Overall Validity
Vartiainen,[10] 2000	136	RCS	+	+	−	−	NA	H	+	−	NR	NR	±	+	M
Dornhoffer and Gardner,[11] 2001	200	RCS	−	NR	−	+	+	H	+	NR	NR	±	−	+	M
Redaelli de Zinis,[16] 2008	50	RCS	±	NR	+	−	+	H	+	−	NR	NR	+	+	H
Stankovic,[12] 2008	758	RCS	±	+	−	+	+	H	+	+	NR	±	+	+	H
Bared and Angeli,[17] 2010	105	RCS	+	NR	−	−	+	H	+	NR	NR	±	−	+	M
Felek et al,[13] 2010	239	RCS	+	NR	−	+	+	H	+	NR	NR	−	−	+	M
Mardassi et al,[18] 2011	70	RCS	+	NR	−	−	+	H	NR	NR	NR	NR	−	+	L
Maeng and Kim,[14] 2011	2079	RCS	+	+	−	−	+	H	+	NR	NR	±	−	+	M
Lee et al,[19] 2014	52	RCS	+	NR	−	−	+	H	NR	NR	NR	±	−	+	L
Ragheb et al,[20] 1987	455	RCS	±	NR	NR	−	+	M	NR	NR	NR	−	±	[k]	L
Vartiainen and Nuutinen,[21] 1992	264	RCS	±	NR	NR	−	+	M	+	NR	NR	NR	+	+	H
Vartiainen and Nuutinen,[22] 1993	431	RCS	±	NR	NR	−	+	M	NR	NR	NR	NR	−	+	L
Albu et al,[23] 1998	544	RCS	−	NR	−	−	+	L	NR	NR	NR	±	±	+	L
Quaranta et al,[24] 2001	40	RCS	±	NR	−	−	+	M	+	NR	NR	NR	+	+	H
Martin and Harner,[25] 2004	68	RCS	+	NR	−	−	NA	L	+	NR	NR	±	−	+	M
Vassbotn et al,[26] 2005	73	RCS	−	NR	NR	−	+	L	−	+	NR	−	−	+	M
Schmerber et al,[27] 2006	111	RCS	−	−	−	−	+	L	+	NR	NR	NR	−	+	M
De Vos et al,[28] 2007	140	RCS	NR	NR	−	−	+	L	+	NR	NR	±	−	+	M
Truy et al,[29] 2007	168	RCS	±	NR	−	−	−	L	NR	NR	NR	−	−	+	L
Alaani and Raut,[30] 2010	97	PCS	NR	NR	−	−	+	L	+	NR	NR	±	+	+	H
Umit et al,[31] 2010	192	RCS	±	NR	−	−	+	M	+	NR	NR	NR	+	+	H
Iseri et al,[32] 2011	97	RCS	±	NR	−	−	+	M	NR	NR	NR	NR	NR	+	L
Quaranta et al,[33] 2011	57	RCS	±	NR	−	−	+	M	NR	NR	NR	±	−	+	L
Kalcioglu et al,[34] 2013	120	RCS	+	NR	−	−	NA	M	−	NR	NR	±	−	+	L
Querat et al,[35] 2014	128	RCS	±	NR	−	−	+	M	−	NR	NR	±	+	+	M

Abbreviations: AAO-HNS, American Academy of Otolaryngology–Head and Neck Surgery; H, high; L, low; M, medium; NA, not applicable; NR, not reported; OCD, ossicular chain damage; PCS, prospective case series; RCS, retrospective case series.

[a] Plus sign indicates chronic otitis media and cholesteatoma; plus/minus sign, chronic otitis media or cholesteatoma; minus sign, other diseases.

[b] Plus sign indicates acquired cholesteatoma only; minus sign, congenital cholesteatoma also included.

[c] Plus sign indicates inclusion of patients aged at least 18 y; minus sign, patients younger than 18 y included.

[d] Plus sign indicates OCD classified using Austin(-Kartush) criteria; plus/minus sign, OCD classified as damage or no damage for each ossicle separately, status of all ossicles reported; minus sign, OCD classified as damage or no damage for each ossicle separately, not all ossicle statuses reported or only partial ossicular replacement prosthesis/total ossicular replacement prosthesis mentioned.

[e] Plus sign indicates hearing outcome specified as air-bone gap after reconstruction of the ossicular chain when needed; minus sign, hearing outcome specified as conductive hearing loss only or outcome specified otherwise.

[f] Plus sign and minus sign indicate loss to follow-up of less than 20% and more than 20%, respectively.

[g] Plus sign indicates that missing data were mentioned and quantified in the study, with method of handling described, or there were no missing data; minus sign indicates that missing data were mentioned in the study, but the method of handling them was not described.

[h] Plus sign indicates that OCD was measured by the same surgeon in a uniform and protocolled manner; plus/minus sign, OCD was measured by the same surgeon in a nonuniform and protocolled manner; minus sign, determinant was measured by different surgeons.

[i] Plus sign indicates follow-up time of hearing outcome measurement of at least 1 y, with a standardized time of measurement; plus/minus sign indicates follow-up time of hearing outcome measurement at least 3 y or nonstandardized time of measurement (range includes only follow-up ≥1 y); minus sign indicates follow-up time for hearing outcome of less than 1 y.

[j] Plus sign indicates that hearing outcome was measured according to the frequencies of the AAO-HNS Committee on Hearing and Equilibrium guidelines.

[k] The AAO-HNS 1995 guidelines were not in use at the time of publication; however, outcome was measured according to similar rules.

Table 2. Characteristics of Studies Reporting on the Prognostic Value of Ossicular Chain Damage on Postoperative Hearing Outcome (Air-Bone Gap)

Source	Age, Mean (range), y	Diagnosis	Surgical Procedure	Prosthesis Used	Follow-up, Mean (Range), mo	Audiometry, mo[a]
Vartiainen,[10] 2000	<10 to >60	COM NR, C+	CWD	Autologous ossicles/bone	62.4 (24-108)	NR
Dornhoffer and Gardner,[11] 2001	29.3 (4-73)	COM+, C+, other diseases[b]	PORP or TORP, with CWU/CWD if indicated	Dornhoffer PORP or TORP	11.6 (4-60)	NR
Redaelli de Zinis,[16] 2008	(17-78)	COM+, C+	Primary or revision CWD	Hydroxyapatite or titanium	12	12
Stankovic,[12] 2008	NR	COM NR, C+	Adults: CWU/CWD Children: CWU/CWD	Autologous bone/cartilage	<12	NR
Bared and Angeli,[17] 2010	38 (6-77)	COM+, C+/C−	CWU/CWD or second-look	Autologous bone/cartilage, titanium and hydroxyapatite	19 (3-84)	3, 6, 12 (and annually)
Felek et al,[13] 2010	31 (8-67)	COM+, C+/C−	CWU with ossiculoplasty	Autologous or allograft bone/cartilage, glass ionomer cement, polyethylene, hydroxyapatite	26.8 (6-96)	6
Mardassi et al,[18] 2011	43 (5-77)	COM+, C+	PORP or TORP, with CWU if indicated	Titanium Vario	9.8 (3-36)	NR
Maeng and Kim,[14] 2012	NR	COM+, C+/C−	Tympanoplasty with mastoidectomy	NR	(6-256)	NR
Lee et al,[19] 2014	51 (14-76)	COM+, C+/C−	Mastoidectomy, with tympanoplasty if indicated	Hydroxyapatite and titanium	NR	6

Abbreviations: C−, cholesteatoma absent; C+, cholesteatoma present; COM+, chronic otitis media present; CWD, canal wall down; CWU, canal wall up; NR, not reported; PORP, partial ossicular replacement prosthesis; TORP, total ossicular replacement prosthesis.

[a] Time when audiometry was performed postoperatively.

[b] Other diseases includes atelectasis and incus dislocation after temporal bone fracture, among others.

included studies did an independent surgeon classify the OCD type; neither was OCD assessment performed in a uniform and protocol-prescribed manner in any of the included studies.

Patient Characteristics

Extracted data on patient characteristics are presented in Table 2. In 4 studies, patients with COM with and without cholesteatoma were included.[13,14,17,19] Two studies only included patients with both COM and cholesteatoma.[16,18] Two studies included patients with cholesteatoma but did not define COM status.[10,12] One study included patients with cholesteatoma but, in addition, included patients (28.0%) with various surgical indications (eg, conductive hearing loss, atelectasis, perforation).[11] Hearing outcomes, reported in the latter study, were sufficiently homogenous in comparison with the other 8 studies to justify inclusion in the present review. Included patients received different surgical treatments between and within studies (Table 2). Two studies applied the canal-wall-down procedure,[10,16] whereas 1 study used the canal-wall-up procedure.[13] Two studies applied a mastoidectomy, combined with tympanoplasty when this was indicated.[14,19] Various prosthesis types were used to reconstruct the ossicular chain (Table 2). One study did not specify the type of prosthesis that was applied.[14] Mean duration of follow-up between included studies ranged from 9.8 to 62.4 months postoperatively. Three studies measured hearing outcome at 6 months postoperatively,[13,17,19] 2 studies at 12 months postoperatively,[16,17] and the remaining 5 studies did not report when audiometry was performed.[10-12,14,18]

Hearing Results

Hearing results of studies using Austin-Kartush criteria[6,15] are displayed in Table 3. Two studies[10,14] included patients without OCD who could be categorized into Austin-Kartush[6,15] group 0. Only 2 studies[11,12] reported results in all 4 Austin[6] groups (Table 3). Hearing results of studies reporting OCD of individual (parts of) ossicles are presented in Table 4.

Pooled results of patients in Austin-Kartush[6,15] groups B (I^2 = 0%), C (I^2 = 46.7%), and D (I^2 = 0%) showed significant (P < .001) differences in favor of group B when mean ABGs of group B (11.1 [95% CI, 10.3-11.8] dB) were compared with group C (15.7 [95% CI, 14.6-16.7] dB; P < .001) and group D (16.5 [95% CI, 15.2-17.9] dB; P < .001) (see eFigure in the Supplement). In case of an absent malleus, presence or absence of the stapes did not influence postoperative hearing outcomes (Austin-Kartush[6,15] group C vs D; P = .32).

Mean ABG results for patients in Austin-Kartush[6,15] group A ranged from 8.3 (95% CI, 7.9-8.7) to 13.8 (95% CI, 12.8-14.8) dB[11-13] and were too heterogeneous for pooling (I^2 = 98.1%). Pooling of Austin-Kartush[6,15] group 0 results was not possible because 1 study[10] did not provide standard deviations. Studies including patients in Austin-Kartush[6,15] group 0 reported mean ABGs of 11.4 (95% CI, 10.7-12.1)[14] and 16.2 (95% CI, not reported) dB.[10] Only 1 study reported mean ABG results on patients in Austin-Kartush[6,15] group E: 20.1 (95% CI, 16.9-23.3) dB.[13]

Hearing outcomes reported in studies that assessed the influence of individual ossicle damage are presented in Table 4. We were able to pool results of patients with an absent malleus handle (I^2 = 0%): mean postoperative ABG was 25.1 (95% CI, 21.9-28.4) dB (see eFigure, D in the Supplement). Heterogeneity between different studies reporting on all other categories was too high to pool results (I^2 range = 72.7%-95.0%). Studies including patients with an intact malleus handle reported mean ABGs of 18.9 (95% CI, 15.7-22.1)[17] and 27.0 (95% CI, 20.2-33.8) dB.[16] Bared and Angeli[17] reported a significant

Table 3. Results of Studies Reporting on the Prognostic Value of Ossicular Chain Damage on Postoperative Hearing Outcome (Air-Bone Gap) by the Austin-Kartush Criteria

Source	Austin-Kartush Classification Group[a]						
	0	A	B	C	D	E	F
Vartiainen,[10] 2000							
Ears, No.	19						
Air-bone gap, mean (95% CI), dB	16.2 (NR)						
Dornhoffer and Gardner,[11] 2001							
Ears, No.		80	46	34	40		
Air-bone gap, mean (95% CI), dB		11.5 (10.1-12.9)	11.9 (10.1-13.7)	17.7 (14.2-21.2)	16.3 (13.2-19.4)		
Stankovic,[12] 2008							
Ears, No.		331	200	110	117		
Air-bone gap, mean (95% CI), dB		8.3 (7.9-8.7)	10.9 (10.1-11.7)	15.0 (13.7-16.3)	16.6 (15.1-18.1)		
Felek et al,[13] 2010							
Ears, No.		198		64		31	
Air-bone gap, mean (95% CI), dB		13.8 (12.8-14.8)		17.1 (14.7-19.5)		20.1 (16.9-23.3)	
Maeng and Kim,[14] 2012							
Ears, No.	1236						
Air-bone gap, mean (95% CI), dB	11.4 (10.7-12.1)						
Overall (all studies)							
Ears, No.			246	208	157		
Air-bone gap, mean (95% CI), dB	NA	NA	11.1 (10.3-11.8)[b,c]	15.7 (14.6-16.7)[c]	16.5 (15.2-17.9)[b]	NA	NA

Abbreviation: NA, not applicable; NR, not reported.

[a] Group O indicates an intact malleus, incus, and stapes; group A refers to a present malleus and stapes; group B refers to a present malleus and an absent stapes; group C indicates an absent malleus and present stapes; group D refers to an absent malleus and stapes; group E represents a malleus head fixation; and group F indicates stapes fixation.

[b] $P < .001$ (calculated by us) between pooled results in groups B and D.

[c] $P < .001$ (calculated by us) between the pooled results in groups B and C.

difference between patients with intact and absent malleus handle: mean ABG, 18.9 (95% CI, 15.7-22.1) vs 24.4 (95% CI, 20.2-28.6) dB ($P = .04$) (Table 4). However, Redaelli de Zinis[16] found a nonsignificant difference between similar groups.

Only 1 study reported the influence on hearing outcome of the destruction of the incus: in these patients, a mean ABG of 22.6 (95% CI, 20.8-24.5) dB was reported.[14]

Two studies reported outcomes when the stapes was present: mean ABG of 20.8 (95% CI, 17.6-24.0)[17] and 24.5 (95% CI, not reported) dB.[10] Two studies reported results when only the stapes footplate was present preoperatively: 30.9 (95% CI, 28.7-33.1)[14] and 33.8 (95% CI, not reported) dB.[10] Incudo-stapedial joint destruction was reported in only 1 study with a mean ABG of 22.1 (95% CI, 20.4-23.9) dB.[14] All 3 studies reporting on the presence or absence of the stapes suprastructure showed no significant difference in hearing outcomes between groups.[16,18,19] Mean ABG outcomes for studies including patients with presence of the stapes suprastructure were 13.5 (95% CI, 10.3-16.7),[19] 15.1 (95% CI, 11.8-18.3),[18] and 21.9 (95% CI, 15.0-28.8) dB.[16] When the stapes structure was absent, mean ABG results were 12.8 (95% CI, 9.5-16.1),[19] 19.5 (95% CI, 14.9-24.1),[18] and 30.2 (95% CI, 24.7-35.8) dB[16] (Table 4).

Preoperative intact chain integrity resulted in mean ABGs of 11.4 (95% CI, 10.6-12.1)[14] and 16.2 (95% CI, not reported) dB.[10] A disrupted ossicular chain resulted in mean ABGs of 20.5 (95% CI, not reported)[10] and 25.0 (95% CI, 23.9-26.0) dB.[14] Maeng and Kim[14] found a statistically significant difference between the latter 2 groups ($P < .05$).

Four authors performed multivariate linear regression analyses to assess the prognostic value of the malleus status (Bared and Angeli,[17] Dornhoffer and Gardner,[11] and Mardassi et al[18]) or presence of OCD (Maeng and Kim[14]) in relation to the postoperative hearing results (ABG).

Table 4. Results of Studies Reporting on the Prognostic Value of Ossicular Chain Damage in Individual (Parts of) Ossicles on Postoperative Hearing Outcome (Air-Bone Gap)

Source	Malleus		Incus	Stapes				Other		
	Handle Intact	Handle Absent	Long Process Destruction	Present/ Intact	Supra-structure Absent[a]	Supra-structure Intact[b]	Footplate Only	Incudo-Stapedial Joint Destruction	Chain Integrity Intact	Chain Integrity Disrupted
Vartiainen,[10] 2000										
Patients, No.				64			31		19	13
Air-bone gap, mean (95% CI), dB				24.5 (NR)			33.8 (NR)		16.2 (NR)	20.5 (NR)
Redaelli de Zinis,[16] 2008										
Patients, No.	24	26			28	22				
Air-bone gap, mean (95% CI), dB	27.0 (20.2-33.8)	26.1 (20.2-32.0)			30.2 (24.7-35.8)	21.9 (15.0-28.8)				
P value	.75				.05					
Bared and Angeli,[17] 2010										
Patients, No.	64	36		63	42					
Air-bone gap, mean (95% CI), dB	18.9 (15.7-22.1)	24.4 (20.2-28.6)		20.8 (17.6-24.0)	20.9 (16.8-25.0)					
P value	.04[c]			.95[c]						
Mardassi et al,[18] 2001										
Patients, No.					33	37				
Air-bone gap, mean (95% CI), dB					19.5 (14.9-24.1)	15.1 (11.8-18.3)				
P value					.11					
Maeng and Kim,[14] 2012										
Patients, No.			251		137		164	291	1236	843
Air-bone gap, mean (95% CI), dB			22.6 (20.8-24.5)		30.1 (26.7-33.6)		30.9 (28.7-33.1)	22.1 (20.4-23.9)	11.4 (10.6-12.1)	25.0 (23.9-26.0)
P value									<.05	
Lee et al,[19] 2014										
Patients, No.					16	36				
Air-bone gap, mean (95% CI), dB					12.8 (9.5-16.1)	13.5 (10.3-16.7)				
P value					.80					
All studies										
Patients, No.		62								
Air-bone gap, mean (95% CI), dB	NA	25.1 (21.7-28.5)	NA	NA	NA	NA	NA	NA	NA	NA

Abbreviations: NA, not applicable; NR, not reported (and calculation not possible on the basis of available data); NS, not significant.

[a] Stapes suprastructure absent = total ossicular replacement prosthesis.

[b] Stapes suprastructure intact = partial ossicular replacement prosthesis.

[c] Indicates *P* values from original studies; all other *P* values were calculated by us.

Discussion

The aim of this systematic review and meta-analysis was to identify whether the level of OCD could predict the postoperative hearing outcome (ABG) in patients with COM with and without cholesteatoma. The 9 included studies had high relevance and carried a low to high risk of bias. To our knowledge, this is the first systematic review to report the prognostic value of OCD on postoperative hearing prognosis, expressed in ABG.

Pooled results of studies using the Austin-Kartush criteria[11-13] showed that malleus presence predicted a significantly ($P < .05$) better postoperative hearing outcome compared with an absent malleus, independent of the condition of the stapes. This finding is supported by the individual results of Stankovic[12] and Felek et al,[13] who showed significant ($P < .05$) better hearing outcomes in patients in Austin-Kartush group A (intact malleus and stapes) than in those in Austin-Kartush group C (absent malleus, intact stapes). Furthermore, Stankovic[12] showed a significant difference in hear-

ing outcome between patients in Austin[6] groups A and D (absent malleus and stapes), in favor of group A.

Regarding studies reporting on status of separate ossicles, Bared and Angeli[17] reported a significant (P = .04) difference between patients in whom the malleus handle was absent or present. All 3 studies reporting on absence or presence of the stapes suprastructure found no significant hearing outcome difference between these groups.[16,18,19] These findings further stress the importance of the effect of malleus handle status on hearing outcomes, independent of the stapes status, or parts of the stapes.

No studies reported on incus presence or absence. In addition, only 2 studies[10,14] reported the results of patients in Austin-Kartush[6,15] group 0. These studies did not report on other Austin-Kartush[6,15] groups. Drawing conclusions on the influence of incus status, as a predictor of hearing outcome, is therefore not possible in this review.

Yung and Vowler[41] defined a postoperative ABG of less than 20 dB as success and an ABG of greater than 20 dB as surgical failure in a multivariate analysis of patients who had undergone surgery for COM. Similar to our findings, the status of the malleus showed to be a significant predictor of postoperative hearing outcome (P = .02). In addition, the presence of the stapes did not significantly influence their multivariate model. This finding is in line with our results, indicating the significance of malleus status, independent of the condition of the stapes. Wilson et al[42] applied dichotomous outcome definitions similar to those of Yung and Vowler[41] in a study of patients with cholesteatoma. Their results showed that both the malleus and stapes condition were significant (P < .05) predictors of long-term hearing outcome. This finding contradicts our findings. A possible explanation might be that the mean follow-up by Wilson et al[42] was 63.6 months, whereas the mean follow-up in our review ranged between 9.8 and 62.4 months. Furthermore, Wilson et al[42] only included patients treated with a canal-wall-up procedure, whereas in our review several surgical procedures were assessed. Inclusion of more aggressive surgical approaches, such as canal-wall-down mastoidectomy, may result in larger postoperative conductive hearing loss levels.

This review has several strengths and limitations. Four authors (E.F.B., M.N.G., N.J.K., A.S.H.J.L.) independently screened articles and performed critical appraisal, which improved objectivity and uniformity. We decided not to include studies that reported ABG in bins (most frequently reported as <20 or >20 dB) because this disables data pooling and decreases the applicability in daily practice: informing patients about their likely exact postoperative hearing results. Studies by Yung and Vowler,[41] Glasscock,[43] and Wilson et al[42] were thus excluded.

Although heterogeneity analysis allowed a meta-analysis to be performed, several remarks have to be made about differences among included studies in patient characteristics, surgical techniques used, and outcome measurement. Included studies evaluated patients with COM with or without cholesteatoma. However, Dornhoffer and Gardner[11] included 56 patients (28.0%) with diagnoses of other diseases, such as atelectasis, incus necrosis, traumatic incus dislocation, and malleus head fixation (Table 2). No specific analysis was performed for each of these abnormalities, which could have influenced hearing outcomes and pooled results. Nonetheless, this study had high overall relevance and a medium risk of bias and was therefore still included in pooling of the results. In addition, inclusion was supported by a sufficient outcome of the heterogeneity test (I^2 < 50%).

Second, patients received different types of ossicular reconstructive surgery within and between studies (Table 2). None of the included studies required correction for the type of delineated surgery. Each operative approach may result in different postoperative conductive hearing loss,[12] which should be taken into account when results are interpreted.

Third, differences in method and timing of outcome measurement could have influenced the measured hearing outcome. Five of the 9 studies did not report when postoperative audiometry was performed.[10-12,14,18] In addition, the range in reported follow-up times among studies was 3 to 256 months, and some studies did not report it (Table 2). The moment when postoperative hearing outcome was assessed could have influenced the results: this could have been too soon after surgery in several studies and could explain differences in results between studies. Four studies even excluded patients who were lost to follow-up, possibly inducing selection bias.[10,25,39,40]

Fourth, 5 studies did not perform multiple regression analysis to assess possible confounders.[10,12,13,16,19] Therefore, the association between OCD and postoperative hearing results could have been influenced by other factors. Four studies did carry out multiple regression analysis, but it must be noted that the performed analysis only accounts for the reported confounders.[11,14,17,18]

Finally, all included studies were retrospective case series, which marks the need for future prospective studies with a higher level of evidence. For future studies, we recommend the use of the Austin-Kartush criteria[6,15] to measure OCD and the AAO-HNS guidelines in audiology for reporting hearing outcomes at standardized intervals to maximize comparability of results.

Conclusions

This meta-analysis enables health care professionals to predict postoperative hearing results (ABG) in patients with COM, with or without a cholesteatoma, defined according to the specific preoperative OCD level. Results showed that in patients with COM with cholesteatoma, OCD was associated with a significantly worse hearing outcome compared with an intact ossicular chain. The condition of the malleus was the most important predictor of postoperative hearing outcome (ABG), independent of the condition of the stapes. Our recommendations are based on retrospective case series, which indicates the need for future studies with a higher level of evidence.

ARTICLE INFORMATION

Submitted for Publication: May 16, 2015; final revision received July 13, 2015; accepted July 28, 2015.

Published Online: October 22, 2015. doi:10.1001/jamaoto.2015.2269.

Author Contributions: Dr Bruijnzeel had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. Mr Blom, Mss Gunning and Kleinrensink, and Mr Lokin served as co–first authors, each with equal contribution to the manuscript.

Study concept and design: Blom, Gunning, Kleinrensink, Lokin, Bruijnzeel, Smit, Grolman.
Acquisition, analysis, or interpretation of data: Blom, Gunning, Kleinrensink, Lokin, Bruijnzeel, Smit.
Drafting of the manuscript: Blom, Gunning, Kleinrensink, Lokin, Bruijnzeel, Smit.
Critical revision of the manuscript for important intellectual content: All authors.
Statistical analysis: Blom, Gunning, Kleinrensink, Lokin.
Administrative, technical, or material support: Bruijnzeel.
Study supervision: Bruijnzeel, Smit, Grolman.

Conflict of Interest Disclosures: None reported.

Funding/Support: Prof Grolman receives unrestricted grants from Cochlear, MED-EL, and Advanced Bionics.

Role of the Funder/Sponsor: The funders had no role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; preparation, review, or approval of the manuscript; and decision to submit the manuscript for publication.

REFERENCES

1. Lerut B, Pfammatter A, Moons J, Linder T. Functional correlations of tympanic membrane perforation size. *Otol Neurotol*. 2012;33(3):379-386.

2. Miyamoto RT. Otitis media (chronic). Merck Manual website. http://www.merckmanuals.com/professional/ear-nose-and-throat-disorders/middle-ear-and-tympanic-membrane-disorders/otitis-media-chronic?qt=chronic%20otitis%20media&alt=sh. Updated 2013. Accessed November 14, 2014.

3. van de Heyning P, Mulder JS. Aandoeningen van het trommelvlies en het middenoor. In: Huizing EH, Snow GB, de Vries N, Graamans K, van de Heyning P, eds. *Keel-Neus-Oorheelkunde en Hoofd-Halschirurgie.* 2nd ed. Houten, Netherlands: Bohn Stafleu van Loghum; 2009:67-69.

4. Jeng FC, Tsai MH, Brown CJ. Relationship of preoperative findings and ossicular discontinuity in chronic otitis media. *Otol Neurotol*. 2003;24(1):29-32.

5. Kurihara A, Toshima M, Yuasa R, Takasaka T. Bone destruction mechanisms in chronic otitis media with cholesteatoma: specific production by cholesteatoma tissue in culture of bone-resorbing activity attributable to interleukin-1 alpha. *Ann Otol Rhinol Laryngol*. 1991;100(12):989-998.

6. Austin DF. Ossicular reconstruction. *Arch Otolaryngol*. 1971;94(6):525-535.

7. Chole RA, McGinn MD, Tinling SP. Pressure-induced bone resorption in the middle ear. *Ann Otol Rhinol Laryngol*. 1985;94(2, pt 1):165-170.

8. Yetiser S, Satar B, Aydin N. Expression of epidermal growth factor, tumor necrosis factor-alpha, and interleukin-1alpha in chronic otitis media with or without cholesteatoma. *Otol Neurotol*. 2002;23(5):647-652.

9. Desloovere C, van Zanten GA. Onderzoek van het oor en het gehoor. In: Huizing EH, Snow GB, de Vries N, Graamans K, van de Heyning P, eds. *Keel-Neus-Oorheelkunde en Hoofd-Halschirurgie.* 2nd ed. Houten, Netherlands: Bohn Stafleu van Loghum; 2009:35.

10. Vartiainen E. Ten-year results of canal wall down mastoidectomy for acquired cholesteatoma. *Auris Nasus Larynx*. 2000;27(3):227-229.

11. Dornhoffer JL, Gardner E. Prognostic factors in ossiculoplasty: a statistical staging system. *Otol Neurotol*. 2001;22(3):299-304.

12. Stankovic MD. Audiologic results of surgery for cholesteatoma: short- and long-term follow-up of influential factors. *Otol Neurotol*. 2008;29(7):933-940.

13. Felek SA, Celik H, Islam A, Elhan AH, Demirci M, Samim E. Type 2 ossiculoplasty: prognostic determination of hearing results by middle ear risk index. *Am J Otolaryngol*. 2010;31(5):325-331.

14. Maeng JW, Kim HJ. Effects of middle ear lesions on pre and postoperative hearing outcomes in patients with chronic otitis media. *Korean J Audiol*. 2012;16(1):18-26.

15. Kartush JM. Ossicular chain reconstruction: capitulum to malleus. *Otolaryngol Clin North Am*. 1994;27(4):689-715.

16. Redaelli de Zinis LO. Titanium vs hydroxyapatite ossiculoplasty in canal wall down mastoidectomy. *Arch Otolaryngol Head Neck Surg*. 2008;134(12):1283-1287.

17. Bared A, Angeli SI. Malleus handle: determinant of success in ossiculoplasty. *Am J Otolaryngol*. 2010;31(4):235-240.

18. Mardassi A, Deveze A, Sanjuan M, et al. Titanium ossicular chain replacement prostheses: prognostic factors and preliminary functional results. *Eur Ann Otorhinolaryngol Head Neck Dis*. 2011;128(2):53-58.

19. Lee JI, Yoo SH, Lee CW, Song CI, Yoo MH, Park HJ. Short-term hearing results using ossicular replacement prostheses of hydroxyapatite versus titanium. *Eur Arch Otorhinolaryngol*. 2015;272(10):2731-2735.

20. Ragheb SM, Gantz BJ, McCabe BF. Hearing results after cholesteatoma surgery: the Iowa experience. *Laryngoscope*. 1987;97(11):1254-1263.

21. Vartiainen E, Nuutinen J. Long-term hearing results of one-stage tympanoplasty for chronic otitis media. *Eur Arch Otorhinolaryngol*. 1992;249(6):329-331.

22. Vartiainen E, Nuutinen J. Long-term results of surgical treatment in different cholesteatoma types. *Am J Otol*. 1993;14(5):507-511.

23. Albu S, Babighian G, Trabalzini F. Prognostic factors in tympanoplasty. *Am J Otol*. 1998;19(2):136-140.

24. Quaranta N, Fernandez-Vega Feijoo S, Piazza F, Zini C. Closed tympanoplasty in cholesteatoma surgery: long-term (10 years) hearing results using cartilage ossiculoplasty. *Eur Arch Otorhinolaryngol*. 2001;258(1):20-24.

25. Martin AD, Harner SG. Ossicular reconstruction with titanium prosthesis. *Laryngoscope*. 2004;114(1):61-64.

26. Vassbotn FS, Møller P, Silvola J. Short-term results using Kurz titanium ossicular implants. *Eur Arch Otorhinolaryngol*. 2007;264(1):21-25.

27. Schmerber S, Troussier J, Dumas G, Lavieille JP, Nguyen DQ. Hearing results with the titanium ossicular replacement prostheses. *Eur Arch Otorhinolaryngol*. 2006;263(4):347-354.

28. De Vos C, Gersdorff M, Gérard JM. Prognostic factors in ossiculoplasty. *Otol Neurotol*. 2007;28(1):61-67.

29. Truy E, Naiman AN, Pavillon C, Abedipour D, Lina-Granade G, Rabilloud M. Hydroxyapatite versus titanium ossiculoplasty. *Otol Neurotol*. 2007;28(4):492-498.

30. Alaani A, Raut VV. Kurz titanium prosthesis ossiculoplasty—follow-up statistical analysis of factors affecting one year hearing results. *Auris Nasus Larynx*. 2010;37(2):150-154.

31. Umit T, Ozgur Y, Bilgehan G, Volkan SA, Sezim SA. Results of primary ossiculoplasty and prognostic factors in canal wall-down tympanoplasty. *J Craniofac Surg*. 2010;21(2):407-410.

32. Iseri M, Ustundag E, Ulubil A, Ozturk M, Bircan O. Synchronous ossiculoplasty with titanium prosthesis during canal wall down surgery for advanced cholesteatoma: anatomical and hearing outcomes. *J Laryngol Otol*. 2012;126(2):131-135.

33. Quaranta N, Zizzi S, Quaranta A. Hearing results using titanium ossicular replacement prosthesis in intact canal wall tympanoplasty for cholesteatoma. *Acta Otolaryngol*. 2011;131(1):36-40.

34. Kalcioglu MT, Tan M, Fleerakkers J. The use of bone cement for ossicular chain defects. *Eur Arch Otorhinolaryngol*. 2013;270(11):2849-2855.

35. Quérat C, Martin C, Prades JM, Richard C. Canal wall up tympanoplasty for cholesteatoma with intact stapes: comparison of hearing results between cartilage and PORP on stapes and impact of malleus removal and total reinforcement of the tympanic membrane by cartilage. *Eur Ann Otorhinolaryngol Head Neck Dis*. 2014;131(4):211-216.

36. Higgins JPT, Green S, eds. *Cochrane Handbook for Systematic Reviews of Interventions.* 5.1.0 ed. London, England: Cochrane Collaboration; 2011.

37. American Academy of Otolaryngology–Head and Neck Surgery Foundation. Committee on hearing and equilibrium guidelines for the evaluation of results of treatment of conductive hearing loss. *Otolaryngol Head Neck Surg*. 1995;113(3):186-187.

38. Olszewska E, Wagner M, Bernal-Sprekelsen M, et al. Etiopathogenesis of cholesteatoma. *Eur Arch Otorhinolaryngol*. 2004;261(1):6-24.

39. Graphpad Software: Unpaired T-test and confidence interval calculator. http://www.graphpad.com/quickcalcs. Updated 2015. Accessed September 26, 2015.

40. Higgins JP, Thompson SG, Deeks JJ, Altman DG. Measuring inconsistency in meta-analyses. *BMJ*. 2003;327(7414):557-560.

41. Yung M, Vowler SL. Long-term results in ossiculoplasty: an analysis of prognostic factors. *Otol Neurotol*. 2006;27(6):874-881.

42. Wilson KF, London NR, Shelton C. Tympanoplasty with intact canal wall mastoidectomy for cholesteatoma: long-term hearing outcomes. *Laryngoscope*. 2013;123(12):3168-3171.

43. Glasscock ME III. Ossicular chain reconstruction. *Laryngoscope*. 1976;86(2):211-221.