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Original Article

Comparison of Total Endoscopic Ear Surgery and Microscopic Postauricular Canal–Wall–Down Approach on Primary Acquired Cholesteatoma

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BACKGROUND: This study aimed to compare total endoscopic ear surgery (TEES) and microscopic postauricular canal-wall-down tympanomastoidectomy (CWD) in cholesteatoma surgery in our clinic.

METHODS: This study included 59 patients, of whom 30 and 29 were operated on with CWD in 2016-2018 and TEES in 2019-2021, respectively and compared regarding intraoperative findings, hearing outcomes, long-term outcomes, and recidivism rates between groups. This study excluded patients in stage IV according to the European Academy of Otology and Neurotology/Japan Otological Society Staging System on Middle Ear Cholesteatoma, aged < 18, with congenital cholesteatoma, who underwent revision surgery.

RESULTS: Two patients in the TEES group had recidivism (6.9%), with recurrent disease observed in both patients and residual disease in none, whereas 3 patients in the CWD group had recidivism (10%), including recurrent disease in 2 and residual disease in 1 patient. Tympanic membrane perforation occurred in 2 (6.9%) and 1 (3.3%) patients in the TEES and CWD groups, respectively. The 2 groups revealed no significant difference in terms of recidivism and perforation rates ($P = 1.000$, $P = .612$). The CWD group had a longer mean operation time (225.54 ± 47.86 minutes) than the TEES group (160.55 ± 24.98 minutes) ($P < .001$). The 2 groups demonstrated no significant difference regarding pre- and postoperative air–bone gap (ABG) and ABG gain ($P = .105$, $P = .329$, $P = .82$, respectively).

CONCLUSION: Total endoscopic ear surgery provides similar results in terms of hearing, recidivism, and long-term outcomes with the microscopic CWD approach. However, the CWD approach is still important, especially in patients in advanced stages.

KEYWORDS: Cholesteatoma, canal-wall-down, endoscopic ear surgery

INTRODUCTION

The pathogenesis of primary acquired cholesteatoma is presented in different theories but with no general agreement.[1,2] Surgery is the only treatment option for cholesteatoma; however, consensus on the ideal surgical approach remains unestablished.

In the past, microscopic postauricular or transcanal approaches were classically used for the treatment of cholesteatoma; however, the endoscopic transcanal approach has been widely adopted recently because of its wider view, lack of a separate incision, and less invasiveness.[3] Endoscopic ear surgery can be performed in patients with advanced stages and complications, and its limitations and indications have changed over time.[4] On the other hand, the postauricular microscopic approaches remain of importance, especially for cases where the cholesteatoma extends beyond the lateral semicircular canal (LSSC).

This study retrospectively compared patients who underwent microscopic postauricular canal-wall-down tympanomastoidectomy (CWD) and total transcanal endoscopic ear surgery (TEES) in our clinic. We aimed to compare the recidivism rates, complication rates, and hearing results between the 2 groups.

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MATERIAL AND METHODS

This study included 59 patients, of whom 30 and 29 were operated on with CWD in 2016-2018 and TEES in 2019-2021, respectively. Before 2019, CWD was routinely performed in all patients with cholesteatoma; however, after 2019, TEES was performed in all patients, excluding those with a limited number of extratemporal complications and those with cholesteatoma extensively spreading to the mastoid. In this study, the patients who underwent CWD before 2019 were compared with those who underwent TEES after 2019. This retrospective study reviewed patient records through our hospital's computer program (Probel, Izmir). The local ethics committee of İzmir Bozyaka Training and Research Hospital approved this study (Decision number: 2022/97). The study was conducted following the Declaration of Helsinki principles. This study included patients aged >18 years, who were operated on for cholesteatoma with CWD or TEES, and whose cholesteatoma was preoperatively confirmed by high-resolution temporal computed tomography (HRCT) and otoendoscopy. This study excluded patients in stage IV according to the European Academy of Otology and Neurotology/Japan Otological Society (EAONO/JOS) Staging System on Middle Ear Cholesteatoma,[5] aged <18, with congenital cholesteatoma, who underwent revision surgery, and without proper postoperative follow-up and adequate data.

This study used the EAONO/JOS Staging System to stage the included cases. The EAONO/JOS Staging System indicated that in stage I, the cholesteatoma is located in the primary site, either the attic (A) for pars flaccida cholesteatoma or the tympanic cavity (T) for pars tensa cholesteatoma, congenital cholesteatoma, and cholesteatoma secondary to a tensa perforation; while the cholesteatoma is found in 2 or more sites in stage II, extracranial complications or pathologic conditions associated with the cholesteatoma are found in stage III, and intracranial complications are present in stage IV. This study excluded individuals in stage IV to ensure greater similarity between the groups.

All patients in the study were operated on under general anesthesia. Endoscopic ear surgery was performed as total TEES, described by Cohen et al[6] as class 3, using 0º and 30º, 3 mm rigid endoscopes (Karl Storz), camera system, and high-resolution monitor (Karl Storz). Tragal cartilage was harvested as graft material, and cartilage and perichondrium were used. Superior and inferior canal incisions were made in the external auditory canal skin at 6 and 12 o'clock positions following local anesthetic infiltration. The epitympanum and mesotympanum were exposed by raising the tympano-meatal flap. The cholesteatoma was removed after the atticotomy with a curette or a drill if required, and ossiculoplasty was performed in case of ossicular chain destruction. The operation was terminated following the tympanic membrane reconstruction with the perichondrium and tympano-meatal flap repositioning. There was no need to switch to using a microscope in the TEES group. In cases where the cholesteatoma extended to the mastoid, transcanal inside-out mastoidectomy and atticotomy were performed in the TEES group to reach the cholesteatoma sac. Only 1 case required endoscopic CWD procedure. In that case, mastoid obliteration and posterior canal wall reconstruction with cartilage and fascia were performed after the removal of cholesteatoma. In other cases in which the posterior canal wall was intact but atticotomy performed, reconstruction was done with tragal cartilage according to the size of the defect. Figures 1A, B, and C show a right attic cholesteatoma and retraction pocket, oval window after the removal of the cholesteatoma, and ossiculoplasty with a total ossicular reconstruction prosthesis (TORP) during TEES.

MAIN POINTS

- Total endoscopic ear surgery (TEES) is a good alternative for microscopic approaches in appropriate cases, improving access to hidden areas such as sinus tympani.
- Total endoscopic ear surgery is a safe approach for the removal of cholesteatoma with low recidivism and complication rates.
- Even complicated cases may be operated on with TEES as experience increases.
- Postauricular microscopic approach is still important, especially for cases where the cholesteatoma extends beyond the lateral semicircular canal.

In the CWD group, the graft was harvested from the temporal muscle fascia or tragal cartilage following the postauricular incision. Subsequently, tympanomeatal flap elevation, cholesteatoma sac exposure, and canal-wall-down mastoidectomy were performed with the microscope (Zeiss OPMI Vario 700, Jena, Germany), and the cholesteatoma was removed. Meatoplasty was performed after ossiculoplasty and tympanic membrane reconstruction with the temporal muscle fascia or tragal cartilage perichondrium.

Age, gender, side, graft material used, and tympanoplasty type were recorded for all patients, as well as postoperative complications, such as facial palsy, vertigo, otorrhea, perforation, and intraoperative features, such as facial nerve dehiscence, labyrinthine fistula, and tegmen defect. Patients' complaints, temporal bone preoperative HRCT images, pre- and postoperative otoscopic and endoscopic examination notes, surgery notes, and pre- and postoperative audiograms were examined. All patients were assessed with pure-tone audiograms and speech discrimination scores preoperatively and 6 months postoperatively. The 4-tone pure-tone average was used to determine hearing levels. The audiological outcomes were reported following the Committee on Hearing and Equilibrium criteria.[7] Diffusion-weighted magnetic resonance imaging (MRI) was used for patients with suspected recurrence and residual cholesteatoma at postoperative examinations.

Our study defined recurrent disease as tympanic membrane/attic retraction detection on clinical examination, and residual disease as cholesteatoma detection behind the intact tympanic membrane on diffusion MRI or second-look surgery, as described by Killian et al.[8] Recidivism was used to define the sum of recurrent disease and residual disease.[9] Auditory success was defined as an air–bone gap (ABG) of ≤20 dB or 10 dB gain in air conduction in postoperative audiometry. Patients with facial paralysis were staged according to the House–Brackmann facial nerve grading system.

Statistical analysis was performed with IBM Statistical Package for the Social Sciences Statistics (SPSS), version 23.0 (IBM SPSS Corp., Armonk, NY, USA). The numerical variables were presented as mean ± SD, while categorical variables were described as numbers and percentages. The Kolmogorov–Smirnov and Shapiro–Wilk tests were used to determine normal distribution following the normality

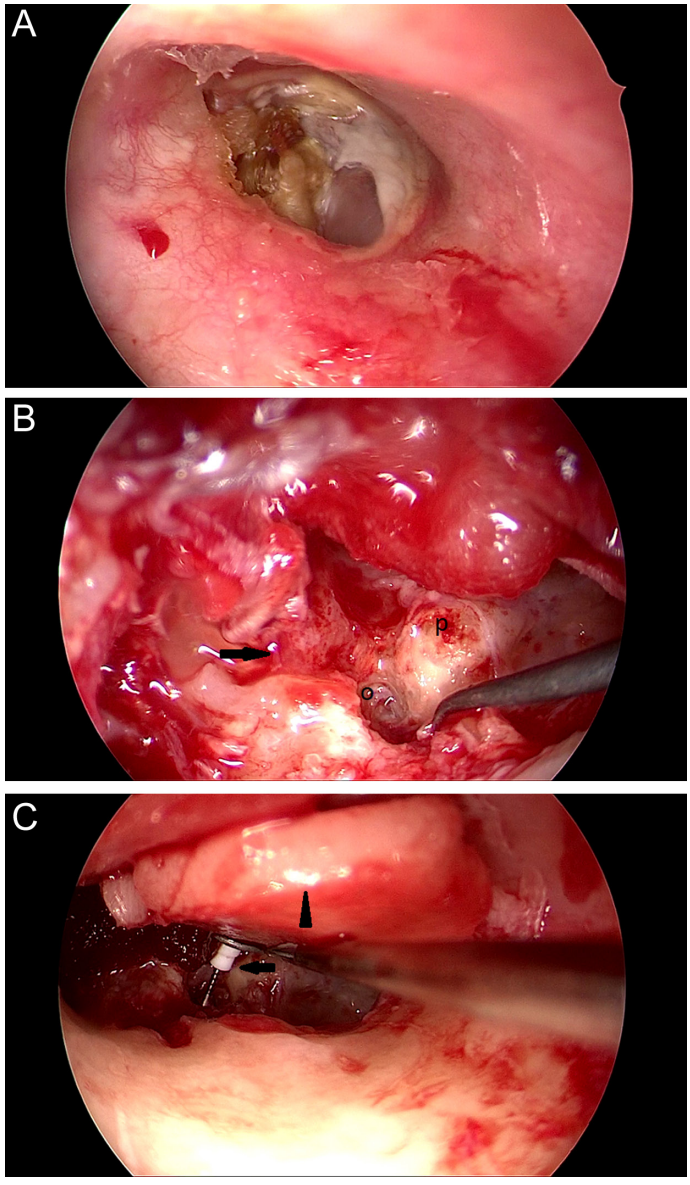

Figure 1. (A) Right ear attic cholesteatoma and retraction pocket eroding the long crus of incus. (B) Following the cholesteatoma removal from the oval window. p: promontorium. o: oval window. Arrow: granulation tissues on the facial canal and epitympanum. (C) Tympanic membrane reconstruction with tragal cartilage and perichondrium, and ossiculoplasty with a titanium TORP. Arrow: TORP. Arrowhead: tragal cartilage. TORP, total ossicular reconstruction prosthesis.

assessment. Student *t*-test, Fisher exact test, and chi-square test were used to compare continuous and categorical variables between the groups as appropriate. Paired t-test was used for paired variables. *P*-values < .05 were considered statistically significant.

RESULTS

The TEES and CWD groups comprised 29 and 30 patients, respectively. Table 1 shows the demographic and clinical characteristics of patients included in the study. The mean age of the TEES and CWD groups was 36.37 ± 14.82 and 42.06 ± 13.03 years, with 12 males (41.4%) and 19 females (58.6%) and 21 males (70%) and 9 females (30%), respectively. The groups demonstrated no difference in terms of mean age (P = .123) but with a significant gender difference (P = .027). The average follow-up period was 33.06 ± 10.80 months (minimum: 19, maximum: 58) and 48.16 ± 13.27 months (minimum: 21, maximum: 84) in the TEES and CWD groups, respectively. The follow-up period was significantly longer in the CWD group (P < .001).

Table 1. Characteristics of Patients

	TEES	CWD	*P*
Age (years) (mean ± SD)	36.37 ± 14.82	42.06 ± 13.03	.123
Sex			**.027**
Male	12 (41.4%)	21 (70%)	
Female	19 (58.6%)	9 (30%)	
Affected side			.218
Right	9 (31%)	14 (46.7%)	
Left	20 (69%)	16 (53.3%)	
Stage[a]			N/A
Stage 1	16 (55.2%)	9 (30%)	
Stage 2	11 (37.9%)	15 (50%)	
Stage 3	2 (6.9%)	6 (20%)	
Stage 4	0	0	
Follow-up period (months) (mean ± SD)	33.06 ± 10.80	48.16 ± 13.27	**<.001**

The bold fold indicates P < .05.
CWD, canal-wall-down tympanomastoidectomy; N/A, not applicable; SD, standard deviation; TEES, total endoscopic ear surgery.
[a]Stage according to the European Academy of Otology and Neurotology/Japan Otological Society Staging System on middle ear cholesteatoma.

The TEES group included 16 (55.2%), 11 (37.9%), and 2 (6.9%) patients with stages 1, 2, and 3, whereas 9 (30%), 15 (50%), and 6 (20%) patients in the CWD group, respectively, according to the EAONO/JOS staging system.

Table 2 shows the intraoperative findings and clinical outcomes of patients. Facial nerve dehiscence was observed in 3 (10.3%) and 9 (30%) patients in the TEES and CWD groups, respectively, during the operation. Lateral semicircular canal fistula was present in 1

Table 2. Intraoperative Findings and Clinical Outcomes

	TEES	CWD	*P*
Ossicular chain reconstruction			N/A
Not done	6 (20.7%)	0(0%)	
Autograft	16 (55.2%)	19 (63.3%)	
PORP	1 (3.4%)	4 (13.3%)	
TORP	4 (13.8%)	7 (7%)	
Bone cement	2 (6.9%)	0 (0%)	
Operation time (minutes) (Mean ± SD)	160.55 ± 24.98	225.54 ± 47.86	**<.001**
Recidivism	2 (6.9%)	3 (10%)	1.000
Perforation	2 (6.9%)	1 (3.3%)	.612
Facial nerve dehiscence	3(10.3%)	9 (30%)	.061
LSSC fistula	1(3.4%)	4 (13.3%)	.353
Postoperative vertigo	1 (3.4%)	1 (3.3%)	1.000
Auditory success	15 (51.7%)	17(56.7%)	.703

The bold fold indicates P < .05.
CWD, canal-wall-down tympanomastoidectomy; LSSC, lateral semicircular canal; PORP, partial ossicular reconstruction prosthesis; SD, standard deviation; TEES, total endoscopic ear surgery; TORP, total ossicular reconstruction prosthesis.

(3.4%) and 4 (13.3%) patients in the TEES and CWD groups, respectively. Following the bone removal with curettes and burrs in the attic part of the external auditory canal, the LSSC fistula was seen with angled endoscopes and accessed with curved instruments in the TEES group. Intraoperative stapes dislocation and perilymph fistula occurred during the operation in 1 (3.3%) patient in the CWD group. In comparison, bleeding occurred in 1 (3.4%) patient in the TEES group due to the high jugular bulb as an intraoperative complication. Bleeding from the high jugular bulb was endoscopically controlled with epinephrine-soaked cottonoids and bipolar electrocautery. Postoperative vertigo was encountered in 1 (3.4%, and 3.3%, respectively for TEES and CWD) patients in both groups. The operation time was 160.55 ± 24.98 and 225.54 ± 47.86 min in the TEES and CWD groups, respectively. The TEES group's operation time was significantly shorter ($P < .001$).

Ossiculoplasty was not performed in 6 (20.7%) patients in the TEES group because the ossicular chain was intact and mobile. Autografts (incus, malleus, and cortical bone) were applied to 16 (55.2%), partial ossicular reconstruction prosthesis (PORP) to 1 (3.4%), TORP to 4 (13.8%), and bone cement to 2 (6.9%) patients in the TEES group. Autografts were used in 19 (63.3%), PORP in 4 (13.3%), and TORP in 7 (7%) patients in the CWD group. Tragal cartilage perichondrium was used as a graft for tympanic membrane reconstruction in all patients (100%) in the TEES group and perichondrium in 17 (56.7%) and temporal muscle fascia in 13 (43.3%) patients in the CWD group.

The recurrent disease and recidivism were encountered in a total of 2 (6.9%) patients in the TEES group, with no residual disease (0%) during the follow-up period. Recidivism was observed in 3 (10%) patients in the CWD group, including residual disease in 1 patient (3.3 %) and recurrent disease in 2 patients (6.6 %). In the CWD group, an epitympanic cholesteatoma was detected in 1 patient and tympanic membrane retraction occurred in 1 patient. No significant difference was observed between recidivism rates between the 2 groups ($P = 1.000$). Perforation occurred in 2 (6.9%) patients in the TEES group, while perforation occurred in 1 (3.3%) patient in the CWD group, with no significant difference ($P = .612$) (Figure 2).

Preoperative grade 5 facial paralysis of 1 patient in the TEES group completely resolved postoperatively. One of the 2 patients who had preoperative facial palsy in the CWD group was preoperatively grade 3 and completely recovered postoperatively. However, the other patient regressed from preoperatively grade 5 to postoperatively grade 2.

Table 3 shows the mean pure-tone preoperative and postoperative air conduction and bone conduction thresholds, ABG, and ABG closure (preoperative ABG–postoperative ABG) of the patients pre- and postoperatively. No difference was observed between the preoperative bone conduction pure-tone thresholds between the 2 groups ($P = .135$), but a significant difference was found between the preoperative air conduction thresholds ($P = .031$). A significant difference was found between the postoperative bone conduction and air conduction thresholds between the 2 groups ($P = .038$, $P = .035$, respectively). No significant difference was found in pre- and postoperative ABG and ABG closure ($P = .105$, $P = .329$, $P = .82$, respectively). A significant difference was found between the preoperative and postoperative word recognition score (WRS) between the 2 groups ($P = .005$, $P = .005$).

No statistically significant difference was found between preoperative and postoperative paired measurements of both groups' bone conduction thresholds, air conduction thresholds, WRS, and ABG ($P > .05$). Auditory success was achieved in 15 (51.7%) and 17 (56.7%) patients in the TEES and CWD groups, respectively, with no significant difference between the 2 groups ($P = .703$).

DISCUSSION

Our study revealed no difference between the TEES and CWD groups regarding hearing reconstruction and complication rates. Total endoscopic ear surgery is very useful and effective, especially for cases in the early stages. The postauricular and transcanal microscopic approaches were used extensively in ear surgery in our clinic before 2019. On the other hand, endoscopic ear surgery has been increasingly used for tympanoplasty, stapes surgery, and cholesteatoma since 2019.

Canal-wall-down tympanomastoidectomy effectively treats cholesteatoma, but it can disrupt normal anatomy and physiology. The

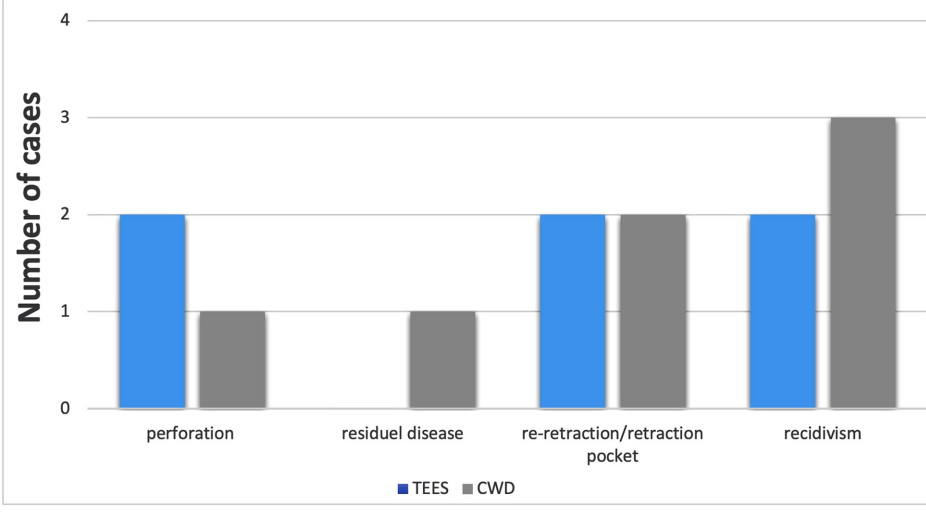

Figure 2. Long-term outcomes. CWD, canal-wall-down tympanomastoidectomy; TEES, total endoscopic ear surgery.

Table 3. Comparison of Preoperative and Postoperative Audiometric Outcomes

	TEES	CWD	*P*
	Mean ± SD	**Mean ± SD**	
Pre-op bone conduction PTA	25.43 ± 17.04	32.15 ±17.04	.135*
Post-op bone conduction PTA	23.21 ± 17.34	33.79 ± 19.86	**.038***
Pre-op air- conduction PTA	48.79 ± 25.59	61.87 ± 19.53	**.031***
Post-op air conduction PTA	46.50 ± 26.65	61.79 ± 26.17	**.035***
Pre-op ABG	23.35 ± 14.60	29.71 ± 15.05	.105*
Post-op ABG	23.31 ± 13.25	26.81 ± 13.32	.329*
ABG gain	0.65 ± 13.00	1.49 ± 15.59	.82*
Pre-op WRS	85.78 ± 22.42	86.67 ± 22.68	**.005****
Post-op WRS	78.80 ± 15.36	76.80 ± 18.92	**.005****

Values on bold indicate statistical significance ($P < .05$).
ABG, air–bone gap; CWD, canal-wall-down tympanomastoidectomy; PTA, pure-tone audiometry; SD, standard deviation; TEES, total endoscopic ear surgery; WRS, word recognition score.
*Student *t*-test.
**Mann–Whitney *U*-test.

posterior canal wall may be reconstructed, but it does not always give successful results. Canal-wall-down tympanomastoidectomy often causes a cavity that cannot clean itself and avoidance of water sports. Canal wall-up mastoidectomy (CWU) with a microscopic postauricular approach is another alternative, where a separate incision is needed, and posterior tympanotomy may be required to access hidden areas, such as sinus tympani and facial recess. The microscopic transcanal or endaural approach is effective in limited cholesteatomas, but its angle of view is less than that of endoscopes. Healthy mastoid cells and mucosa are also needed for opening the ventilation routes, and gas exchange can be disrupted in transmastoid approaches.[2] Healthy mucosa is protected and obstructions in ventilation routes can be opened during surgery with the endoscopic transcanal approach.

Another disadvantage of microscopic CWU approaches is their higher recidivism rates than CWD. Recidivism rates after CWU techniques range from 9% to 70% while recidivism rates after CWD vary between 4% and 17% in the literature.[9-12] Killen et al[8] compared microscopic CWU and EES and reported that residual disease was 17% in both groups and disease recurrence by clinical examination was 18% and 20% in the EES and CWU groups, respectively. Alicandri-ciufelli et al[3] revealed residual disease at 20% and recurrence at 12% and included the exclusive endoscopic approach and the combined approach (endoscopic/microscopic). The retrospective EES series by Glikson et al[13] reported 10% residual disease and 8.3% recurrence. Magliulo and Iannella[14] compared the endoscopic and microscopic approach consisting of 80 patients with attic cholesteatoma and reported no recurrence in either group. Our study revealed a 6.9% and 10% recidivism rate in the TEES and CWD groups, respectively. The recidivism rate was lower in the TEES group although with no significant difference.

Das et al[15] compared the transcanal microscopic group with the middle ear structural visibility index (MESVI) in terms of exposure and access to hidden areas with the endoscopic transcanal approach and revealed better exposure in the endoscopic group. Wu et al[16] also found higher MESVI in the endoscopic group. Better visualization of hidden areas, such as sinus tympani, which is difficult to see with microscopic approaches, with the endoscope provides better clearance of cholesteatoma. We managed to remove the cholesteatoma in a minimally invasive way in the TEES group, often without the need for bone removal.

The extent of cholesteatoma is essential in the choice of surgery. Microscopic approaches and canal wall-down tympanoplasty retain their significance, especially in cases with extensive cholesteatoma accompanied by complications, such as LSSC fistula. Conversely, publications in the literature state that EES can be applied in patients with complications at present.[4,17] Our endoscopic case series revealed that 1 patient had preoperative grade 5 facial palsy, and 1 had an LSSC fistula. In general, EES is successfully performed in patients with limited attic or pars tensa cholesteatoma and complications without extensive cholesteatoma, even with LSSC fistula.

Magliulo and Iannella[14] compared EES and the microscopic approach in treating attic cholesteatoma and revealed that the microscopic approach is faster (87.8 min and 69.7 minutes, respectively). Similarly, Das et al[15] indicated that the endoscopic approach is faster than the microscopic transcanal approach (122.833 ± 16.69, 143.94 ± 9.97, respectively). Our study revealed that the operative time was shorter in the TEES group (160.55 ± 24.98 and 225.54 ± 47.86, respectively). Performing external incision, meatoplasty, and posterior canal wall reconstruction in the CWD group may prolong the operation time. Additionally, the surgeon's experience stands out as an important factor in operation time. Operation time may be prolonged if good bleeding control is not performed due to one-handed manipulation in endoscopic surgery. The operation time may be extended due to the wider spread of cholesteatoma in patients with advanced stages.

Wu et al[16] revealed less postoperative pain in EES compared to the microscopic ear surgery (MES) group. Kakehata et al[18] compared TEES with MES and revealed that TEES was associated with less postoperative pain and less non-steroidal anti-inflammatory drug use. Choi et al[19] and Magliulo et al[14] indicated that the reduced pain in the TEES group can be attributed to the absence of drilling on the mastoid bone, with no external incision.

Das et al[15] revealed no significant difference in terms of hearing results between ABG closure in their study investigating endoscopic and microscopic transcanal approaches. Similarly, Bae et al[20] revealed the hearing improvement to be 6.67 dB in the EES group and 1.75 dB in the microscopic group. However, they did not reveal a significant difference between the 2 groups. Moreover, other studies in the literature revealed no significant difference in hearing gains between the EES group and the microscopic CWU group.[8,16] Additionally, our study revealed no significant difference in the hearing gains between the 2 groups.

The one-handed technique, lack of 2-dimensional view, and depth perception are major disadvantages of endoscopic surgery.[21] Endoscope-holding systems have been developed, but their use in cholesteatoma surgery is minimal.[21] Bleeding is another problem, which is crucial to provide hemostasis. Hypotensive anesthesia by the anesthesia team, topical vasoconstriction, and the use of epinephrine-soaked cottonoids are effective in controlling bleeding. Our

series demonstrated severe bleeding due to a high jugular bulb in 1 patient in the endoscopic group, and bleeding was endoscopically controlled. We had no bleeding-related complications, except for the previously mentioned patient. Thermal tissue damage is a complication that can be encountered at the beginning of the learning curve, especially in relation to experience. It can be prevented by intermittent washing and keeping the lens tip away from the tissue.[13,21,22]

Our study has some limitations. First, the groups were not randomized. Second, the TEES group may experience more recidivism over time due to the varying follow-up periods between the 2 groups. Third, including the CWU group in the microscopic group would have yielded more accurate results. However, the study included cases that underwent CWD because microscopic cholesteatoma surgery was performed with CWD in our clinic. Last, this is a retrospective study.

Total endoscopic ear surgery has come to the fore recently for reasons, such as being more minimally invasive, preserving normal physiology, less postoperative pain, and shorter recovery time. However, the microscopic postauricular approaches and CWD remain important in cases with extensive cholesteatomas extending to the mastoid and in cases with complications. The use of the appropriate technique with the right patient will increase success rates postoperatively. Prospective randomized studies with a larger number of patients are needed on this subject.

Data Availability Statement: The datasets that were used and/or analyzed during the present study are available by the corresponding author upon a reasonable request.

Ethics Committee Approval: This study was approved by Ethics Committee of İzmir Bozyaka Training and Research Hospital (Approval number: 97, Date: June 8, 2022).

Informed Consent: Informed consent was obtained from the patients who agreed to take part in the study.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept – M.E.Z., A.D.; Design – M.E.Z., M.E.C.; Supervision – A.D.; Materials – B.Y., A.D.; Data Collection and/or Processing – B.Y.; Analysis and/or Interpretation – M.E.C., M.E.Z.; Literature Search – M.E.Z.; Writing – M.E.Z.; Critical Review – A.D.

Declaration of Interests: The authors have no conflicts of interest to declare.

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