Original Article

Facial canal dehiscence in cholesteatoma and co-existing surgical findings: a systematic review and meta-analysis

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Background: Dehiscence of the facial canal is an important consideration in cholesteatoma surgery. This study aims to determine the prevalence of intra-operative finding of facial canal dehiscence (FCD) in patients with cholesteatoma who underwent middle ear surgery, and to investigate surgical findings that are associated with FCD.

Methods: The systematic review and meta-analysis was conducted in accordance with the PRSIMA guidelines using the following databases: PubMed, MEDLINE, Embase, and Cochrane Library. The search was completed on 25th October 2021. The selection criteria included studies published in the English literature between 1981–2021 that reported FCD incidence diagnosed intraoperatively during middle ear surgery for cholesteatomatous disease. The pooled prevalence was calculated using a generic inverse variance model with random effects analysis. The Joanna Briggs Institute (JBI) checklist for prevalence studies was used for quality assessment of included articles.

Results: Twenty-seven articles representing 5,848 cases were included for quantitative analysis, with two outliers identified on leave-one-out analysis and excluded. The pooled prevalence of FCD was found to be 24.67% [95% confidence interval (CI): 21.51–27.84%]. The overwhelming majority of dehiscence occurred in the tympanic segment of the facial canal with a pooled prevalence of 93.79% (95% CI: 92.06–95.52%). The prevalence of FCD was comparatively higher in adult, 27.20% (95% CI: 22.18–32.22%) versus paediatric, 15.33% (95% CI: 8.86–21.79%) patients, in revision, 33.54% (95% CI: 27.30–39.78%) versus primary, 24.47% (95% CI: 21.27–27.66%) surgery, and in studies with smaller sample size <300 patients, 26.60% (95% CI: 22.12–31.07%) versus larger sample size, 21.94% (95% CI: 18.14–25.74%). A meta-analysis of twelve studies showed that the presence of a lateral semicircular canal fistula increased the likelihood of FCD with an OR 6.45 (95% CI: 4.07–10.23).

Conclusions: FCD is a common finding during cholesteatoma surgery with increased likelihood in adult and revision cases. Studies have reported an association with other destructive findings to middle ear structures, including the scutum, ossicles, and semicircular canals, highlighting the importance of preoperative clinical and radiographic evaluation to assess the risk of dehiscence.

Keywords: Facial nerve; fallopian canal; facial canal dehiscence; cholesteatoma; middle ear disease

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Introduction

The facial nerve is an important anatomic structure in middle ear surgery and travels within the Z-shaped bony facial canal between the internal acoustic meatus and stylomastoid foramen. Facial canal dehiscence (FCD) is defined as erosion of or discontinuity in the bony structure of the facial canal, allowing for communication between the facial nerve and the middle ear cavity. It may be present in the normal population as a congenital anatomic variant due to incomplete ossification during intra-uterine life and early childhood (1). Pathological dehiscence can be secondary to inflammatory, infectious, or neoplastic processes that affect the middle ear, as well as previous trauma or surgical instrumentation. The tympanic segment of the facial canal is the most common site of FCD, with dehiscence generally occurring in proximity to the oval window (2). The clinical significance of FCD in cholesteatoma is its association with more extensive disease and increased incidence of further destructive findings intra-operatively—this includes labyrinthine fistula and erosion of the ossicular chain, scutum, external auditory canal, and tegmen tympani (3). The importance to the surgeon is that dehiscence of the facial canal increases risk of iatrogenic injury to the facial nerve during middle ear surgery as it lacks a protective bony covering. The gold standard for clinical diagnosis of FCD is intraoperative examination using a microscope. Pre-operative imaging with dedicated computed tomography (CT) petrous temporal bones is useful in predicting FCD and assists surgical planning. It facilitates assessment of the course of the intratemporal facial nerve and, in cases where FCD is not obvious, aids detection of other cautionary erosive findings that should raise suspicion for dehiscence being encountered intraoperatively (4). The objective of this systematic review and meta-analysis is to determine the pooled prevalence of FCD in patients who underwent cholesteatoma surgery and discuss coexisting surgical findings that correlate with FCD. We present this article in accordance with the PRISMA reporting checklist (available at https://www.theajo.com/article/view/10.21037/ajo-23-1/rc) (*Figure 1*).

Methods

Study design and search strategy

A systematic review and meta-analysis were performed in accordance with the PRISMA guidelines. An a priori study protocol was not lodged. A literature review was performed on 25th October 2021 using the following databases, including studies from their earliest date of cataloguing: PubMed (which includes MEDLINE data), MEDLINE, Embase, and Cochrane Library. Two main search domains were used, which were combined with the Boolean operator "And", whilst search terms contained within each domain were combined with the Boolean operator "Or". The keywords within the first search domain were "cholesteatoma", and within the second search domain were "facial nerve", "facial canal", "fallopian canal", and "dehiscence". The reference lists of all included articles were searched by the authors to identify further articles that met the inclusion criteria. The Google Scholar database was utilised to supplement the literature review.

Approval from the ethics institutional review board was not required for this study as it is a systematic review and meta-analysis of published literature and it does not require collection of patient data.

Study selection and eligibility criteria

Two authors (S Ananthapadmanabhan, G Budiono) independently assessed the titles, abstracts, and full-text articles of potentially eligible studies using pre-determined inclusion criteria. Studies that reported the incidence of FCD in patients with cholesteatoma were included, in which dehiscence was diagnosed by intraoperative examination. All age groups including studies reporting on adult, paediatric, or combined populations were included. Both prospective and retrospective studies were included. Exclusion criteria included case reports, unpublished studies, studies without surgical confirmation of FCD, and studies with mixed pathology data sets in which the cholesteatoma cohort could not be isolated. Studies that focussed solely on medially invasive and extensive cholesteatomas or

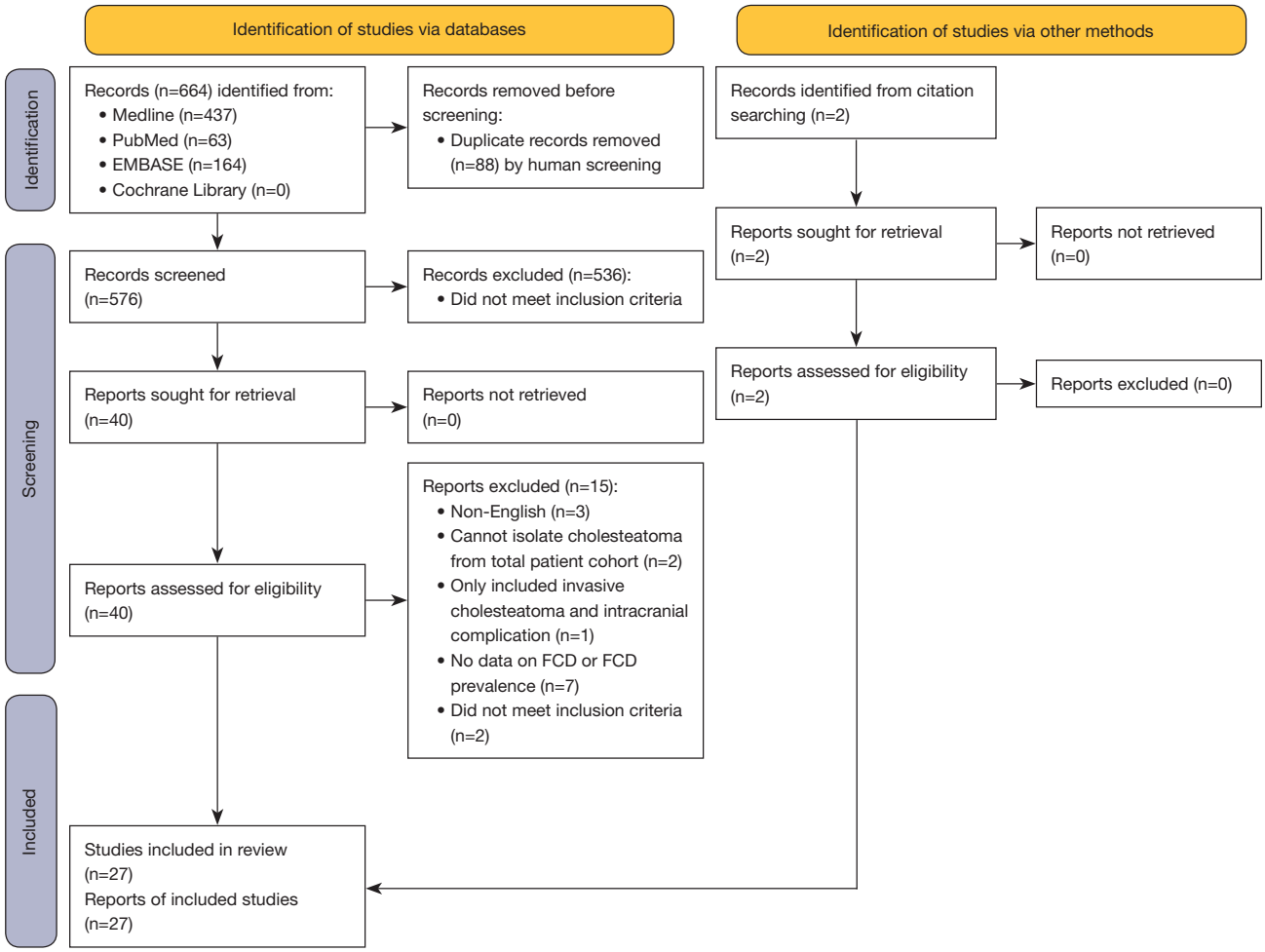

Figure 1 Results of the literature search with PRISMA flow diagram showing the study selection for the meta-analysis. PRISMA, Preferred Reporting Items for Systematic reviews and Meta-Analyses; FCD, facial canal dehiscence.

cholesteatomas with intracranial complications were excluded as the incidence of FCD would be grossly inflated. The search was limited to the English language and articles published between 1981–2021.

Titles and abstracts were first independently assessed by the authors (S Ananthapadmanabhan, G Budiono) to screen for eligible studies by applying the inclusion and exclusion criteria described. To maximise inclusivity in the early stage of the systematic review, we included all studies deemed eligible by at least one author. A full-text manuscript of screened articles was then conducted to determine final eligibility for inclusion in the meta-analysis. If disagreements arose, the input of a senior colleague (V Sivapathasingam) was sought until consensus was reached.

Quality assessment

Quality assessment of the included articles was performed using validated, standardized tools. The methodological quality of the included studies was critically appraised using the Joanna Briggs Institute (JBI) Checklist for Prevalence Studies (5) and the quality of the research findings were graded using the Oxford Centre for Evidence-Based Medicine Levels of Evidence (6). The JBI checklist is a validated tool consisting of nine items and scored from 0 to 9, with one point awarded for each item achieved. A high risk of bias was attributed to studies that achieved 5 of less points. The appraisal was performed by two authors (S Ananthapadmanabhan, G Budiono) and if there were discrepancies in identifying the study as high or low risk,

the opinion of a senior colleague was consulted. Studies were awarded an evidence grade of 1b for prospective cohort studies or 2b for retrospective cohort studies.

Data extraction

The following data were extracted independently by the authors (S Ananthapadmanabhan, G Budiono) from each study, where reported: total participants, inclusion and exclusion criteria for patient selection, method of diagnosing FCD, incidence of FCD, segment of FCD, whether the operation was primary or revision surgery, proportion of adult and paediatric patients, and the presence of other erosive surgical findings was extracted. The proportion of FCD was calculated from the number of cases with surgical diagnosis of dehiscence of the facial canal divided by the total number of total patients with cholesteatoma who underwent surgery.

Statistical analysis

Statistical analysis was performed using commercially available software STATA version 17.0 (StataCorp LLC, Texas, USA) and Review Manager (Version 5.4, The Cochrane Collaboration, 2020). A P value <0.05 was considered statistically significant and confidence intervals of 95% were used. Forest plots for pooled prevalence were created using the generic inverse variance method with random-effects model. Standard error (SE) to calculate pooled prevalence was calculated using the formula SE = square root of $p \times (1 - p)/n$, where p is the prevalence of FCD within a sample size of n patients. Publication bias was investigated using a funnel plot with Egger's regression and Begg's rank test. Leave-one-out (LOO) sensitivity analysis was used to identify studies that disproportionately influenced the pooled prevalence. A subgroup analysis was performed where possible to determine possible sources of heterogeneity in the dataset. Heterogeneity was determined using the τ^2, I^2, and Q statistic. Meta-regression analysis was performed to determine if moderator variables contributed significantly to data heterogeneity. The sub-groups were divided based on sample size, adults versus paediatric cohort, and primary versus revision surgery. Forest plots of the pooled odds ratio (OR) was calculated using the Mantel-Haenszel test.

Results

Characteristics of included studies

The database search yielded 664 studies from MEDLINE (n=437), PubMed (n=63), Embase (n=164), and Cochrane Library (n=0) and 88 duplicate studies were removed. The PRISMA flow chart for study selection is shown in *Figure 1*. Twenty-seven articles, including 23 retrospective (3,4,7-27) and 4 prospective (28-31) studies, were suitable for quantitative analysis in the meta-analysis, comprising 5,848 patients with 1,449 instances of FCD. A summary of the characteristics of the included studies is provided in *Tables 1,2*.

Bias assessment of included studies

A funnel plot (*Figure 2*) demonstrated an asymmetrical distribution of effect sizes with most studies plotted outside the 95% confidence interval (CI) limit lines. Egger and Begg's test for publication bias was Z=3.47, P=0.0005 and Z=2.46, P=0.014 respectively. A small-study effect was evident. Publication bias is not an expected finding as prevalence studies do not report significance levels or compare variables. It is likely that the asymmetric distribution of the funnel plot is related to the heterogeneity amongst included studies. Methodological diversity related to patient selection and surgery performed was likely the main source of bias leading to moderator variables that created inconsistencies between effect sizes across studies. Each study had specific inclusion and exclusion criteria, detailed in *Table 2*. Examples of confounding factors that could affect FCD incidence include cohort size, proportion of adult and paediatric patients, primary or revision surgery, location and size of cholesteatoma, and type of middle ear surgery performed. In cases where adequate data with respect to these moderator variables was available, a sub-group analysis was performed. Given the overall heterogeneity, presence of moderator variables, and inter-study variability in patient selection, a random-effects model was used in the meta-analysis.

A LOO sensitivity analysis (Figure S1) identified two studies by Choi *et al.* (10) and TanrivermiŞ Sayit *et al.* (22) as outliers, which were excluded from the remainder of the analysis. The pooled prevalence changed from 27.21% (95% CI: 22.90–31.51%) to 24.67% (95% CI: 21.51–27.84%) (*Figure 3*).

Table 1 Characteristics of included studies

Author, year	Country/region	N	Study type	JBI and Oxford score	Diagnostic method to detect FCD in surgery
Arias-Marzán, 2019 (7)	Spain	57	Retrospective	5, 2b	Intra-operative microscopic examination
Baklacı, 2020 (3)	Turkey	151	Retrospective	6, 2b	Intra-operative microscopic examination and palpation
Bayazit, 2002 (8)	Turkey	49	Retrospective	5, 2b	Intra-operative microscopic examination
Bizakis, 2006 (9)	Greece	201	Retrospective	4, 2b	Intra-operative examination
Bulğurcu, 2017 (27)	Turkey	245	Retrospective	4, 2b	Intra-operative microscopic examination and palpation
Choi, 2014 (10)	South Korea	64	Retrospective	4, 2b	Intra-operative microscopic examination and facial nerve monitor
Di Martino, 2005 (28)	Germany	160	Prospective	4, 1b	Intra-operative examination
Faramarzi, 2017 (11)	Iran	499	Retrospective	6, 2b	Intra-operative microscopic examination and palpation
Genc, 2014 (12)	Turkey	93	Retrospective	4, 2b	Intra-operative microscopic examination and palpation
Gulotta, Visconti, 2020 (13)	Italy	527	Retrospective	6, 2b	Intra-operative microscopic examination and palpation
Gulotta, Pace, 2020 (14)	Italy	469	Retrospective	6, 2b	Intra-operative microscopic examination and palpation
Gülüstan, 2014 (15)	Turkey	334	Retrospective	4, 2b	Intra-operative examination
Jaswal, 2008 (29)	India	80	Prospective	2, 1b	Intra-operative examination
Kalcioglu, 2019 (16)	Turkey	318	Retrospective	6, 2b	Intra-operative microscopic examination
Lin, 2004 (17)	Taiwan region	117	Retrospective	7, 2b	Intra-operative microscopic examination
Magliulo, 2011 (18)	Italy	336	Retrospective	6, 2b	Intra-operative microscopic examination and palpation
Magliulo, 2018 (19)	Italy	80	Retrospective	5, 2b	Intra-operative microscopic examination and palpation
Moody, 2007 (30)	USA	416	Prospective	4, 1b	Intra-operative examination
Ocak, 2016 (20)	Austria	50	Retrospective	4, 2b	Intra-operative examination
Ozbek, 2009 (21)	Turkey	118	Retrospective	5, 2b	Intra-operative microscopic examination and palpation
Sahin, 2020, (4)	Turkey	186	Retrospective	6, 2b	Intra-operative microscopic examination and palpation
TanrivermiŞ Sayit, 2019 (22)	Turkey	113	Retrospective	4, 2b	Intra-operative examination
Selesnick, 2001 (23)	USA	67	Retrospective	4, 2b	Intra-operative examination and palpation
Shinnabe, October 2014 (24)	Japan	310	Retrospective	4, 2b	Intra-operative examination and palpation
Shinnabe, September 2014 (25)	Japan	252	Retrospective	4, 2b	Intra-operative examination and palpation
Trinidade, 2014 (31)	UK	401	Prospective	6, 1b	Intra-operative microscopic examination and palpation
Wang, 2006 (26)	Taiwan region	155	Retrospective	7, 2b	Intra-operative microscopic examination

JBI, joanna briggs institute; FCD, facial canal dehiscence.

Table 2 Patient baseline demographics, patient inclusion and exclusion criteria, and risk of bias in selection criteria

Author, year	N	Mean age (years)	Male, n (%)	Paediatric, n (%)	Revision, n (%)	Patient selection	FCD, n (%)
Arias-Marzán, 2019 (7)	57	41	36 (63.2)	7 (12.2)	18 (31.6)	Inclusion: adults and children with primary or revision surgery for cholesteatoma Exclusion: nil Bias risk: high—does not specify type of cholesteatoma surgery performed	17 (29.8)
Baklacı, 2020 (3)	151	42	85 (56.3)	–	0 (0)	Inclusion: adults and children with COM with acquired cholesteatoma with primary tympanomastoidectomy Exclusion: history of previous COM surgery, temporal bone trauma, congenital cholesteatoma, other middle ear pathology, lack of preoperative HRCT scans, or congenital inner ear anomalies Bias risk: high—excludes revision cases and tympanoplasty without mastoidectomy (i.e., small pars tensa cholesteatomas)	51 (33.8)
Bayazit, 2002 (8)	49	–	–	–	–	Inclusion: mixed cohort of 219 adult and children with middle ear surgery for chronic otitis media; 49/219 had cholesteatoma Exclusion: nil Bias risk: low—operations performed by single surgeon and does not exclude based on revision status or surgery type	9 (18.4)
Bizakis, 2006 (9)	201	43	121 (60.2)	44 (21.9)	–	Inclusion: adults and children with primary or revision canal wall down mastoidectomy for cholesteatoma Exclusion: canal wall up mastoidectomy Bias risk: high—only includes CWD mastoid surgery which may overestimate FCD incidence	31 (15.4)
Bulğurcu, 2017 (27)	245	–	–	–	0 (0)	Inclusion: adults and children with primary tympanomastoidectomy Exclusion: temporal bone fracture, temporal bone neoplasm, tympanoplasty without mastoidectomy, revision surgery, stapes surgery, explorative tympanotomy Bias risk: high—excludes revision surgery and non-mastoid cholesteatoma surgery	49 (20.0)
Choi 2014, (10)	64	54	29 (45.3)	–	–	Inclusion: mixed cohort of 212 adults and children with chronic otitis media undergoing primary tympanomastoid surgery; 64/212 had cholesteatoma Exclusion: previous otologic surgery, preoperative facial nerve palsy, temporal bone fracture or tumour Bias risk: high—excludes revision cases and tympanoplasty without mastoidectomy (i.e., small pars tensa cholesteatomas)	41 (64.1)

Table 2 (*continued*)

Table 2 (*continued*)

Author, year	N	Mean age (years)	Male, n (%)	Paediatric, n (%)	Revision, n (%)	Patient selection	FCD, n (%)
Di Martino, 2005 (28)	160	–	–	–	74 (46.3)	Inclusion: comparative study of 357 routine primary or revision middle ear operations, of which 160 had cholesteatoma, versus 300 temporal bone specimens from 150 autopsies Exclusion: history of facial palsy, malformations of facial nerve, temporal bone tumours Bias risk: low—included different types of cholesteatoma surgery	14 (8.8)
Faramarzi, 2017 (11)	499	30	211 (49.0)	–	99 (19.8)	Inclusion: 431 adult and children representing 499 ears undergoing primary or revision CWU or CWD tympanomastoidectomy for cholesteatoma Exclusion: inadequate documentation, tympanic surgery only Bias risk: high—excludes tympanic surgery without mastoidectomy	90 (18.0)
Genc, 2014 (12)	93	–	–	–	0	Inclusion: mixed cohort of 154 patients with chronic otitis media, with 93 having cholesteatoma, undergoing primary mastoidectomy Exclusion: previous tympanoplasty or tympanotomy, mastoidectomy, stapes surgery Bias risk: high—excludes revision surgery and non-mastoidectomy surgery	30 (32.3)
Gulotta, Visconti, 2020 (13)	527	–	301 (57.1)	57 (10.8)	–	Inclusion: adult and children with CWU or CWD mastoidectomy for acquired cholesteatoma Exclusion: congenital cholesteatoma, non CWU/CWD surgery Bias risk: high—excludes non mastoidectomy surgery	125 (23.7)
Gulotta, Pace, 2020 (14)	469	47	267 (56.9)	0	96 (20.5)	Inclusion: adult patients with primary or revision mastoidectomy for cholesteatoma Exclusion: children Bias risk: high—excludes non mastoidectomy surgery and paediatric patients	121 (25.8)
Gülüstan, 2014 (15)	334	–	192 (57.5)	61 (18.3)	23 (6.9)	Inclusion: adult and children with primary or revision CWU or CWD mastoidectomy for cholesteatoma Exclusion: non CWU/CWD surgery Bias risk: high—excludes non mastoidectomy surgery	79 (23.7)
Jaswal, 2008 (29)	80	–	–	–	–	Inclusion: mixed cohort of 146 patients with chronic otitis media, with 80 having cholesteatoma, undergoing radical or modified radical mastoidectomy Exclusion: non mastoid surgery Bias risk: high—excludes non mastoidectomy surgery	18 (22.5)

Table 2 (*continued*)

Table 2 (*continued*)

Author, year	N	Mean age (years)	Male, n (%)	Paediatric, n (%)	Revision, n (%)	Patient selection	FCD, n (%)
Kalcioglu, 2019 (16)	318	–	–	–	–	Inclusion: mixed cohort of 372 adult and children undergoing CWU or CWD mastoidectomy for chronic otitis media, with 318 having cholesteatoma Exclusion: non mastoid surgery Bias risk: high—excludes non mastoidectomy surgery	37 (11.6)
Lin, 2004 (17)	117	–	49 (41.9)	–	8 (6.8)	Inclusion: adult and children with primary or revision tympanoplasty with or without mastoidectomy for middle ear cholesteatoma Exclusion: nil Bias risk: low—included different surgery types	39 (33.3)
Magliulo, 2011 (18)	336	–	188 (56.0)	38 (11.3)	78 (23.2)	Inclusion: adult and children undergoing primary or revision CWU or CWD mastoidectomy for cholesteatoma Exclusion: non mastoid surgery Bias risk: high—excludes non mastoidectomy surgery	91 (27.1)
Magliulo, 2018 (19)	80	40	48 (60.0)	0	0	Inclusion: adult patients with attic cholesteatoma who underwent primary microscopic ear surgery and transcanal exclusive endoscopic ear surgery Exclusion: mesotympanum cholesteatoma, wide mastoid involvement, revision surgery Bias risk: high—excludes non-attic cholesteatoma and revision cases	16 (20.0)
Moody, 2007 (30)	416	–	237 (57.0)	–	129 (31.0)	Inclusion: adult and children who underwent tympanoplasty with or without mastoidectomy for cholesteatoma Exclusion: ears previously operated on by same author Bias risk: high—excludes revision surgery	78 (18.8)
Ocak, 2016 (20)	50	34	31 (62.0)	–	–	Inclusion: mixed cohort of 206 adult and children who underwent tympanoplasty with or without mastoidectomy for various middle ear pathologies; 50/206 had cholesteatoma Exclusion: nil Bias risk: low—includes different surgery types	13 (26.0)
Ozbek, 2009 (21)	118	–	–	–	–	Inclusion: mixed cohort of 265 adult and children who underwent primary or revision mastoidectomy for middle ear disease, 118/265 had cholesteatoma Exclusion: inadequate documentation, malignant tumours of temporal bone, middle ear surgery without mastoidectomy Bias risk: high—excludes non mastoidectomy surgery	44 (37.3)

Table 2 (*continued*)

Table 2 (*continued*)

Author, year	N	Mean age (years)	Male, n (%)	Paediatric, n (%)	Revision, n (%)	Patient selection	FCD, n (%)
Sahin, 2020 (4)	186	39	118 (63.4)	19 (10.2)	61 (32.3)	Inclusion: adult and children with middle ear cholesteatoma with mastoid involvement undergoing primary or revision CWU or CWD mastoidectomy	68 (36.6)
						Exclusion: non mastoid surgery	
						Bias risk: high—excludes non mastoidectomy surgery	
TanrivermiŞ Sayit, 2019 (22)	113	36	76 (67.3)	–	0	Inclusion: adult and children with middle ear cholesteatoma undergoing primary surgery	62 (54.9)
						Exclusion: revision surgery	
						Bias risk: high—excludes revision surgery	
Selesnick, 2001 (23)	67	–	–	–	–	Inclusion: adult and children who underwent primary or revision cholesteatoma surgery	22 (32.8)
						Exclusion: nil	
						Bias risk: low—includes different surgery types	
Shinnabe, October 2014 (24)	310	9.2 (paed) 45 (adult)	–	37 (11.9)	–	Inclusion: adult and children with cholesteatoma who had tympanoplasty	97 (31.3)
						Exclusion: nil	
						Bias risk: high—did not specify revision status of patients	
Shinnabe, September 2014 (25)	252	42	–	–	–	Inclusion: adult and children with either pars tensa or pars flaccida cholesteatoma	85 (33.7)
						Exclusion: mixed pars tensa and flaccida cholesteatoma	
						Bias risk: high—excludes two route cholesteatomas	
Trinidade, 2014 (31)	401	35.9	237 (59.1)	–	–	Inclusion: mastoidectomy surgery for cholesteatoma	76 (19.0)
						Exclusion: nil	
						Bias risk: high—excludes non mastoidectomy surgery	
Wang, 2006 (26)	155*	–	65 (42.8)	–	10 (6.5)	Inclusion: primary or revision tympanoplasty with or without mastoidectomy for cholesteatoma	46 (29.7)
						Exclusion: nil	
						Bias risk: low—includes different surgery types	

*, 152 patients representing 155 cases of primary or revision tympanoplasty with or without mastoidectomy for cholesteatoma. COM, chronic otitis media; CWD, canal wall down; CWU, canal wall up; FCD, facial canal dehiscence; HRCT, high-resolution computed tomography; paed, paediatric.

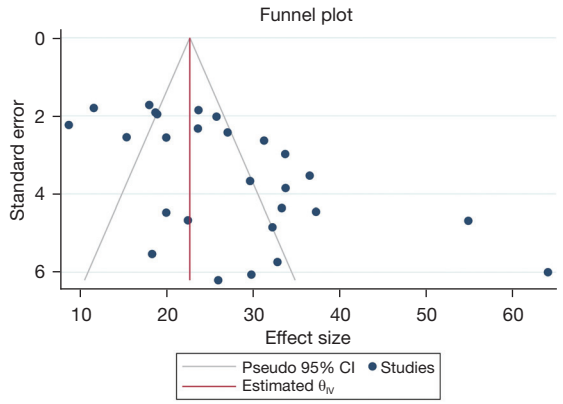

Figure 2 Funnel plot used to assess the distribution of effect size estimates with x-axis representing prevalence of facial canal dehiscence in reported study (n=27) and y-axis representing the standard error. A vertical line is drawn at the value of the summary effect and oblique lines representing the areas bound by 95% CI limit lines. CI, confidence interval.

Meta-analysis of pooled prevalence and sub-group analysis

The pooled prevalence of FCD was 24.67% (95% CI: 21.51–27.84%) with the representative Forest plot shown in *Figure 3B*. The Cochran's Q statistic was 183.61 (df =24, P<0.01) representing significant heterogeneity amongst included studies. The I^2 statistic was 87.57% indicating the overall heterogeneity could be accounted for by methodological differences between studies. The proportion of dehiscences that occurred in the tympanic segment of the facial canal was 93.79% (95% CI: 92.06–95.52%), which was consistent amongst the included studies. The tau (τ^2) statistic was 2.5, the Cochran's Q was 15.69 (P=0.27), and the I^2 statistic was 24.19%, indicating low heterogeneity.

Sub-group and meta-regression analysis was performed for the moderator variables of primary versus revision surgery, adult versus paediatric patients, and cohort size less than or greater than 300 patients, with representative Forest plots of pooled prevalence and bubble plots of the regression analysis provided (*Figures 4-6* and Figures S2-S4 respectively).

The pooled prevalence of FCD was higher in patients undergoing revision surgery (33.54%, 95% CI: 27.30–39.78%) compared to primary surgery (24.47%, 95% CI: 21.27–27.66%). The test of group difference was significant [Q(1) =6.43, P=0.01]. Meta-regression analysis showed this to be a significant moderator variable contributing to study heterogeneity (Z=–2.57, P=0.01, and R^2=21.87%). A meta-analysis of studies that allowed comparison between primary and revision cohorts showed an OR of 1.67 (95% CI: 1.23–2.27) favouring higher FCD incidence in the latter, with a test for overall effect demonstrating significance (Z=3.29, P=0.0010) (*Figure 7*).

The pooled prevalence of FCD was higher in adult patients (27.20%, 95% CI: 22.18–32.22%) compared to paediatric patients (15.33%, 95% CI: 8.86–21.79%) (*Figure 4*). A test of group difference was significant [Q(1) =8.08, P<0.01]. Meta-regression analysis showed that age was a significant moderator variable that accounted for some heterogeneity within the analysis (Z=2.78, P=0.005, and R^2=42.83%). A meta-analysis of studies that compared reported data for both adult and paediatric patients showed the OR of 1.83 (95% CI: 0.96–3.47) favouring higher FCD incidence in the former, however a test for overall effect was not significant (Z=1.84, P=0.07) and the confidence interval of the summary estimate crossed the line-of-no-effect (*Figure 8*). A LOO sensitivity analysis (Table S1) identified that this result is likely due to an outlier study that reported a higher dehiscence rate in children (22.7%, n=44) compared to adults (13.4%, n=157) (9). When omitting this study from analysis, we report an OR 2.25 (95% CI: 1.30–3.91) favouring dehiscence in adults which was statistically significant (Z=2.90, P=0.004).

When investigating the effect of sample size, the pooled prevalence of FCD was higher in the smaller studies (26.60%, 95% CI: 22.12–31.07%) compared to larger studies (21.94%, 95% CI: 18.14–25.74%), but a test of group difference was not significant [Q(1) =2.42, P=0.12]. When n=150 and n=200 patients was considered the limit to divide between small and large studies, meta-regression analysis showed no significance in cohort size contributing to the observed heterogeneity.

Twelve studies investigated the association between FCD and lateral semicircular canal fistula (LSCCF) (3,4,11,15,17,18,21,23,25,26,30,31). The pooled prevalence of LSCCF in this cohort was 7.10% (95% CI: 5.57–8.62%) and the pooled prevalence of FCD in patients with LSCCF was 67.84% (95% CI: 57.16–78.51%). The prevalence of LSCCF was likely inflated as most studies had low LSCCF rates that authors did not comment on its association with FCD. Meta-analysis of these 12 studies demonstrated a pooled OR of 6.45 (95% CI: 4.07–10.23) favouring higher

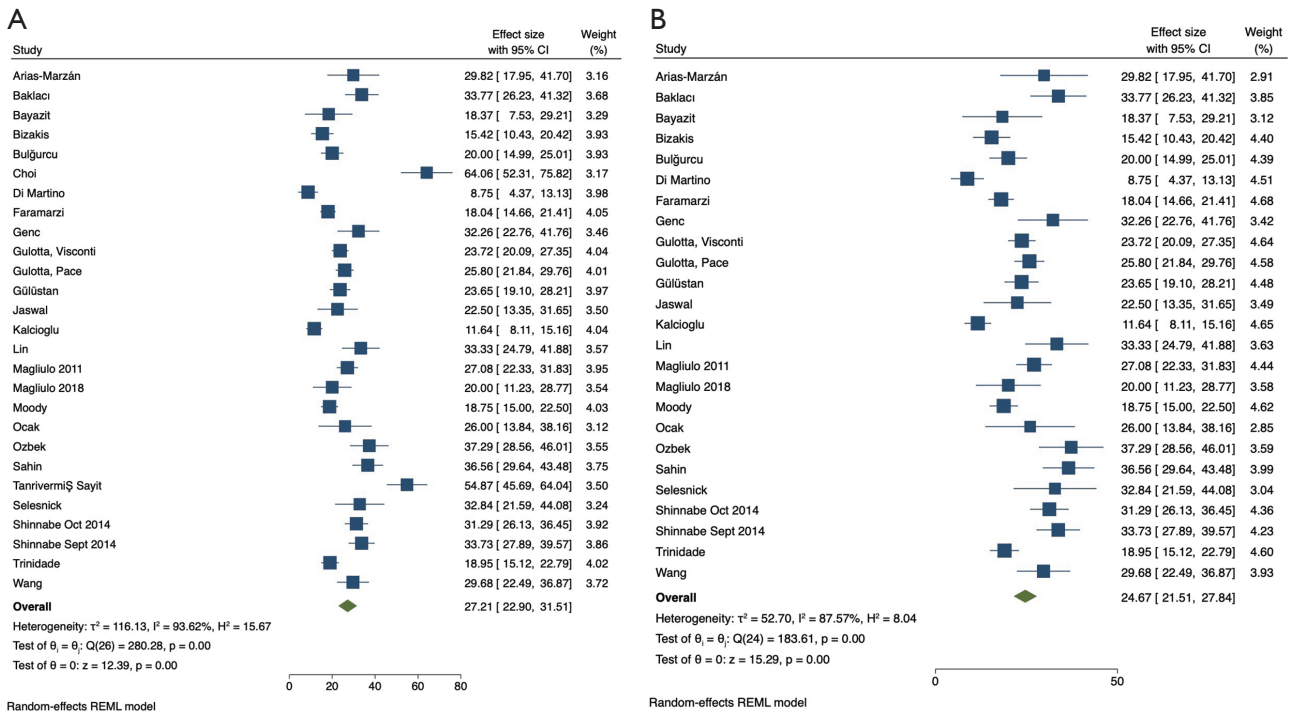

Figure 3 Forest plot of the pooled prevalence of facial canal dehiscence in all included studies using a random-effects model. (A) With all identified studies; (B) after leave-one-out analysis performed with exclusion of two outlier studies. CI, confidence interval; REML, restricted maximum likelihood.

incidence of FCD in patients with LSCCF (*Figure 9*).

Discussion

Summary of main results

This is the first meta-analysis to investigate the pooled prevalence of FCD at the time of cholesteatoma surgery, and we estimate it to be 24.67% (95% CI: 21.51–27.84%). The tympanic segment is consistently demonstrated to be the most common localization of dehiscence with a pooled prevalence of 93.79% (95% CI: 92.06–95.52%). The prevalence of FCD was comparatively higher in adult (27.20%, 95% CI: 22.18–32.22%) versus paediatric (15.33%, 95% CI: 8.86–21.79%) patients and in revision (33.54%, 95% CI: 27.30–39.78%) versus primary (24.47%, 95% CI: 21.27–27.66%) surgery.

FCD in the literature

FCD is a discontinuity in the bony structure of the facial canal, which exposes the facial nerve and may allow herniation into the middle ear cavity. It occurs in cholesteatomatous disease due to two main pathogenic mechanisms (32). Firstly, cholesteatomas are inherently destructive lesions that erode bone by exerting chronic mechanical pressure within the middle ear. Secondly, longstanding inflammation of middle ear mucosa induces osteitis and osteonecrosis of the bony walls of the middle ear and mastoid, with upregulation of osteolytic enzymes, inflammatory mediators, osteoclast-mediated resorptive activity, and adverse bone remodelling processes. FCD increases the risk of preoperative facial nerve palsy, due to inflammatory involvement of the nerve or cholesteatoma invasion into the epineurium, as well as the risk of postoperative palsy, due to accidental surgical injury. Previous studies have estimated the incidence of iatrogenic facial nerve injury to be 0.3–3.6% in primary surgery and 4–10% in revision surgery (33).

Historical studies in cadaveric models of the petrous temporal bone have reported a high incidence of FCD (1,2,34,35). Anatomic and histologic studies by Dietzel *et al.*, Baxter *et al.*, and Moreano *et al.*, estimated a dehiscence rate of 57%, 55%, and 56% respectively (2,34,35). Bilaterality

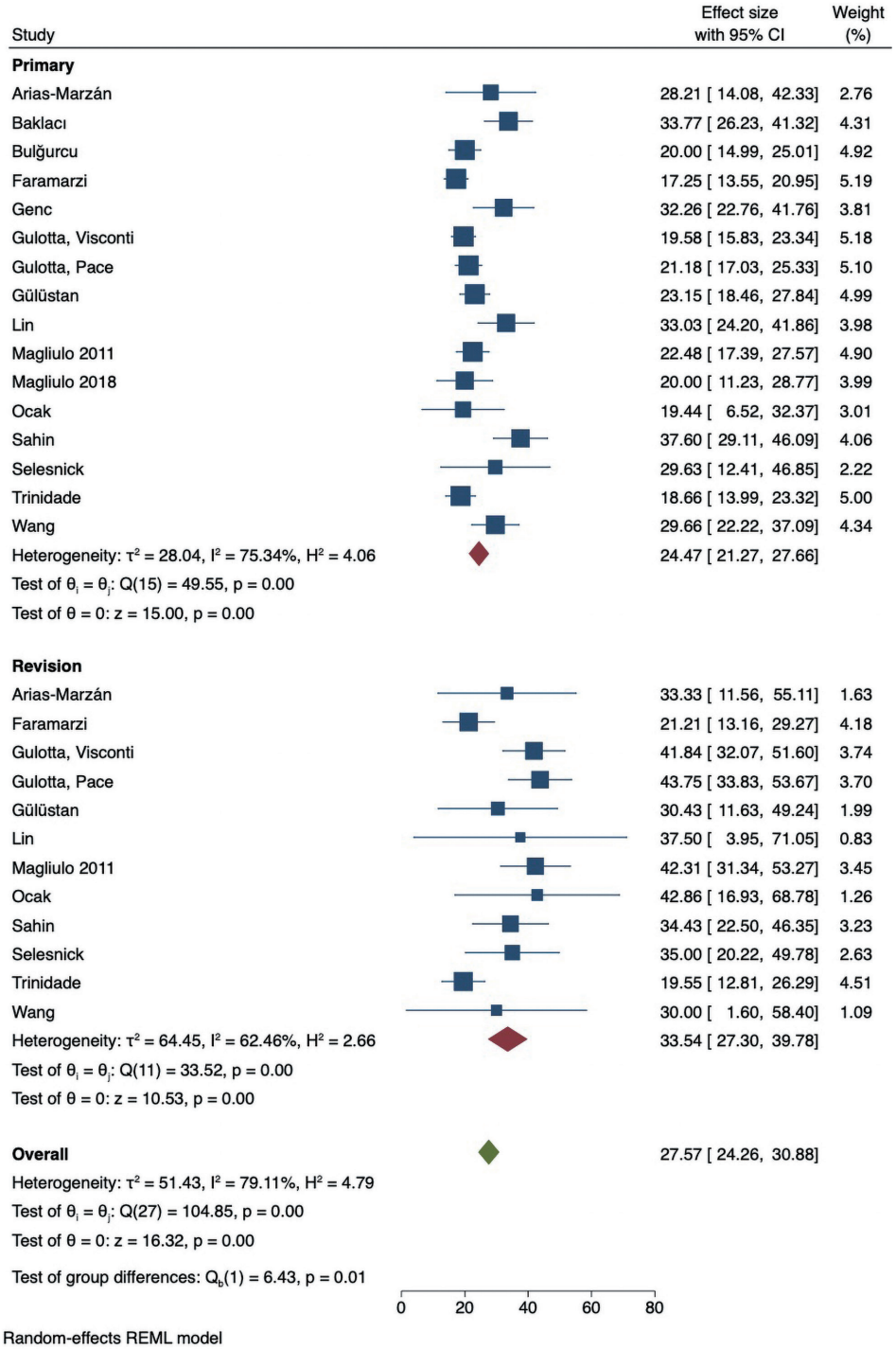

Figure 4 Forest plot of the pooled prevalence of facial canal dehiscence in primary (top) and revision (bottom) surgery using a random-effects model. CI, confidence interval; REML, restricted maximum likelihood.

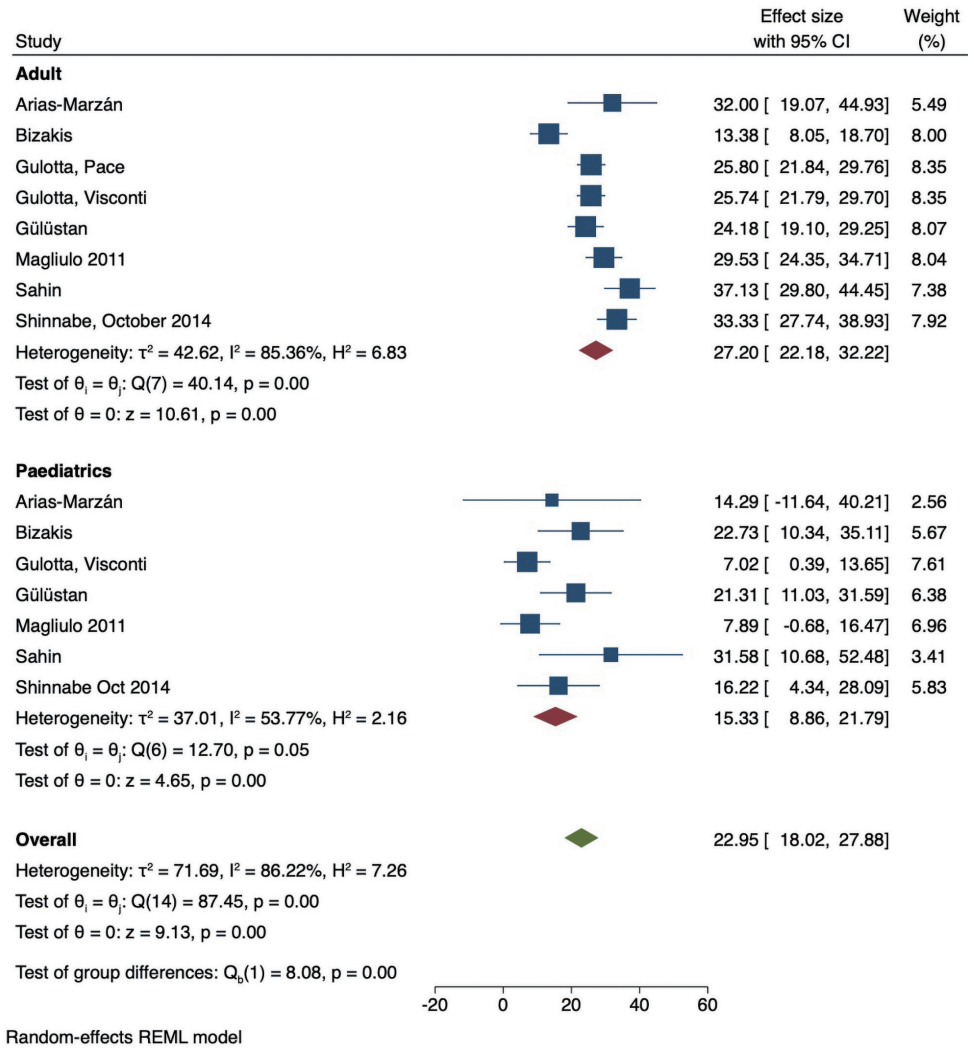

Figure 5 Forest plot of the pooled prevalence of facial canal dehiscence in adults (top) and paediatrics (bottom) patients using a random-effects model. CI, confidence interval; REML, restricted maximum likelihood.

was reported in 76.3% of cases suggesting that the cause of FCD as an anatomic variation in the normal population is likely due to interference in facial canal ossification during foetal development. The authors introduced the concept of microdehiscences, with comparatively higher rates of microdehiscences in adult populations whereas paediatric populations had higher rates of macrodehiscences—this inverse trend is likely due to ongoing ossification in childhood, converting large dehiscences into smaller ones (35). The high incidence in anatomic and histologic studies compared to clinical studies may be due to injuries introduced in the preparation of the specimens. Dehiscences detected in these studies are often microscopic and unnoticeable or of negligible clinical significance to the surgeon, with those less than 1 mm unable to be visualised at the time of surgery. These studies also report a high rate of microdehiscences along the inferior or inferomedial aspect of the tympanic segment, which may be difficult to recognize intraoperatively (2,22,36). Clinical studies investigating FCD in patients undergoing stapes surgery, a cohort used as a surrogate for control or "normal" ears, have reported dehiscence rates of 3.3% by Tange *et al.* (n=427) (37), 5.2% by Trinidade *et al.* (n=172) (31), and 11.4% by Li *et al.* (n=1,465) (38).

The tympanic segment of the facial canal is consistently described as the most common site of dehiscence, with

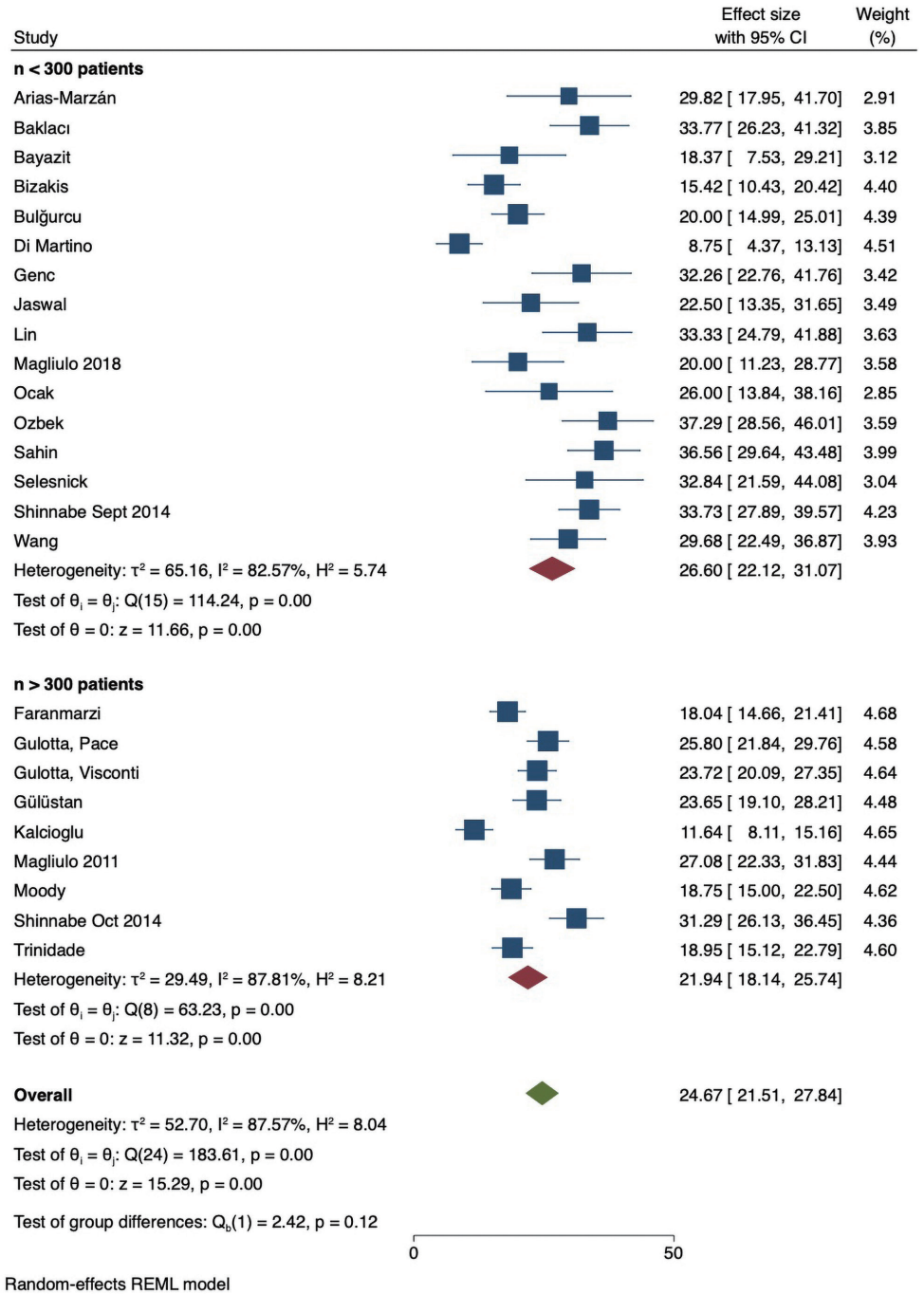

Figure 6 Forest plot of the pooled prevalence of facial canal dehiscence in studies with n<300 (top) and n>300 (bottom) patients using a random-effects model. CI, confidence interval; REML, restricted maximum likelihood.

multiple explanations proposed. The bony covering is thinnest in the tympanic segment and most vulnerable to erosion by inflammation and mechanical pressure. Cadaveric models from foetuses and neonates have provided insight into the embryological basis of congenital dehiscences (1,39). Facial canal ossification commences from an apical and canalicular ossification center, proceeding in an anterior-to-posterior direction towards each other (1). Ossification

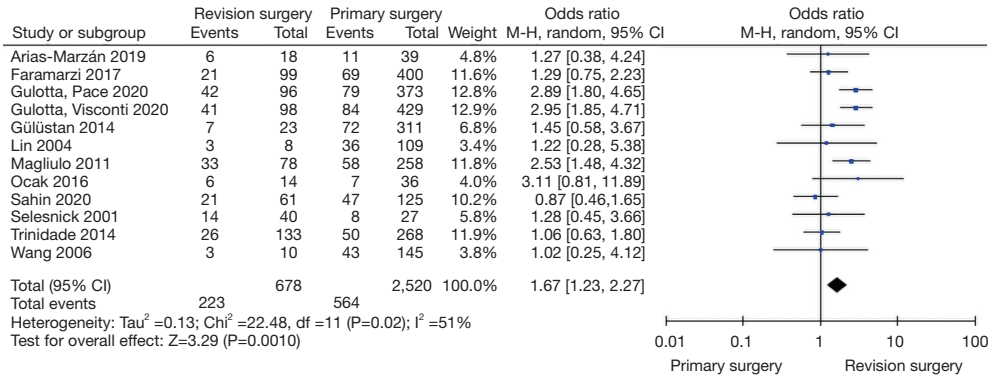

Figure 7 Forest plot showing odds ratio of facial canal dehiscence in primary versus revision cholesteatoma surgery using a random-effects model. CI, confidence interval; M-H, Mantel-Haenszel test.

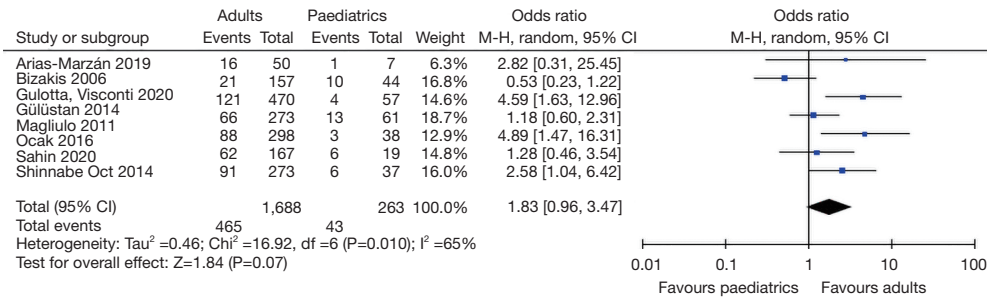

Figure 8 Forest plot, using a random-effects model, showing odds ratio of facial canal dehiscence in adult versus paediatric patients in included studies where both patient subgroups could be compared. CI, confidence interval; M-H, Mantel-Haenszel test.

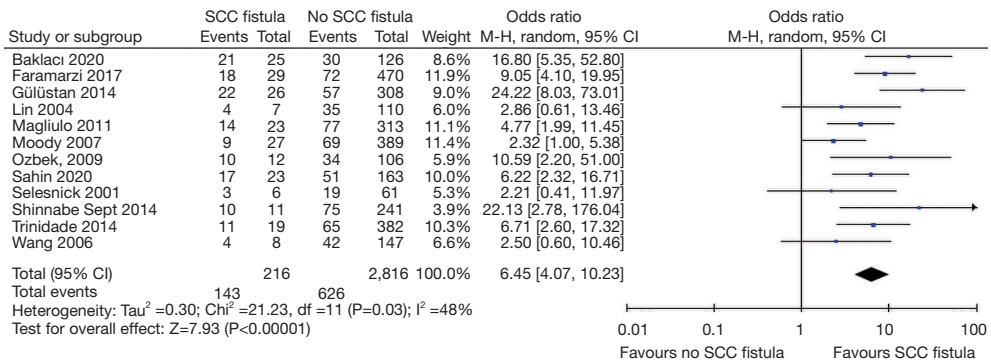

Figure 9 Forest plot, using a random-effects model, showing odds ratio of facial canal dehiscence in patients with and without semicircular canal fistula. CI, confidence interval; M-H, Mantel-Haenszel test; SCC, semicircular canal.

is incomplete at birth and all temporal bones have micro- or macro-dehiscences in the tympanic segment (1), which are considered variations of normal development. Development continues post-partum with fusion of the two ossification centres in the region of the oval window approximately one year after birth and ossification continuing into early childhood replacing macrodehiscences (1,39). It is hypothesized that failure of this fusion is responsible for congenital dehiscences in the tympanic segment, near the oval window niche, and accounts for FCD in individuals without otologic disease (1,39,40). The high rate of tympanic segment dehiscences in this meta-

analysis is consistent with current knowledge about the site of origin of cholesteatomas and their expected growth patterns (23,41). Pars tensa cholesteatomas are generally limited to the tympanic cavity, with some extension into the epitympanum, and progress directly around the tympanic facial canal, with posterior mesotympanic variants more likely to involve the posterior tympanic spaces such as the sinus tympani and facial recess (42). Pars flaccida cholesteatomas have more dispersed growth patterns within the tympanum and are more likely to progress towards the aditus ad antrum and the mastoid (43). Finally, because of the tendency for tympanic segment involvement or invasion by cholesteatoma, it is this region where mechanical dissection during surgery is required, introducing risk of creating iatrogenic dehiscences (23).

Multiple studies have cited higher rates of dehiscence in CSOM with cholesteatoma (C-CSOM) compared to CSOM without cholesteatoma (CSOMwoC) (10,12,20,21,29). Genc *et al.* showed that 88% of CSOM patients with FCD had cholesteatomatous disease, demonstrating a statistically significant association (12). A study by Kalcioglu *et al.* of 372 tympanomastoidectomy patients showed a similar dehiscence rate with 11.6% (37/318) in the C-CSOM cohort compared to 9.3% (5/54) in the CSOMwoC cohort, with no statistically significant association (P=0.822) (16). However, when analysing adult and paediatric patients separately, the dehiscence rates were significantly higher in the C-CSOM cohort within both sub-groups.

Primary versus revision surgery and FCD

Revision surgery was shown to be significantly associated with higher incidence of FCD compared to primary surgery. This is consistent with previous studies in the literature that have reported higher dehiscence rates at the time of revision cholesteatoma surgery, as shown in *Figure 4*. This could be explained by (I) surgical trauma due to instrumentation and microdissection of the facial canal during primary surgery, and (II) revision surgery reflecting patients with longer duration and progression of bony erosion in residual or recurrent cholesteatomatous disease. Sahin *et al.* was the only study in the meta-analysis that had a higher dehiscence rate at primary surgery (37.6%) compared to revision (34.4%), though this was not statistically significant (4). Whilst all other studies reported a higher dehiscence rate in revision surgery, a statistically significant association between FCD and revision surgery was only reported in four studies (13,14,18,20), with the remainder showing no significance (7,11,15,17,23,26,31). This could possibly be explained by the comparatively low patient numbers in the revision cohort, which would require larger magnitude in the difference between dehiscence rates to reach significance, as well as differences amongst authors in the candidates selected for revision surgery, the site and size of the cholesteatoma, and the type of revision surgery performed. Three papers have reported on the association between FCD incidence and disease duration, categorized as greater or less than 5 years, with a significant relationship in each study favouring dehiscence in patients with longer disease burden (13,14,18).

Adult versus paediatrics and FCD

Few studies investigated the association between age and FCD, with the majority reporting higher dehiscence rates in the adult cohort. This observation is likely due to longer disease duration and exposure to chronic inflammation and mechanical pressure in adult patients, and higher likelihood of having previous surgery. This theory is supported by Gulotta *et al.* (13) who reported a non-significant difference in dehiscence between adults (11.3%, n=106) versus children (6.2%, n=16) in those with disease duration less than 5 years, compared to a significant difference between adults (29.9%, n=364) and children (7.3%, n=41) when disease duration was greater than 5 years. A 2011 study by Magliulo *et al.* reported a significant OR of 4.96 (95% CI: 1.51–25.97) favouring dehiscence in adults, with this cohort often having more extensive disease (18). They were the only study to look at the effect of primary versus revision surgery in adult and paediatric cohorts, and reported that revision surgery in adult patients had the highest incidence of FCD. Ozbek *et al.* (21) demonstrated that dehiscence risk increased by 2.88 times in patients over the age of 16 years; however, this included a cohort of mixed middle ear pathologies in which cholesteatoma could not be isolated for analysis. Shinnabe *et al.* showed a significantly lower incidence of dehiscence in children (16.8%) compared to adults (33.3%) and that FCD rates were influenced by the type of cholesteatoma (24).

FCD and co-existing surgical findings

High resolution CT petrous temporal bones is the standard imaging modality in patients planned for cholesteatoma surgery. Previous studies investigating the radiologic-surgical correlation of diagnosing FCD from preoperative

imaging have reported wide variability in sensitivity and specificity (7,18,44-46). This is due to difficulties in evaluating the thin bone of the facial canal, especially in thicker slices where partial volume averaging from adjacent soft tissue may be a confounding factor. Other studies have investigated the role of coexisting surgical findings that may predict FCD—these include the presence of LSCCF or erosion of the scutum (3,12), ossicular chain (4,15,16,27), dural plate of the mastoid tegmen (3,4,11,21,25), or the posterior wall of the external auditory canal (PWEAC) (3,15,29). We report a significant association between LSCCF and FCD in a meta-analysis of 12 studies with an OR 6.45 (95% CI: 4.07–10.23) (3,4,11,15,17,18,21,23,25, 26,30,31). Shinnabe *et al.*, demonstrated that the presence of LSCCF was only significant in predicting FCD in pars flaccida cholesteatomas (25). Baklacı (3) and Genc (12) *et al.* showed an association between FCD and scutum erosion, with 43.2% and 55.6% of patients with scutum erosion respectively having FCD compared to 7.5% and 8.25% of patients without scutum erosion having FCD. This finding is important for pars flaccida cholesteatomas as both studies excluded patients who underwent tympanoplasty without mastoidectomy, resulting in exclusion of small pars tensa cholesteatomas. The relationship between FCD and dehiscence of the dural plate of the mastoid tegmen is uncertain, with some studies reporting significant association (3,4,11,21,25) and others not (26,29). This may be related to the low incidence of dural exposure. The presence of multiple surgical findings raises the likelihood of FCD. A regression analysis by Baklacı *et al.* (3) showed that LSCCF combined with erosion of the scutum or the PWEAC strongly correlated with FCD with OR 34.3 and 31.6 respectively. Ossicular chain erosion is frequently encountered at the time of cholesteatoma surgery, with the incus being most commonly involved. The presence of a stapes defect, either in isolation or combined with incudal or pan-ossicular erosion, increased the risk of FCD (4,15,16) in three studies, with only Shinnabe *et al.* (25) showing no association. Hence, these erosive changes, which are often easier to visualize on CT imaging, may be used as cautionary findings to predict encountering FCD intraoperatively.

Study limitations

The limitations of this meta-analysis mainly related to the methodology used in the included studies, especially with respect to patient selection where most studies had a high risk of bias (*Table 2*). A high degree of heterogeneity in the pooled prevalence of FCD was noted, which was partially explained by the moderator variables investigated in the sub-group analysis. The sensitivity analysis showed two outlier studies, which were excluded from the meta-analysis. Overall, we feel that our estimate of the pooled prevalence should be generalizable despite the observed heterogeneity. Variability in sample sizes introduced a small-study effect, with higher incidence in studies with fewer recruited patients, however this was shown to not be clinically significant on a test of group differences and meta-regression analysis.

In general, the included studies used appropriate selection criterion but some recruited participants with specific indications that can introduce confounding bias into the meta-analysis—for example, the 2018 study by Magliulo *et al.* (19) exclusively studied attic cholesteatomas, disregarding those arising from the mesotympanum. Most studies did not specify the location or type of the cholesteatoma, whether arising from the pars flaccida or pars tensa, and a comparison between these two entities that demonstrate different growth patterns could not be made. Heterogeneity was apparent with respect to the type of cholesteatoma surgery performed. Whereas some studies exclusively investigated mastoidectomy, others included patients who had tympanoplasty with or without mastoidectomy. It is expected that patients who required mastoidectomy would have had more extensive disease with erosive changes to the facial canal. Studies that excluded patients who had tympanoplasty alone would be omitting small pars tensa cholesteatomas, raising the risk of overestimating FCD incidence. Mastoid segment dehiscences would not be visualised in patients who had tympanoplasty alone, however if a mastoidectomy was not required then it is reasonable to assume that the mastoid facial canal would not have been involved by the cholesteatoma. Data in the literature is not presented in a way to allow subgroup analysis between tympanoplasty with or without mastoidectomy. Size of the dehiscence is not recorded and it is likely that this will be associated with the presence of co-existing destructive surgical findings. FCD may be present as a congenital variant and whether the cholesteatoma is the cause of the dehiscence may be determined by its size, location, and association with other erosive findings.

Whilst all studies stated that dehiscence was diagnosed by intraoperative examination of the facial canal, ten studies did not specifically state the use of the microscope

in diagnosis and it is uncertain if these authors used microscopic or endoscopic visualisation. The reported incidence of dehiscence is also dependent on the practice of the operating surgeon, both in terms of detecting and accurately diagnosing it as FCD. There were no standardized criteria amongst different studies and interobserver variability in detecting bony dehiscence is unknown.

In multiple studies, authors presented data in a way that it was difficult to extract data for the sub-group analysis and meta-regression (i.e., they did not separate data by adults versus children or primary versus revision surgery). This was more common in mixed cohorts of cholesteatoma and non-cholesteatomatous ear pathologies. There was inadequate data to compare the effects of primary and revision surgery in children and adults separately.

Overall, this systematic review and meta-analysis highlights that FCD is a common intraoperative finding in cholesteatoma surgery, including up to one-third of revision surgeries. Given, the potential challenges in determining FCD on preoperative imaging, it is important to consider other clinical risk factors and radiographic findings in the patient workup, discussed in our review, to estimate the likelihood of encountering dehiscence. Furthermore, this can preoperative patient counselling about surgical risk and assist with surgical planning, with the option to consider a canal wall down procedure in recurrent cholesteatoma or extensive disease with FCD or other associated cautionary findings.

Conclusions

The pooled prevalence of FCD at the time of cholesteatoma surgery is 24.67%, with the tympanic segment of the facial canal being the most common localisation and adult and revision cases having higher dehiscence rates. Dehiscence of the facial canal may coexist with other destructive findings such as LSCCF and erosion of the ossicular chain erosion, scutum, and PWEAC. The association with revision cases and erosion of the scutum, ossicles, and semicircular canals highlights the importance of thorough preoperative clinical and radiographic assessment to estimate the risk of FCD and prevent injury to the nerve.

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Footnote

Reporting Checklist: The authors have completed the PRISMA reporting checklist. Available at https://www.theajo.com/article/view/10.21037/ajo-23-1/rc

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Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://www.theajo.com/article/view/10.21037/ajo-23-1/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. Approval from the ethics institutional review board was not required for this study as it is a systematic review and meta-analysis of published literature and it does not require collection of patient data.

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Supplementary

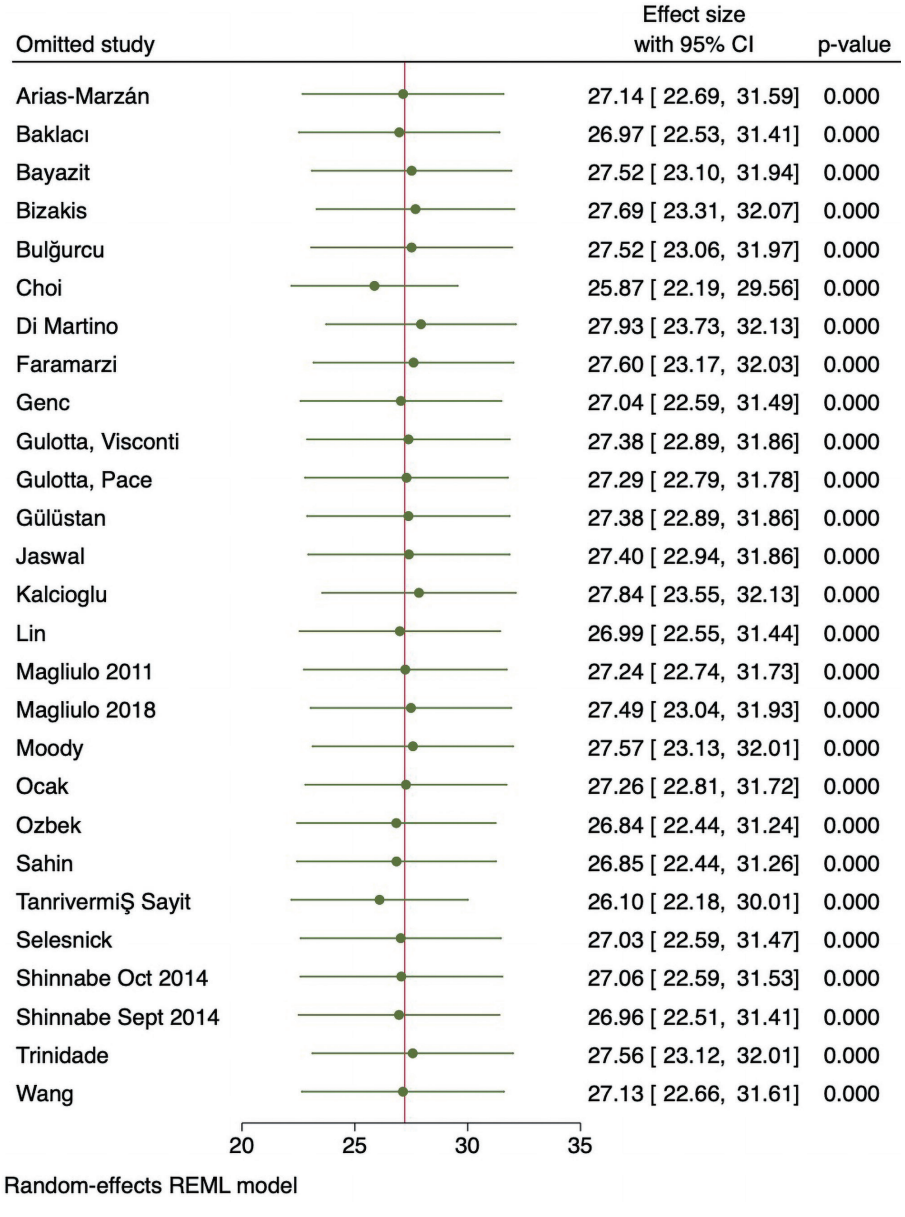

Figure S1 Leave-one-out sensitivity analysis performed to investigate the impact on effect sizes and pooled prevalence after exclusion of any one study. CI, confidence interval; REML, restricted maximum likelihood.

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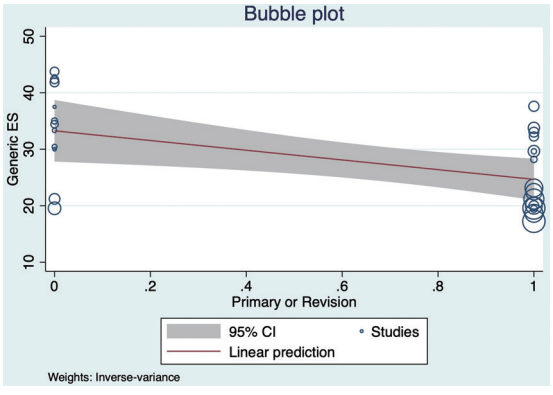

Figure S2 Bubble plot, or meta-regression scatter plot, with regression line (red) and 95% CI bounds (grey) to evaluate the effect of primary and revision surgery on incidence of FCD. On the x-axis, 0 and 1 corresponds to the revision and primary surgery cohorts respectively. CI, confidence interval; ES, effect size; FCD, facial canal dehiscence.

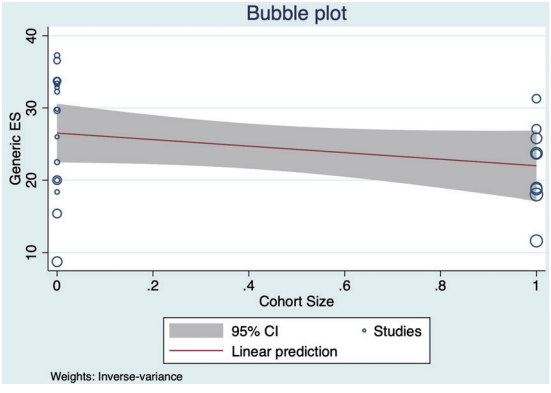

Figure S4 Bubble plot, or meta-regression scatter plot, with regression line (red) and 95% CI bounds (grey) to evaluate the effect of cohort size (less than or greater than 300 patients) on incidence of FCD. On the x-axis, 0 and 1 corresponds to the n<300 and n>300 cohorts respectively. CI, confidence interval; ES, effect size; FCD, facial canal dehiscence.

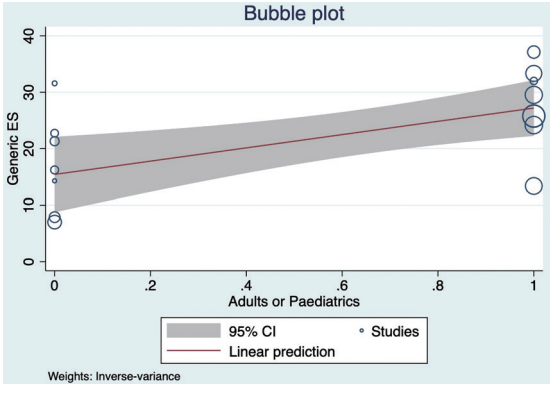

Figure S3 Bubble plot, or meta-regression scatter plot, with regression line (red) and 95% CI bounds (grey) to evaluate the effect of age groups (adults or paediatrics) on incidence of FCD. On the x-axis, 0 and 1 corresponds to the paediatric and adult cohorts respectively. CI, confidence interval; ES, effect size; FCD, facial canal dehiscence.

Table S1 Leave-one-out sensitivity analysis performed for calculating the odds ratio of FCD in adult patients compared to paediatric patients

Omitted study	Odds ratio (95% CI)	Test for overall effect
None	1.83 (0.96–3.47)	Z=1.84 (P=0.07)
Arias-Marzán, 2019, (7)	1.78 (0.90–3.55)	Z=1.65 (P=0.10)
Bizakis, 2006, (9)	2.25 (1.30–3.91)	Z=2.90 (P=0.004)
Gulotta, Visconti, 2020, (13)	1.54 (0.91–2.92)	Z=1.32 (P=0.19)
Gülüstan, 2014, (15)	2.05 (0.92–4.55)	Z=1.77 (P=0.08)
Magliulo, 2011, (18)	1.57 (0.82–3.01)	Z=1.35 (P=0.18)
Sahin, 2020, (4)	1.97 (0.92–4.21)	Z=1.76 (P=0.08)
Shinnabe, October 2014, (24)	1.73 (0.82–3.67)	Z=1.43 (P=0.15)

The odds ratio is calculated using the Mantel-Haenszel test with a random-effects model and 95% confidence intervals. On omission of Bizakis *et al.*, the test for overall effect is significant and the confidence interval of the summary effect does not cross the line-of-no-effect. CI, confidence interval; FCD, facial canal dehiscence.

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