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Residual Cholesteatoma After Endoscope-guided Surgery in Children

*†Adrian L. James, *†Sharon Cushing, and *†Blake C. Papsin

**Department of Otolaryngology–Head and Neck Surgery, University of Toronto; and †Department of Otolaryngology–Head and Neck Surgery, Hospital for Sick Children, Toronto, Ontario, Canada*

Objective: Endoscopes can facilitate surgery within tympanomastoid recesses that are not visible with the operating microscope. This study investigates whether use of endoscopes to guide dissection of cholesteatoma leads to lower rates of residual cholesteatoma than using the endoscope only for inspection after microscope-guided dissection.
Study Design: Comparative cohort study.
Setting: Tertiary pediatric center.
Patients: Two hundred thirty-five patients with acquired or congenital cholesteatoma in children <18 years having intact canal wall surgery and follow-up >12 months.
Interventions: Comparison of group (A) microscope surgery followed by endoscopic inspection, with group (B) endoscope-guided dissection.
Main Outcome Measures: Residual cholesteatoma rates, controlling for site of initial cholesteatoma, detection by second-stage surgery, and length of follow-up.
Results: Analysis of all patients showed endoscopic dissection was associated with less residua in the middle ear (risk difference = 0.12; $p = 0.026$, Kaplan–Meier log rank analysis; number needed to treat = 9) but not at other sites. When restricting analysis to ears that were evaluated with second look surgery, no significant reduction in residual disease was found after endoscopic dissection at any site (e.g., retrotympanic residua: 12% Group A versus 7% Group B (NS, Fisher exact test). Endoscopic dissection allowed more permeatal surgery. No complications were attributable to endoscope use. Wound complications occurred in 4% of open cases.
Conclusion: Endoscopes enhance surgical access to tympanomastoid recesses. In conjunction with the availability of the operating microscope, angled instruments, and KTP laser, endoscope-guided dissection provides a small incremental benefit for prevention of residual cholesteatoma, and facilitates a minimally invasive approach. **Key Words:** Cholesteatoma—Endoscopic ear surgery—Recidivism—Residual.

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Residual cholesteatoma, in which un-cleared remnants of keratinizing squamous epithelium survive and grow after incomplete surgical clearance, was recognized by Politzer as long ago as 1891 (1) and still occurs in as many as 35% of patients (2). This form of recidivism must be distinguished from recurrent cholesteatoma, in which disease is newly acquired from tympanic membrane retraction after previous complete surgical removal (3). The likelihood of residual disease may be greater with more extensive cholesteatoma, especially when trapped in inaccessible recesses, and with presentation during childhood (4–6).

The proportion of patients *reported* to have residual disease is also dependent on the method of assessment, choice of denominator, and completeness of follow-up (7). Staged surgical exploration is perhaps the most sensitive means of detecting early, occult residual cholesteatoma, but tends to be reserved for selected patients, being advocated more commonly for canal wall up tympanomastoidectomy (2). More recently nonecho planar diffusion weighted magnetic resonance imaging (DWI-MRI) has been used to detect occult residual disease, but has limited sensitivity for smaller lesions (8,9). Residual disease can only be detected in clinic with otoscopic inspection when it is sufficiently close to the surface of the tympanic membrane or alternatively with erosive complications. Ears that have not been followed long enough, or have not been evaluated with staged surgery or imaging, may harbor occult residual cholesteatoma. It is therefore appropriate to consider reporting rates of residual cholesteatoma in those who have been evaluated with second-stage surgery separately and also by length of follow-up. It is also important to note that residual disease is most likely to occur at its initial location, so it is appropriate to count residua by each previously involved tympanomastoid subsite. Some

Address correspondence and reprint requests to Dr. Adrian L. James, Associate Professor, Department of Otolaryngology–Head and Neck Surgery, Hospital for Sick Children, 555 University Avenue, Toronto, ON M5G 1X8, Canada; E-mail: adr.james@utoronto.ca

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authors also quote the rate of "unexpected" residual disease in their series in contrast to patients where remnants were known to be left in situ and expected to persist as residua (5,10).

It is likely that the risk of residual disease is reduced by meticulously dissecting the matrix off bone in continuity so as not to leave behind any remnants (5). Application of KTP laser to submicroscopic deposits or remnants on ossicles has been shown to effectively reduce the rate of residual disease (11,12). Endoscopic inspection of hidden recesses after microscope-guided dissection has been shown to reveal otherwise occult remnants, so allowing removal and prevention of residual disease (13–16). It is thought that endoscope-guided dissection may further reduce the risk of residual disease though this has not been demonstrated convincingly (5,15,17–19).

This manuscript reviews the prevalence of residual disease in a consecutive cohort of children having intact canal wall (ICW) surgery for cholesteatoma over a 9-year period. It evaluates the impact of introducing endoscope-guided dissection on residual disease rates half way through this time period, and controls for extent and location of initial disease, length of follow-up and method of screening for occult disease.

MATERIALS AND METHODS

Ethical approval for this study was granted by the Research Ethics Board at the Hospital for Sick Children, Toronto, ON, Canada.

Detailed records of the presentation, operative procedure, and outcome of a consecutive series of surgeries for cholesteatoma by a single surgeon (A. J.) were recorded prospectively on an extensive database from 2005. Inclusion criteria for the study were: age at presentation under 18 years, no history of surgery for cholesteatoma before referral, initial surgery completed by ICW technique, at least 1 year of follow-up after initial surgery.

Data were extracted on: location of initial cholesteatoma within tympanomastoid subsites, number of surgeries, age at surgery, use of endoscopy for dissection, and the presence and location of residual cholesteatoma at subsequent surgery, or at follow-up with DWI-MRI. Patients were dichotomized into two groups according to how endoscopes were used. In the first time period (Group A: 2005–2009), endoscopes were used for inspection of hidden tympanomastoid recesses to check for remnants of cholesteatoma matrix left after microscope-guided dissection. Endoscopes were never used to guide dissection in Group A patients. In the second time period (Group B: 2009–2013) endoscopes were used when felt to be needed to guide primary dissection of matrix from hidden recesses. Most commonly this was for cholesteatoma in the retrotympanum or medial epitympanum. With increasing surgical experience, endoscopic dissection was used more extensively during the time course of Group B so that ultimately some cases were completed totally endoscopically.

The primary outcome measure was set a priori as a comparison between Groups A and B of residual cholesteatoma in the retrotympanum at second-stage surgery, expecting this to be the site of maximum advantage for endoscopic dissection. Retrotympanum was defined as including the facial recess, subpyramidal space, sinus tympani, and sinus subtympanicum (16). Secondarily comparison between Groups A and B was to be made for residual disease rates at any site using two denominators: number of patients with second-stage surgery and total number of patients. Statistical analysis was completed using SigmaPlot 11 (Systat Software Inc., San Jose, CA, U.S.A.), including Kaplan–Meier analysis to control for the shorter of duration of follow-up in Group B. χ^2 test was used to test for difference in proportions of larger sample sizes and Fisher's exact test for smaller samples.

Surgical Technique

Principles used for selection of patients for ICW surgery were as described previously (20). Surgery was completed in both Groups A and B in accordance with the minimally invasive functional principles typical of contemporary surgical practice (5). A postauricular approach was used in the majority of patients and a cortical mastoidectomy drilled for access to cholesteatoma that could not be reached through the canal after scutum removal. Angled instruments developed by Thomassin et al. (21) (Karl Storz GmbH & Co. KG, Tuttlingen, Germany) were used to remove disease from the retrotympanum with both microscope and endoscope-guided surgery. Endoscopes were used for inspection after dissection to check for matrix remnants. KTP laser was applied at settings of <1 W at sites from where cholesteatoma had been removed, though not over the facial nerve, to ablate matrix fixed to the stapes, and to ablate granulation tissue (22). Defects of the scutum and tympanic membrane were typically reconstructed with cartilage. Second-stage surgery was typically planned approximately 1 year later for extensive disease or when friable matrix was removed piecemeal. DWI-MRI was used sporadically as an additional screen for residual cholesteatoma 3 years after completion of surgery or before discharge from follow-up.

In Group A, retrotympanic dissection was completed under the microscope, assisted by a Buckingham mirror for visualization, or by drilling off bone toward the facial nerve (approach demonstrated in Fig. 1). In Group B, endoscopes were used to guide dissection in areas hidden from view with the microscope when necessary (Fig. 2) using the same instruments available for group A, including the KTP laser. Further details of endoscopic technique were reported previously (23,24).

RESULTS

From the consecutive series of 385 ears with cholesteatoma in 363 children, 72 were excluded as having had previous cholesteatoma surgery before referral, 40 as

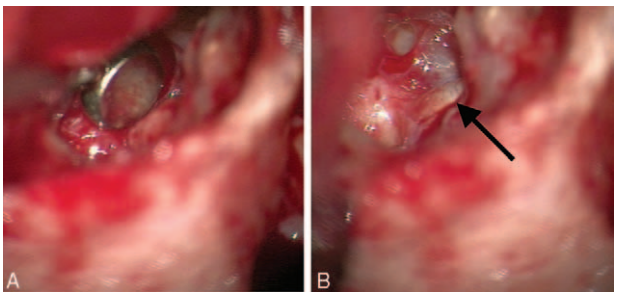

FIG. 1. Second-stage intact canal wall tympanomastoidectomy after initial surgery without endoscopic dissection (left ear). The posterior canal wall runs from top right to bottom left corner of these images obtained with the operating microscope. A cyst of residual disease is visible in the upper facial recess area initially only with a mirror (*A*), but more readily after drilling away bone of the annulus posteriorly (*B*, *black arrow*).

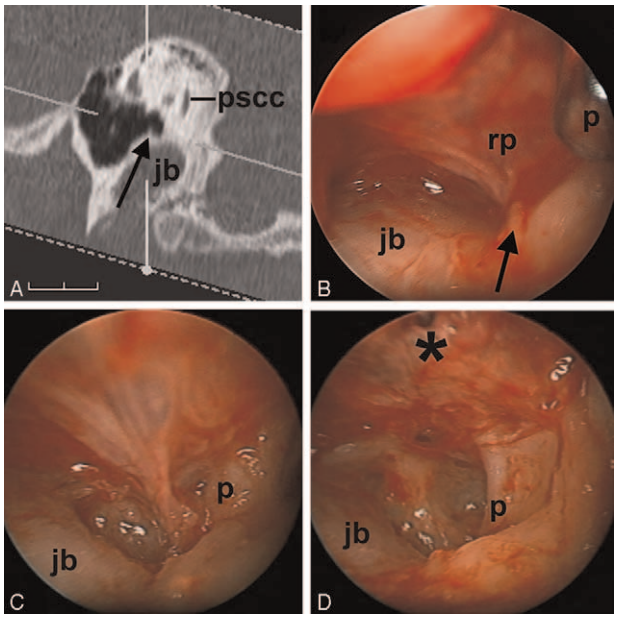

FIG. 2. Primary acquired cholesteatoma associated with retraction of the left pars tensa into the sinus tympani. A small bony septation partially impedes access to the sinus tympani as marked with an *arrow* in (*A*) sagittal reconstruction of temporal bone CT scan at the level of the posterior semicircular canal (pscc) and jugular bulb (jb) and (*B*) endoscopic intraoperative image of the retraction pocket (rp) just inferior to the pyramidal eminence (p). Removal of the spicule of bone with endoscopic guidance improves access (*C*) allowing intact elevation of the pocket (*) with endoscopic dissection (*D*).

initially having canal wall down surgery, and 38 as having inadequate follow-up (i.e., initial surgery less than 1 yr ago), leaving a total of 235 ears in 220 children for further analysis. The median age at first surgery was 10.9 years (1.0–17.9 yr). Almost half as many more cases occurred in males as females (152/235 = 65%). Origin of the cholesteatoma was found to be congenital in 29 (12%), and acquired from the pars tensa alone in 138 (59%), pars flaccida in 49 (21%), both tensa and flaccida in 10 (4%), or implantation in 7 (5%) and ear canal in one. As shown in Table 1, there were no significant differences between these parameters in groups A and B. Extent and location of cholesteatoma (Tables 1 and 2) were also similar in both groups but more patients in Group B had an intact ossicular chain. Median length of maximum follow-up was inevitably longer in Group A than Group B (74 versus 38 mo; $p < 0.001$ Mann–Whitney), necessitating the use of survival analysis to control for the increased likelihood of residual disease becoming visible with longer follow-up.

Second-stage surgery was completed in 121 patients (51%). Residual cholesteatoma was detected at the second stage of surgery in 45 patients, representing 19% of all patients, or 37% of those having a second operation. There were no cases of "expected" residual disease as complete removal was always intended and thought to have been achieved. DWI-MRI screening for occult residual cholesteatoma in 21 patients, at a mean

TABLE 1. *Demographic details of cholesteatoma patients*

Demographic	Group A	Group B	*p* Value
Total	108	127	
Age (median, yr)	10.6	11	0.39 ^{MW}
Sex (male:female)	75:33 (69%)	77:51 (59%)	0.14 ^{X2}
Cholesteatoma origin			
Pars tensa only	60 (56%)	77 (61%)	0.39 ^{X2}
Pars flaccida only	22 (20%)	27 (21%)	0.89 ^{X2}
Tensa and flaccida	4 (4%)	6 (5%)	1 ^{F}
Congenital	16 (15%)	13 (10%)	0.32 ^{F}
Implantation	5 (5%)	3 (2%)	0.48 ^{F}
Ear canal	1 (1%)	1 (1%)	1 ^{F}
Cholesteatoma extent			
Mills stage (median)	2	2	0.12 ^{MW}
Intact ossicles pre-op	20 (19%)	39 (31%)	0.03 ^{X2}
Intact ossicles post-op	18 (17%)	38 (30%)	0.02 ^{X2}
Time to residual disease detection (median, months)	12	14	0.3 ^{MW}

Group A: endoscopes were used only for inspection when necessary after microscope-guided cholesteatoma dissection.

Group B: endoscopes and the operating microscope were used to guide dissection of cholesteatoma.

Mills staging of extent of disease is the sum of number of tympanomastoid subsites containing cholesteatoma (33).

^{F} indicates Fisher exact test; ^{MW}, Mann–Whitney test; ^{X2}, χ^2 test.

duration of 4 years postoperatively, revealed no additional cases of residual disease. It is of note that fewer second-stage surgeries were considered necessary after endoscopic dissection was used because of increased confidence in the integrity of matrix removal (61% versus 43% in Groups A and B respectively; $p < 0.01$ χ^2 test).

Group A included 108 patients, in whom endoscopes were only used for inspection, and 127 in Group B in whom endoscopic dissection was used when needed. Residual cholesteatoma was detected in 26 (24%) of Group A ears and 19 (15%) of Group B ears (NS χ^2 test). Of those patients in whom second look surgery was performed, residual disease was found in 39% of Group A (from 66 ears) and 35% of Group B (from 55 ears) (NS χ^2 test).

The proportion of ears with cholesteatoma at different subsites within the tympanomastoid cavity is summarized in Table 2, showing locations of initial and residual cholesteatoma at initial and second-stage surgery, respectively. When considering the primary outcome measure for this study, it can be surmised that cholesteatoma was found in retrotympanic recesses in a total of 106 (45%) of all patients at first surgery. Retrotympanic residual cholesteatoma occurred in only six patients of these patients (5.7%), with no significant reduction in risk by using endoscopic dissection (Fisher exact test). Two cases of retrotympanic disease occurred after endoscopic dissection, one likely arising from under the arch of an intact stapes superstructure and having time to grow into the subpyramidal space as second look surgery was delayed to 19 months for patient preference; the other

TABLE 2. *Number of patients of cholesteatoma and residual cholesteatoma by tympanomastoid subsite*

	Primary Surgery		Second Surgery		Residual		Cholesteatoma
Subsite	n	(% of Total)	n	(% of Second Look)	n	(% Primary)	(% of Second Look)
Group A: microscope dissection ± endoscopic inspection							
Total	108	(100%)	66	(61%)	26	(24%)	(39%)
Middle ear	87	(81%)	54	(82%)	19	(22%)[a]	(35%)
Retrotympanum	45	(42%)	33	(50%)	4	(9%)	(12%)
Attic	71	(66%)	58	(88%)	13	(18%)	(22%)
Antrum	43	(40%)	41	(62%)	3	(7%)	(7%)
Mastoid	23	(21%)	21	(32%)	4	(17%)	(19%)
Group B: microscope ± endoscope dissection							
Total	127	(100%)	55	(43%)	19	(15%)	(35%)
Middle ear	94	(74%)	47	(85%)	10	(11%)[a]	(21%)
Retrotympanum	61	(48%)	29	(53%)	2	(3%)	(7%)
Attic	79	(62%)	55	(100%)	9	(11%)	(16%)
Antrum	43	(34%)	41	(75%)	3	(7%)	(7%)
Mastoid	18	(14%)	14	(25%)	0	(0%)	(0%)

Primary-surgery column indicates the number of patients with cholesteatoma at each tympanomastoid subsite, with percentage of the total number of patients for groups A and B. Second-surgery column indicates the number of patients for each subsite which had a second-stage procedure, with percentage of the number of patients having a second stage of surgery.

The number of patients found to have residual cholesteatoma at second-stage surgery is indicated for each subsite, with proportion given as a percentage by number at each subsite at primary surgery and by number of patients having a second stage.

[a]Significant difference between groups A and B ($p < 0.05$; Fisher exact test).

likely arose from hidden residua within perifacial air cells opening between the facial recess and fossa incudis. Further subgroup analysis revealed no cases of residual cholesteatoma within the sinus tympani in Group B (i.e., after endoscopic dissection), but this was not a statistically significant improvement from Group A in which there were only two cases of residual disease in the sinus tympani. Although the proportions of ears with residual disease were generally lower in Group B, in which endoscopic dissection was available, this difference only reached statistical significance when considering middle ear residua as a proportion of all cases. As shown in Figure 3, Kaplan–Meier survival analysis controlling for the shorter duration of follow-up in Group B confirms a significant reduction in residual disease when endoscopic dissection was available for the middle ear ($p = 0.026$, Kaplan–Meier log rank statistic). This benefit equates to a number needed to treat of nine patients with endoscopic dissection to prevent one case of residual disease in the middle ear. A significant benefit was not found for the mesotympanum when considering the proportion of residual disease in patients who had second look surgery. Kaplan–Meier analysis excluded the possibility that the trend to less residual disease in Group B was secondary to the shorter duration of follow-up.

The majority of cases were completed by an open postauricular approach. Introduction of endoscopic dissection allowed per-meatal surgery to be completed in 23 cases (18% of Group B) compared with none in Group A. There were no significant differences in canal wall preservation or ossicular preservation rates between the two groups.

No complications were attributable to endoscopic dissection. Complications attributable to an open approach included postoperative wound infections or mastoid abscesses in five patients (2%) and four (2%) keloid scars. One transient facial nerve palsy followed a postoperative mastoid abscess in Group B. No activity from the facial nerve monitor had occurred intraoperatively and the palsy could not be attributed to any specific surgical event. No other significant complications occurred.

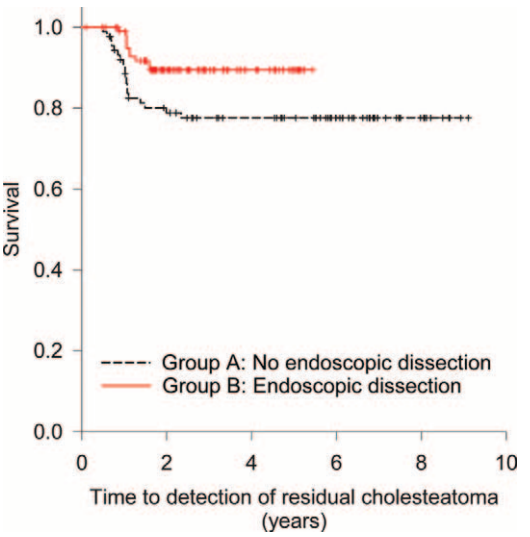

FIG. 3. Kaplan–Meier survival curves showing time to detection of residual cholesteatoma with (Group B) and without (Group A) the availability of endoscopic dissection for cholesteatoma in the middle ear (including meso- and retrotympanum). Endoscopic dissection significantly reduces the risk of residual disease in this location (risk difference = 0.12 at 2.5 yr; n > 54 each group; $p = 0.026$).

DISCUSSION

This series finds that endoscope-guided dissection of cholesteatoma from the middle ear leads to an overall reduction in residual disease with a number needed to treat of around nine cases (being the number of ears in which endoscopic dissection could be used to ensure one less case of residual disease). This benefit was independent of the shorter length of follow-up after endoscopic dissection compared with the other study group in which endoscopes were only used for inspection after microscope-guided dissection. However, no reduction in residual cholesteatoma was found as a result of endoscopic dissection at any other site, including the primary outcome of retrotympanic disease. Furthermore, this analysis does not control for the possibility of occult residual cholesteatoma in patients who had no second look surgery. When restricting analysis to patients in whom the true status of residual disease was evaluated by second look surgery, no statistically significant difference in proportion of patients with residual disease was noted for cholesteatoma at any site.

Endoscopic dissection of cholesteatoma, whether as a part of a totally endoscopic permeatal approach or when combined with the microscope and an open approach, has gained popularity since initial reports in the 1990s (18,19,25,26) but as yet has not been universally shown to reduce residual disease rates (5,17). This is in contrast with the first report of endoscopic cholesteatoma surgery by Thomassin, in which endoscopy reduced the residual disease rate observed at second surgery from 47.7 to 10.7% (18) equivalent to a number needed to treat of 2.7 patients. This dramatic improvement can be attributed to the simultaneous introduction of at least three factors: endoscopic inspection, endoscopic dissection, and specially designed angled instruments (21). The same angled instruments were used in both groups of the current series as was endoscopic inspection and use of the KTP laser. It could be argued that the smaller reduction in residual disease rates noted in the current series reflects the incremental benefit of using endoscopes for primary dissection rather than simply inspecting the dissected site with endoscopes. Although endoscopes were not used at all for dissection in Group A, they were introduced progressively into Group B and used more extensively by the surgeon as expertise increased, so the learning curve may have led to under-representation of the potential benefit of endoscope-guided dissection in experienced hands. The current data will be meaningful to those adopting endoscopic dissection in their practice. In due course, data from outcomes with greater experience including totally endoscopic surgery will be available.

The sinus tympani is widely considered to be a site at high risk of residual disease (12,14,27–29). The comparatively low prevalence in this study is perhaps attributable to careful methodical application of the above techniques. There were only two cases, which both occurred in Group A (i.e., without endoscopic dissection). These two cases can be reported as a sinus tympani residual disease rate of anywhere between 0.8 and 6.1% of patients (i.e., 6.1% of 33 second surgeries for retrotympanic disease in Group A, 1.8% of all of Group A, or 0.8% of all patients). That such a wide range of residual disease rates can legitimately be quoted in one location from a single study illustrates the importance of describing definitions of residual disease clearly. Incomplete removal at the first stage of surgery perhaps resulted from the blind dissection of matrix which occurs when operating with a microscope in this area. Despite the large cohort of patients in this study, no statistically significant benefit was found with endoscope-guided retrotympanic dissection, likely in part because of the small numbers of patients with residual disease, despite the relatively large series. The statistical significance of mesotympanic clearance was also lost when comparing with the smaller denominator of patients undergoing second look surgery.

Endoscopic dissection was introduced during this series because of the surgeon's perception that retrotympanic dissection under direct vision was favorable compared with the alternatives of blind dissection with the operating microscope using palpation (tactile feedback of angled dissectors against bone), mirror-guided dissection, or more extensive bone removal, and then endoscopic inspection to confirm adequate clearance. It is found, for example, in some patients (Fig. 2) that the clear view allows precise removal of small bony septations hidden in the sinus tympani that would otherwise trap matrix remnants. Other benefits of endoscopic dissection that can be recognized by the surgeon include greater confidence of matrix removal with direct observation reducing the need for staged surgery, less radical bone removal to obtain access, and greater feasibility of permeatal surgery. Use of the endoscope through the mastoid is also found to be beneficial for dissecting disease from the medial epitympanum under an intact ossicular chain (23) and the rare requirement of retrofacial dissection (24).

The benefits from advances in the surgical technique perceived by practicing surgeons do not necessarily provide easily measurable improvements in patient-focused outcome measures. Although no dramatic reduction in residual disease was found, some benefits to the patient are demonstrated in this series by the significant increase in permeatal surgery after introduction of endoscopic dissection. Across the time course of Group B, 18% of cases were completed permeatally, with an increasing proportion being totally endoscopic as experience increased. This avoids the risk of significant wound complications observed in 4% of open approaches. Postoperative discomfort and length of stay may also be reduced, and these expectations may lead to the anecdotal impression that children and their parents prefer the option of "incisionless" ear surgery. An additional benefit for the patient has been the reduced requirement of a second stage of surgery, to some extent because of the greater confidence in effective clearance with endoscopic dissection. Although DWI-MRI was

only used sporadically in this series, the observation that scanning has not as yet identified any residual disease missed by lack of surgical exploration suggests that case selection for second-stage surgery has been appropriate to date. Despite this encouraging finding, the rate of occult disease within ears that have not been re-explored inevitably remains unknown.

Variables that may be thought to increase the likelihood of residual disease in this series include the focus on pediatric patients and selection of ICW surgeries (4,6). Children also have a higher proportion of pars tensa retraction cholesteatoma than adults (30), and congenital cholesteatoma is also common in this location (31) so increasing the potential for sinus tympani residua. The narrower pediatric meatus (32) can impair permeatal access though this is offset to some extent with endoscopy by the wider freedom of movement possible with the shorter meatus (24). It is reassuring to note in these circumstances that the techniques used in this series can assure a relatively low risk of residual disease in the sinus tympani even in the pediatric setting.

Canal wall down surgery exenterates some potential hiding places for matrix remnants, but residual disease does still occur, in several reputable series as frequently as with ICW surgery (3,10,12). Removal of the canal wall therefore does not seem justifiable simply for the prevention of residual disease, particularly for children in whom clinic-based cavity management can be challenging and pose a life-long burden. Hearing outcomes may also be better when the canal is preserved (20). Consequently, it is appropriate to consider techniques such as endoscopy that may facilitate prevention of residual disease while preserving the ICW.

Although children are thought to be at high risk of residual cholesteatoma, meticulous dissection with availability of operating microscope, endoscopic inspection, angled instruments, and KTP laser can minimize this risk. Use of endoscopes to guide dissection of the cholesteatoma matrix out of hidden recesses may help to reduce this risk further.

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