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Minimally Invasive Transcanal Endoscopic Ear Surgery

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Abstract

Endoscopes have rapidly become widely accepted in the performance of ear surgery. Current chapter describes surgical technique and benefits and limitations for endoscopic eradication of cholesteatoma, endoscopic tympanoplasty, endoscopic stapedotomy and endoscopic cochlear implantation.

Minimally invasive endoscopic and endoscope-assisted surgical techniques are increasingly being employed in the surgical management of cholesteatoma. Endoscopic surgeries distinctly reduced residual cholesteatomas and the indications of later tympanotomy thanks to the good visualization of residual cholesteatoma sites, such as the anterior and posterior epitympanic spaces, sinus tympani, facial recess, and hypotympanum. Minimally invasive transcanal endoscopic approach can be applied as for primary cholesteatomas as well as for revision of CWU cases, when residual/recurrent cholesteatoma is confined to the middle ear, and in CWD or radical cavities, when residual/recurrent disease is hidden in the supratubal recess, sinus tympani or under pseudo-membrane in the large mastoid cavities.

The use of endoscopes in myringoplasty is especially helpful in patients with narrow external canals, anterior defects and bone overhang, when perforation’s margins are barely, if at all, visible under a microscope.

The transcanal endoscopic stapedotomy can be beneficial in improving the visibility and accessibility of the stapes and the oval window niche, avoiding manipulation of the chorda tympani nerve and blind fracture of the stapedial crurae.

An endoscopic cochlear implantation involves entering the middle ear by means of endoscopic transcanal tympanotomy and insertion of the electrode array into the scala tympani via the round window under direct endoscopic control. The main benefits of the endoscopic transcanal approach to cochlear implant are improving the visibility...
and accessibility of the round window membrane, obviating the need to divide the chorda tympani nerve in order to obtain adequate exposure of the middle ear structures, and eliminating the risk of the facial nerve injury since it is not in the direction of drilling.

**Keywords:** endoscopic surgery, approach, tympanoplasty, stapedectomy, cochlear implant

1. Introduction

The introduction of endoscopes completely changed the surgical approach to the middle ear pathologies. Management of cholesteatoma continues to pose a surgical challenge, and the choice of surgical technique depends on the extension of the disease, the surgeon's own experience and skills, published data, and the patient's socioeconomic circumstances. Minimally invasive endoscopic and endoscope-assisted surgical techniques are increasingly being employed in the surgical management of cholesteatoma.

2. Endoscopic surgery for cholesteatoma

Exclusive transcanal endoscopic approach (TEA) can be used for the resection of a primary cholesteatoma or for endoscopic revision of an accessible residual/recurrent cholesteatoma in the post-mastoidectomy cavity. In endoscope-assisted ear surgery (EAES), the endoscopes are introduced intraoperatively for completion of surgery performed under a microscope.

Endoscopic ear surgery (EES) and EAES distinctly reduced residual cholesteatomas and the indications of later tympanotomy thanks to the good visualization of residual cholesteatoma sites, such as the anterior and posterior epitympanic spaces, sinus tympani, facial recess, eustachian tube and hypotympanum [1-10]. Moreover, it was found that retraction pockets extending into the facial recess may be more readily removed by using endoscopes than by converting to an intact canal wall mastoidectomy with a facial recess approach [10,11].

The vast majority of cholesteatomas starts to develop in the middle ear and its extensions, and only later involves the mastoid cavity. Thus, the most logical access to a cholesteatoma has not yet advanced to the mastoid is the transcanal approach. However, the endoscopic approach depends on the experience and skills of the surgeon. In addition, otosurgeons are accustomed to using both hands at surgery while in the EES one hand is occupied with the endoscope and the other performs the manipulations for the eradication of the pathology, suctioning, hemostasis and subsequent reconstructions [10].

A cholesteatoma is defined as being accessible with TEA when it does not extend beyond the level of the lateral semicircular canal [11]. In case of cholesteatoma inaccessible even with
angled instruments under direct vision of angled endoscopes traditional mastoidectomy is performed. The optimal surgical approach to residual/recurrent cholesteatoma is a controversial issue since residual lesions can be missed and cholesteatoma tends to recur despite the variety of surgical options. The common sites of residual lesions and recurrences are sinus tympani, attic, anterior epitympanic space, facial recess and the supratubal region, and they can all be visualized and accessed using the TEA [3,5-7,12-26].

Preoperative assessment includes otoscopy and pure tone audiometry in all patients. Recent studies have shown that non-echo planar (non-EPI) diffusion-weighted (DW) magnetic resonance imaging (MRI) can accurately predict the presence and extent of cholesteatoma in both primary and residual cases [27-31]. The size of lesion determined by the non-EPI DW images correlated well with intra-operative findings, with error margins lying within 1 mm [28-31]. Non-EPI DW MRI can distinguish cholesteatoma from other tissues and from mucosal reactions in the middle ear (ME) and mastoid, and it can also demonstrate the extent of the lesion [27-31]. Thus, we prefer performing the non-EPI DWI MRI prior to primary cholesteatoma surgery as well as before revision procedures [31]. Non-EPI DW images allow avoiding the irradiation, and this point is extremely important for all patients, especially children [32]. The choice of approach as in primary as well as in revision surgery depends on the extent of disease and on the preoperative otoscopic and radiological findings (Figures 1-8). We already found that cholesteatoma < 8 mm in size and confined to the ME or its extensions can be eradicated with a minimally invasive TEA, while endoscope-assisted retroauricular mastoidectomy is the preferable procedure for larger lesions [31].

Many primary and some residual/recurrent lesions can be accessed with endoscopes. However, prior to undergoing the intervention, all the patients are informed of the possibility of extending their surgery to a transmastoid approach in the event that the cholesteatoma could not be satisfactorily eradicated by the transcanal endoscopic approach.

2.1. Surgical technique

The operating room setup, instrumentation and surgical technique were similar to those proposed by Tarabichi [11-14]. Rigid 3-mm diameter, 0°, 30° and 45° endoscopes, angled picks and forceps and routine otologic micro-instruments are used for all the TEA procedures (the list of the instruments can be seen in the web site of the International Working Group on Endoscopic Ear Surgery). A wide posterior tympanomeatal flap was elevated via the external auditory canal and then transposed inferiorly in cases of cholesteatoma situated in the middle ear (ME) under a closed or perforated tympanic membrane (TM). If needed, the scutum was removed with a bone curette until the cholesteatoma extension and the mastoid antrum could be visualized. The malleus and incus are removed when they are involved in the cholesteatoma or when they limit access to cholesteatoma in the anterior or posterior epitympanic space. When present, the stapes is left intact and meticulously and gently cleaned when it is involved with the cholesteatoma. Scutumplasty is done with tragal cartilage, and TM defects are reconstructed with the palisade technique and perichondrium in the relevant cases. In certain cases, cholesteatoma can be assessed and removed using the endoscopes directly from the radical cavity or from the mastoid cavity remaining after a canal-wall-down (CWD) procedure.
An operating microscope is used when the surgeon needs both hands to complete the removal of the cholesteatoma from the facial nerve or stapes footplate, and occasionally for ossicular chain reconstruction (OCR). Operative time depends on the extension of the disease, ossicular involvement in cholesteatoma and whether OCR is required.

Post-operative follow-up recommendations included repeated clinical examinations, and all the patients are encouraged to perform non-EPI DWI MRI at approximately one year following surgery. Second-look procedures or secondary OCRs usually are planned according to the clinical and MRI findings and the postoperative audiometric results. Whatever the etiology of cholesteatoma, scutumplasty with cartilage yielded good results in terms of prevention of postoperative retraction pockets.

EES has several advantages as compared to traditional mastoidectomy. This is a minimally invasive surgical approach in terms of incision, bleeding, drilling, postoperative pain and healing, and it is curative in terms of the radical eradication of the pathology including hidden areas poorly accessible and thus overlooked by a microscope. In the TEA, bony work can be circumvented leading to a decrease of possible intraoperative complications. This is functional surgery since scutumplasty and reconstruction of the tympanic membrane lead to conditions favorable to the introduction of the water into the external auditory meatus, and primary ossicular chain reconstruction can be done at the same setting. The patient can be discharged on the same day or on the day after surgery, and the hospital stay can be shortened compared to at least 2 days postoperative admission for uneventful retroauricular mastoidectomy. In contrast to mastoidectomy, the EES can be performed under local anesthesia, and there is no need for postoperative wound care. Post-EES healing time is usually painless and is shorter compared to mastoidectomy. The set-up time and costs of the endoscopic procedure are comparable with mastoidectomy and even less since there is no need in drilling, cotton material and cauterization for hemostasis, suturing of the wound, bandage and postoperative wound care. The endoscopes and video-cameras are in routine use for endoscopic sinus surgery and thus are already available in most departments. The routine otologic micro-sets should be completed with some angled picks and forceps.

Although mastoidectomy is a procedure that is familiar to all otosurgeons, it can be complicated by accidental trauma to middle cranial fossa dura, dural exposure in the tegmen and sinodural angle, and brain herniation into the mastoid cavity. Dural and tegmen defect due to dural tears and cerebrospinal fluid leakage may result in pneumocephalus, brain herniation, subdural empyema, epidural or brain abscess [33-39]. In addition to primary cholesteatoma cases, minimally invasive TEA can be applied for revision of canal-wall-up (CWU) cases, when residual/recurrent cholesteatoma is confined to the middle ear, and in CWD or radical cavities, when residual/recurrent disease is hidden in the supratubal recess, sinus tympani or under pseudo-membrane in the large mastoid cavities, when access to cholesteatoma via external ear canal is difficult using the operating microscope due to the limited axis of work [24]. The TEA can be one of the options for eradication of residual/recurrent lesions in addition to traditional CWU and CWD techniques. The TEA avoids drilling in the mastoid region, thereby obviating the risk of dural injury and postoperative intracranial complications. Pre-operative non-EPI DWI MRI can predict cholesteatoma extension and is essential in planning revision surgery.
for residual/recurrent lesions. Screening with non-EPI DWI MRI at one year postoperatively is highly recommended to rule out residual disease, especially in patients who underwent CWU mastoidectomies.

**Figure 1.** A view (with a 0° endoscope) of a left ear primary retraction pocket cholesteatoma.

**Figure 2.** Non-EPI DW coronal images of the same patient presented in Figure 2 shows a 7-mm hyperintense lesion in the left attic (it was managed with TEA).
Figure 3. Endoscopic view of right ear primary retraction pocket cholesteatoma extended to the mastoid cavity.

Figure 4. Non-EPI DW coronal images of the same patient presented in Figure 3 shows a hyperintense lesion occupied whole mastoid cavity (it was managed with CWD mastoidectomy).
Figure 5. Endoscopic view of right ear residual cholesteatoma presented 1 year after CWU mastoidectomy.

Figure 6. Non-EPI DW coronal images of the same patient presented in Figure 5 shows a 6-mm hyperintense lesion in the right attic (it was managed with TEA).
3. Endoscopic myringoplasty

Recently, different endoscopes have been used in the performance of ear surgery in general and myringoplasty in particular, and the surgical success of endoscope-assisted myringoplasty ranges between 80 and 100 % [40-46]. Myringoplasty can be technically difficult, especially in pediatric patients, due to the narrowness of the external auditory canal and the generally small
size of the ear [46]. Moreover, temporalis fascia grafts and myringoplasties for anterior perforations are more likely to fail in children [40-43,47,48]. Surgical management of anterior perforations requires total exposure of the anterior angle, but a microscope may fail to provide a view of the anterior edge in 73% of perforations that can, however, be entirely exposed with an endoscope [44]. As a result, drilling of the anterior part of an external auditory canal is usually unavoidable for the repair of anterior perforations when only a microscopic approach is employed [47].

3.1. Surgical technique

Transcanal endoscopic myringoplasties are performed under local or general anesthesia with a chondro-perichondrial graft that is harvested from the tragus and placed medial to the tympanic membrane remnants, utilizing the underlay technique and 14-mm length, 3-mm diameter, 0° and 30° endoscopes (Figures 9 and 10). Tympanomeatal flap is elevated using the 0° endoscope in all the cases, and the 30° endoscope can be utilized for better visualization of anterior perforations. The margins of perforations are freshened using the 0° or 30° endoscopes. A microscope is used for removal of the sclerotic plaques and releasing adhesions surrounding the ossicles when bimanual manipulations are needed.

![Endoscopic view of a large anterior perforation in the right tympanic membrane.](http://dx.doi.org/10.5772/60551)

We found that an endoscope is very effective in ensuring satisfactory approximation of graft material to the perforation margins in small, medium-sized, large and subtotal perforations as well. The transcanal endoscopic myringoplasty had, in our hands, a 100% rate of surgical success for closure of tympanic membrane defects. This technique is especially helpful in patients with narrow external canals, anterior defects and bone overhang, when perforation's
margins are barely, if at all, visible under a microscope. The choice of chondro-perichondrial graft material and the meticulous removal of myringosclerotic plaques can enhance the surgical outcome of endoscopic myringoplasty performed by an experienced otologist.

Figure 10. Endoscopic view of the same ear as in Figure 9 at the end of the myringoplasty.

4. Endoscopic stapedotomy

Stapedotomy can be technically difficult and challenging due to anatomic variations in size, configuration, shape or irregularity of the external ear canal. The stapes and oval window niche (OWN) can be obscured by the scutum. Excessive removal of the bone for better visualization of the middle ear (ME) structures can rarely result in subluxation of the incus [49-51]. When the posterior part of the bony annulus is removed to visualize the stapes, the chorda tympani nerve (CTN) can be occasionally touched, stretched, manipulated or transected and result in 20-60% of postoperative taste disorders or tongue symptoms [52-57]. The existing data indicate that the CTN should be preserved whenever possible, especially if surgery is bilateral [53,54,57,58]. Bilateral CTN damage can result in transient or permanent bilateral ageusia of the anterior two-thirds of the tongue, as well as a decreased resting salivary flow rate. In addition, the patients may suffer from transient or persistent, distressing xerostomia or tactile dysguesia [58-60]. However, damage to the CTN and subluxation of the ossicles or stapes fracture significantly decreases in the hands of an experience surgeon.

Endoscopic stapedotomy was introduced in our department with the intent to avoid injury to the CTN when attempting to achieve visibility of the ME structures. The CTN was preserved in all cases, and our preliminary audiometric results were comparable with the others [61-63].
4.1. Surgical technique

The position of the patients is the same as for routine otomicroscopic ear surgeries. The external ear canal is injected with lidocaine 1% with 1:100,000 epinephrine. A fully endoscopic transcanal procedure was undertaken using rigid endoscopes 3 mm diameter, 14-cm length, 0° and 30°. Angled picks and curved scissors and forceps are used in addition to the routine otologic micro-instruments. A posterior tympanomeatal flap is elevated transmeatally with the 0° endoscope and then transposed anteriorly. All the surgeries are performed with a 0° endoscope, while a 30° endoscope can be required to better visualize the OWN, the anterior crus of the stapes, the tympanic portion of the facial nerve and the pyramidal eminence in some cases due to bony overhang in the posterior tympanum. Stapes fixation is confirmed by gentle testing of ossicular chain mobility. The stapes tendon is cut with curved micro-scissors and the stapes is separated from the incus in the incudo-stapedial joint. The anterior and posterior stapedial crus are carefully fractured and the superstructure is removed. The distance between the footplate and medial surface of the long process of the incus was measured to determine the required prosthesis size. The hole in the footplate is created with a Skeeter microdrill using a 0.5-mm diameter diamond burr. A platinum/fluoroplastic piston prosthesis (0.4-mm diameter, 4.5/4.75-mm length) is placed into this hole and fitted along the long process of the incus (Figures 11-14). The appropriate ossicular chain movement with the replaced stapes is ensured by malleus palpation. The tympano-meatal flap is repositioned, and the external auditory canal is filled with Gelfoam® soaked in ear drops containing antibiotics.

Figure 11. Endoscopic view of the right middle ear after an elevation of the tympano-meatal flap. Good access to the stapes and oval window niche was achieved without removal of the scutum and without touching the chorda tympani nerve.
Figure 12. Endoscopic view of the right ear: cutting of the stapedius.

Figure 13. Endoscopic view of piston prosthesis placed in the hole that was created in the footplate and covered with a small piece of fat.

The possible benefits of ES are excellent visibility and accessibility of the stapes and the OWN, and avoiding manipulation of the CTN and blind fracture of the stapedial crurae. Assistance
in using the operating microscope can be required when there is the need for two-hand manipulations for proper placing and coupling of the prosthesis, especially during the surgeon’s initial endoscopic procedures. Finally, right-handed surgeon (L.M.) found that the axis of work was initially more comfortable when performing surgery on right ears and that the relative difficulty in creating a hole in the footplate and positioning the prosthesis in left ears could be overcome with more training.

Transcanal fully endoscopic stapedotomy can be utilized in patients with unfavorable external or middle ear anatomy, in candidates for revision or bilateral stapedotomy, in patients with already impaired taste sensation, with food-, smell- or taste-related occupations, and in those for whom the taste of food contributes appreciably to their quality of life.

5. Endoscopic cochlear implantation

Recent developments in cochlear implant electrode array design and modifications of surgical techniques have resulted in improved post-implantation performance by minimizing intracochlear damage during implantation [64]. However, electrodes and the surgical procedures used for their insertion still produce intracochlear trauma. An optimal site for cochleostomy in terms of avoiding insertion trauma during cochlear implantation (CI) has not yet been established. Some authors recommend the insertion of the electrode array through the cochleostomy corresponding to the antero-inferior margin of the round window membrane (RWM), while others contend that atraumatic insertion can be achieved directly through the RWM by removing the antero-inferior overhang of the RW niche, drilling down the crista fenestra, and incising the most lateral aspect of the RWM before insertion [64]. Regardless of the site of electrode insertion, the first step is achieving adequate exposure of the RWM in order to facilitate minimally invasive surgery. However, the topographical relationships among the facial nerve (FN), CTN, and RW showed that the widest route of approach through the facial recess (FR) frequently did not point directly towards the RW, but rather towards the basal turn at the promontory [65]. RWM insertion using the FR approach can be more challenging in pediatric patients, with the visibility of the RWM being limited in 11%-22 % of children even after an "optimal" posterior tympanotomy. An extended membranous cochleostomy or conventional bony cochleostomy may be required in some of these cases [66]. Moreover, the access to the RWM may be compromised in an FR approach due to the bony overhangs, abnormal course of the FN, jugular bulb location or abnormalities, anteriorly located sigmoid sinus, narrow FR and an undeveloped mastoid [67-70].

An endoscopic CI involves entering the ME by means of endoscopic transcanal tympanotomy and insertion of the electrode array into the scala tympani via the RW under direct endoscopic control [71,72]. Limited access to the ME structures can result in electrode misplacement, damage to the FN and injury to the CTN when a CI is carried out with an FR approach [73-78]. Indeed, bilateral sacrificing of the CTN due to a narrow FR in bilaterally implanted children can lead to morbidity that has not yet been investigated in depth. One of the reasons for incorrect electrode insertion using the microscopic approach through the FR can be the
presence of a wide subcochlear canaliculus that could be mistaken with the RW niche [72]. Our experience as well as findings of our colleagues showed that the direct visualization of the RWM using a transcanal endoscopic approach permits electrode insertion through the RWM into the scala tympani with less drilling of the niche comparing to the FR technique [72].

5.1. Surgical technique

The procedures are performed with the patients under general anesthesia. The position of the patients, the skin incisions and the drilling of the implant wells are the same as for routine otomicroscopic CI. The external ear canal is injected with lidocaine 1% with 1:100.000 epi-nephrine. Cortical mastoidectomy until visualization of the incus is performed. A 6 o’clock vertical incision is made in the meatal skin, and a posterior tympano-meatal flap is elevated transmeatally to expose the ME cavity using a rigid 0° endoscope 3 mm in diameter and 14 cm in length held manually, and then transposed anteriorly. The CTN and body of the incus are exposed. Visualization of the incus body serves as a target for drilling and preventing injury to the FN which is located medial to it. The RWM is incised, and the electrodes are passed through the tunnel from the mastoid to epitympanum, medial to the CTN and lateral to the incus into the RW (Figure 15). The tympano-meatal flap is repositioned, and the external auditory canal is filled with Gelfoam® soaked in ear drops containing antibiotics. The surgical procedure can be modified in some procedures as follows: instead of inserting the electrodes through a tunnel that could limit the angle of insertion, an open groove is drilled starting superiorly and laterally to the CTN and ending in the mastoid region. The electrodes are passed through the groove medially to the CTN and laterally to the incus into the scala tympani through the RW, which is then covered with a small piece of temporalis fascia. The groove is filled with bone dust that had been collected during the drilling of the implant well, and covered with a large piece of fascia prior to repositioning of the tympano-meatal flap, aiming to prevent extrusion of the electrode array into the external auditory canal or tracking of the canal skin into the mastoid with cholesteatoma formation. All patients routinely receive intravenous ceftriaxone intra-operatively, followed by a course of oral cephalixin during the first postoperative week.

Fully endoscopic CI with complete electrode insertion via the RW was found more feasible for insertion of Concerto (Medical Electronics, Innsbruck, Austria) electrode followed by HiRes90K (Advanced Bionics Corporation, California, USA) and Nucleus 24 Contour Advance (Cochlear Corporation, Australia) [71].

The main benefits of the TEA to CI are improving the visibility and accessibility of the RWM, obviating the need to divide the CTN in order to obtain adequate exposure of the ME structures, and eliminating the risk of FN injury since the FN is not in the direction of drilling. The open groove technique was used several times in the past by the first author in cases of low-set dura and anteriorly based sigmoid sinus. A follow up of these patients showed that there is no protrusion of the electrode over a period of at least 5 years when the groove is filled with bone dust and is covered with intact skin.

A good knowledge of the endoscopic anatomy of the middle ear and a good practical knowledge of the endoscopic technique are essential to ensure a safe endoscopic CI with good
outcome. An assistance of another surgeon may be required for holding the endoscope during the insertion of the electrode by a right-handed surgeon in the right cochlea and in removal of stylet, when relevant. Moreover, modern electrodes designed for hearing preservation by all companies are very thin and there is the need in bimanual manipulations for their safe and slow insertion requiring the help of an assistant in holding the endoscope. An angle of electrode insertion seems more comfortable in the transcanal approach compared to the epitympanic root of insertion. Right-handed surgeons (e.g. the first author) found that the axis of work was initially more comfortable when performing surgery on left ears and that the relative difficulty in electrode insertion in right ears could be overcome with more training [71]. Complete electrode insertion is achievable into the scala tympani via the round window both in children and adults. This technique can be used as a first surgical option or complementarily to the traditional posterior tympanotomy approach in patients with undeveloped or anomalous mastoid, narrow facial recess, anteriorly based sigmoid sinus, abnormal course of the facial nerve, high jugular bulb, malformed cochlea or distorted anatomy of the middle ear. The main limitation of an endoscopic CI is that it is a difficult one-hand surgery, technically possible only for highly skilled otosurgeons with extensive experience in performing classic approaches as well as various endoscopic ear procedures. In endoscopic CI, one hand is occupied by the endoscope while the other performs manipulations during endoscopic CI including suctioning, hemostasis and subsequent introduction of the electrode into the cochlea [71]. The lack of stereoscopic vision was not considered to be a drawback by the first author in any surgery.

Figure 14. Wide exposure of the middle ear after elevation of the tympano-meatal flap in an endoscopic transcanal cochlear implantation (left ear).
6. Conclusion

The transcanal endoscopic approach is minimally invasive surgery that can be successfully applied for various ear pathologies. Knowledge on middle ear anatomy, ear radiology and an experience in classic techniques is essential before starting the endoscopic approach. The assistance of an operating microscope may be required when there is the need for two-hand manipulations in dissection of the cholesteatoma from the dehiscent facial nerve, ossicles, stapes footplate, and in some cases of ossicular chain reconstruction, introduction of the electrode array into the cochlea. In inexperienced hands, the endoscopic approach can be associated with complications due to direct trauma from the tip of the endoscope to the facial nerve, the ossicular chain and a low-lying tegmen.

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References


