Journal of Visualized Experiments

Endoscopic Cholesteatoma Surgery

--Manuscript Draft--

Article Type:	Invited Methods Collection - JoVE Produced Video
Manuscript Number:	JoVE63315R2
Full Title:	Endoscopic Cholesteatoma Surgery
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TITLE:

Endoscopic Cholesteatoma Surgery

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SUMMARY:

The present protocol describes a step-by-step guide for the complete endoscopic removal of epitympanic cholesteatoma with different techniques for cholesteatoma dissection and bone removal for epitympanectomy.

ABSTRACT:

Implementation of endoscopes in cholesteatoma surgery resulted in considerable changes in the management of cholesteatoma in the last two decades. Compared to the microscopic approach with an excellent but straight-line view and limited illumination, the introduction of endoscopes provides a wide-angled panoramic view. Moreover, angled lenses allow the surgeon to visualize the middle ear and its hidden recesses through a transcanal, minimally-invasive approach. The endoscope enables the surgeon to remove limited cholesteatoma of the middle ear and its recesses using an exclusive endoscopic technique by taking advantage of these benefits. This reduces the rate of residual disease and sparing external incisions and excessive temporal bone drilling as in a transmastoid approach. Since transcanal endoscopic access is mainly a one-handed technique, it implies the need for specific procedures and technical refinements. This article describes a step-by-step guide as a surgical manual for endoscopic removal of epitympanic cholesteatoma. Different techniques for cholesteatoma dissection and bone removal for epitympanectomy, including curettage and powered instruments such as drills and ultrasonic devices with their outcomes, are discussed. This may offer ear surgeons insight into technical refinements and the latest technological developments and open the horizon for different techniques.

INTRODUCTION:

The introduction and successive spread of endoscopic ear surgery led to considerable changes in the treatment of cholesteatoma in the past two decades. The first intraoperative use of endoscopes to prevent residual cholesteatoma was already described in 1993 by Thomassin et al.[1], followed by the first description of exclusive endoscopic cholesteatoma surgery in 1997 for cases of limited cholesteatoma[2]. Compared to the excellent but straight-line view with limited illumination in the microscopic approach, the endoscopic approach provides a panoramic view combined with high resolution, high magnification, and the ability to use angled lenses. The technique experiences increasing interest, despite the loss of binocular vision and two-handed working possibility[3]. As a consequence of the one-handed technique, safe and sufficient hemostasis is required to reap the benefits of superior visualization of the endoscopic technique[4,5].

Traditional microscopic approaches might require a canal wall down (CWD) technique with excessive temporal bone drilling for improved visualization and complete removal of the cholesteatoma[6]. A less invasive alternative for limited cholesteatoma is the canal wall up (CWU) technique, although the limited visualization is often associated with a higher rate of residual cholesteatoma[7]. Endoscopes were therefore incorporated as an adjunct in canal wall up surgery to reduce the residual rate of cholesteatoma after CWU surgery[1,8]. Proceeding from this, the transcanal exclusive endoscopic approach has emerged as a possible alternative approach in cholesteatoma surgery as a minimally invasive approach. This resulted in excellent results in limited cholesteatoma with a comparable rate of residual cholesteatoma compared to the traditional CWD technique[9–11]. Nowadays, the exclusive use of endoscopes in cholesteatoma surgery is increasingly documented in the literature, and indications for exclusive endoscopic approaches are continuously expanding[12]. This work presents an insight into the different technical refinements and latest technological developments for exclusive endoscopic cholesteatoma surgery.

PROTOCOL:

The protocol followed the guidelines of the local institution's human research ethics committee and was approved by the local institutional review board (KEK-BE 2019-00555). All operations were performed in general anesthesia under controlled hypotension in anti-Trendelenburg positioning with standard otological instruments.

1. Preparation of the surgical site

1.1. Manually adjust the endoscope screens (see **Table of Materials**) according to the surgeon's preferred position (sitting or standing).

1.2. Monitor the facial nerve by checking impedances with a nerve monitoring system (see **Table of Materials**) and perform a tap test[13].

1.3. Disinfect the auricle and the retroauricular region with swabs soaked with commercially available povidone-iodine solution (see **Table of Materials**).

1.4. Drape the periauricular region with sterile blankets.

1.5. Clean and rinse the external auditory canal (EAC) with a blunt syringe and Ringer solution (see **Table of Materials**).

1.6. Perform white balancing of the camera with white gauze and apply drops of anti-fog solution to the endoscope lens.

2. Exclusive transcanal endoscopic approach

2.1. Introduce the 0°, 3mm diameter, and 15cm length endoscope in the EAC (see **Table of Materials**) and clean the EAC by removing earwax and cutting the hairs in the EAC.

2.2. Perform local anesthesia with 0.5 mL of diluted epinephrine (1:200) injection (see **Table of Materials**), each using four injection sites in all quadrants of the EAC under endoscopic control. Additionally, inject 0.5 mL of diluted epinephrine (1:200) to the vascular strip in the posterior-superior quadrant of the EAC.

2.3. Inspect the tympanic membrane and the attic region with the 0° endoscope.

2.4. Elevate a tympanomeatal flap tailored to disease extension using an angled round knife and provide hemostasis with epinephrine (1:1000) soaked cottonoids.

NOTE: Additional hemostasis may be applied by electrocoagulation using mono- or bipolar cautery; alternatively, radio-frequency-cautery can be used (see **Table of Materials**). Be careful to use monopolar at the lowest intensities to minimize risks of spread of electricity to the facial nerve.

2.5. Expose the annulus and, if possible, the chorda tympani; open the middle ear cavity, and evaluate in detail the cholesteatoma extension.

2.6. Carefully separate the cholesteatoma matrix from the eardrum and from the chorda tympani.

2.7. Carefully dissect the cholesteatoma involving the middle ear and the incudostapedial area in case of an intact ossicular chain.

2.8. Perform limited atticotomy using unpowered instruments, bone drilling, or ultrasonic devices (see **Table of Materials**) by stepwise removal of the lateral portion of the attic and evaluate the extent of cholesteatoma infiltration by following the steps below.

2.8.1. For attico- and antrotomy with bone drilling: remove larger parts of bone either in an underwater technique[14], followed by cutting burrs at low speed (2000-8000 rpm) or cutting or

coarse diamond burrs at slow speed with only a little irrigation.

NOTE: For the underwater technique, the EAC is filled with 0.9% of NaCl solution, and the endoscope lens is inserted into the EAC with the burrs. Subsequently, drilling for attico- and antrotomy is performed directly under visual inspection. Occasional suction is required due to bone dust and reduced visibility. Utmost care has to be applied to prevent damage to surrounding structures by direct or heat damage. The delicate lens and shaft of the endoscope have to be kept away from the rotatory instruments to prevent its damage.

2.8.2. For attico- and antrotomy with ultrasonic devices: remove the larger parts of bone with the curved tip in an underwater technique to prevent heat damage to bone and soft tissues.

CAUTION: Do not touch the ossicular chain and the cochlea due to possible inner ear hair cell damage due to transmission of micro-vibrations.

2.9. If the cholesteatoma infiltrates deep into the anterior epitympanum or erodes the incus, remove the incus and, if required, the malleus head to entirely remove the cholesteatoma.

2.10. Perform stepwise attico- and antrotomy with different devices (see **Table of Materials**) to follow and completely extirpate the cholesteatoma. Use angled dissectors if appropriate.

2.10.1. For atticotomy with unpowered instruments: remove small parts of bone, especially the scutum, by a bone curette using rotatory movements or chisel and hammer.

3. Middle ear exploration

3.1. After completion of cholesteatoma resection, an entire middle ear exploration with an emphasis on residual cholesteatoma and functional considerations with the greatest sparing of healthy mucosa is performed. Use first 0° then a 45° angled lens.

NOTE: If appropriate, a 70° endoscope may also be used.

3.2. Check anterior epitympanic space, tegmen tympani, posterior epitympanum, antrum until the posterior limit of the lateral semicircular canal.

3.3. Carefully inspect the retrotympanum, including posterior sinus, sinus tympani, subtympanic sinus, and hypotympanum.

3.4. Check Eustachian tube, protympanum, supratubar recess, tensor fold, and isthmus; restore the ventilation route by tissue removal in case of obstruction.

4. Reconstruction of the ossicular chain and scutum

4.1. Perform an incision 5 mm posterior to the tragus edge and cut through to the cartilage,

then harvest a large piece of cartilage with perichondrium on both sides.

4.2. Reconstruct the scutum with a trimmed piece of cartilage and perichondrium for defect closure after attico- and antrotomy.

4.3. Perform underlay tympanoplasty using a trimmed piece of cartilage with overlapping perichondrium in island-graft technique or temporalis fascia for defect closure of the tympanic membrane. Add perichondrium in case of cartilage use for supporting the construction if necessary.

4.4. If the stapes is intact, inspect the incus or head of the malleolus for possible malleolar head or incus interposition ossiculoplasty; otherwise, use double-block cartilage (Malafronte technique[15]) or PORP (partial ossicular replacement prosthesis).

4.5. Use a TORP (total ossicular replacement prosthesis) if the stapes supra-structure is also affected by cholesteatoma and needs to be removed.

4.6. Use resorbable gelatinous sponges to secure the reconstruction, reinforce the reconstruction using a pressed perichondrium layer or cartilage in case of PORP/TORP.

5. Wound closure

5.1. Reposition the tympanomeatal flap and adapt it to the EAC curvature without sutures.

5.2. Splint the tympanic membrane with silicone or silk strips of adequate size for defect coverage.

5.3. Pack the EAC with a resorbable gelatinous sponge and the outer part with an antibiotic (polymyxin, neomycin) and hydrocortisone soaked gauze (see **Table of Materials**).

REPRESENTATIVE RESULTS:

A total of 43 consecutive cases of exclusive endoscopic cholesteatoma surgery were analyzed for this study. One surgeon performed all operations; cases needing conversion to a microscopic or combined approach were excluded. Preoperative computed tomography suspected an epitympanal cholesteatoma extension in every case. The mean age (±standard deviation) at the surgery date was 37.36 years (±15.64 years). Seven cases (16.3%) were revision surgeries, thirty-six cases (83.7%) were patients undergoing first cholesteatoma removal. The left side was operated in 26 cases (60.5%), the right side in 17 cases (39.5%).

Surgical Results

All operations were completed without significant complications like facial nerve palsy or postoperative sensorineural hearing loss, as illustrated in **Figure 1**. Cartilage was used as grafting material in 38 cases (88.4%) and fascia in 5 cases (11.6%). The graft intake rate (GIR) was 90.7% showing 3 cases of postoperative perforations (7.3%). The mean follow-up was 17.4 months (±10

months), with 40 cases (93%) having no recurrent cholesteatoma at the last follow-up.

Audiological Results

Each patient underwent standard audiological testing before and after surgery. One patient was already deaf before surgery; thus, no hearing improvement was expected. Two more patients had no postoperative audiogram. Preoperative air bone gap (ABG) of 23.8 dB ± 12.6 dB improved significantly (paired t-test with $p = 0.0005$) to a postoperative ABG of 18.2 dB ± 10 dB after surgery. The detailed surgical results are presented in **Table 1**.

FIGURE AND TABLE LEGENDS:

Figure 1: Overview of the essential surgical steps.

Table 1: Detailed surgical results.

DISCUSSION:

This article describes a step-by-step guide as a surgical manual for endoscopic removal of limited attic cholesteatoma. Different techniques for cholesteatoma dissection and bone removal techniques for atticotomy as curettage, bone drills, and ultrasonic devices (piezoelectric devices, ultrasonic bone curettes) are presented. However, single-handed surgery requires habituation, and particular care has to be taken to avoid damage to surrounding structures directly or indirectly during attico- and antrotomy with powered instruments.

Since the first description of exclusive endoscopic cholesteatoma surgery for limited cholesteatoma by Tarabichi in 1997[2], several studies have been published reporting its successful application in cases of limited attic cholesteatoma. Tarabichi presented in 2004 a cohort of 73 procedures in 69 patients, who all received transcanal exclusive endoscopic cholesteatoma removal, showing 5 cases of recurrence in a mean follow-up period of 43 months[9]. In 2008, Barakate and Botrill presented 68 procedures of endoscopic cholesteatoma surgery in 66 cases, all of them receiving a second look procedure within a mean of 16 months[16]. In the second look procedure, 10 ears revealed residual disease, and 4 ears presented a recurrence. Migirov et al. demonstrated no residual disease in 18 patients after exclusive endoscopic cholesteatoma eradication after more than 1 year[10]. In 2013 Marchioni et al. reported on 146 patients with attic cholesteatoma and 120 patients undergoing an exclusive endoscopic approach; 26 patients underwent an endoscopic procedure combined with mastoidectomy[11]. Thereof, 7 patients presented with residual cholesteatoma, with no case having limited attic cholesteatoma in the beginning. Thus, the residual and recurrent cholesteatoma rate of 6.4% after endoscopic assisted or exclusive endoscopic removal seems to be comparable to the rate after most CWD procedures with 0%-13.2%, while using a minimally invasive approach[7,17]. In addition, direct comparison of endoscopic with microscopic techniques revealed significantly better middle ear structural visibility, reduced pain scores, and faster wound healing as further advantages of an endoscopic minimally-invasive approach[18,19]. Thus, the endoscopic approach seems to be particularly suitable for limited attic cholesteatoma.

Nevertheless, the inaccessibility of cholesteatoma extending deep into the mastoid remains one of the limiting factors in the success of the transcanal exclusive endoscopic approach. Despite the use of angled optics, complete endoscopic explorability is not always feasible, especially in the case of more excavated retrotympanal regions[20].

Extended atticotomy was mainly performed by curettes or bone drilling until recently. To avoid the rough and time-consuming bone removal with curettes and possible facial nerve or tympanomeatal flap injury caused by drills, ultrasonic devices may provide a safe and precise alternative in cholesteatoma surgery[21]. With the transcanal endoscopic retrograde mastoidectomy technique, even removing cholesteatoma extensions into the antrum in a sclerotic mastoid can be achieved by an exclusive endoscopic transcanal approach[22,23]. However, extensive cholesteatoma formation inside the mastoid or severe hemorrhage might require switching to a microscopic retroauricular approach.

Additionally, there are also recent developments described in the literature to reduce the residual rate of cholesteatoma with chemically or physically assisted dissections. Mesna (sodium 2-mercaptoethanesulfonate) is reported as a possible chemical agent to reduce the residual rate of cholesteatoma by breaking disulfide bridges between different tissues[24,25]. For physically assisted dissection, different types of lasers known from stapes mobilization procedures have also been used in cholesteatoma surgery, resulting in a low recurrence rate around the ossicular chain[26]. In addition to white light endoscopy, other image processing technologies based on spectral separation may further improve cholesteatoma removal by recognizing residual cholesteatoma in the final overview[27].

Therefore, applying endoscopic cholesteatoma surgery with improved technical devices and chemically or physically assisted dissection is promising to further evolve the minimally invasive approach and reduce the residual disease rate.

ACKNOWLEDGMENTS:
Not applicable.

DISCLOSURES:
LA is a consultant for Stryker ENT. All other authors declare no conflict of interest.

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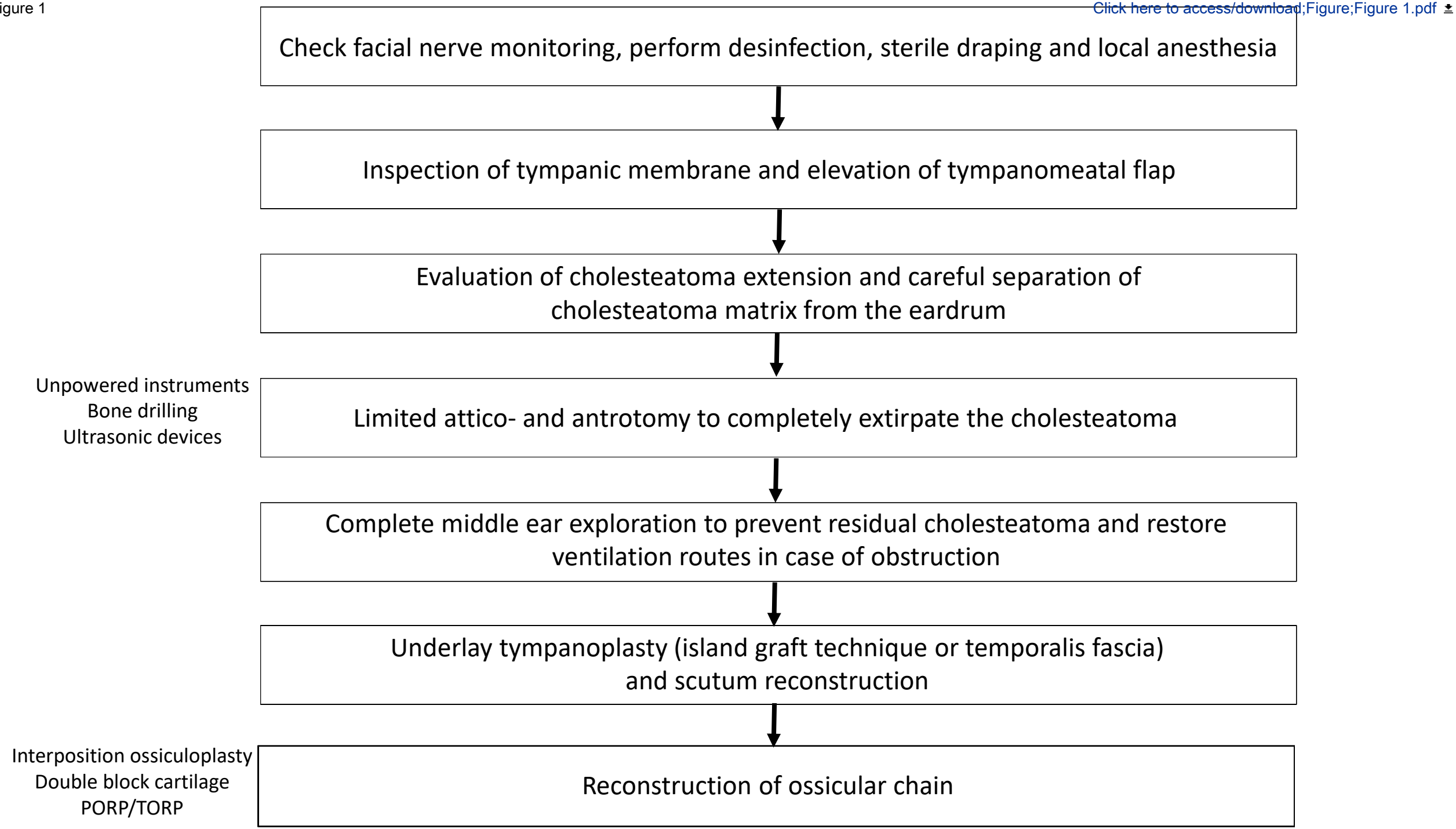
Figure 1



Age	37.4 years (14-80 years)
Side	26 left side
Revision surgery	36 primary surgery
Grafting sucess	39 successful
Grafting material	38 cartilage
Recidive	40 without recidive
Mean ABG	23.8 ± 12.6 dB preoperative

17 right side
7 revision surgery
3 perforations 1 missing follow up
5 fascia
3 with recidive
18.2 ± 10 dB postoperative

Please note that the reviewers raised some significant concerns regarding your method and your manuscript. Please revise the manuscript to thoroughly address these concerns. Additionally, please describe the changes that have been made or provide explanations if the comment is not addressed in a rebuttal letter. We may send the revised manuscript and the rebuttal letter back to peer review.

Editorial comments:

1. Please take this opportunity to thoroughly proofread the manuscript to ensure that there are no spelling or grammar issues.

Done as suggested.

2. Will you be having a patient filming the procedure? This is important. If yes, please confirm whether filming of live surgery is possible at your institute. Are there any restrictions for filming?

We will have a patient for filming the procedure. Filming of the operation is allowed without restriction.

3. Please revise the Introduction to include all of the following:
a) A clear statement of the overall goal of this method

L68-70: We present you an insight into different technical refinements and latest technological developments for exclusive endoscopic cholesteatoma surgery.

b) The rationale behind the development and/or use of this technique

L63-64: Possible alternative approach in cholesteatoma surgery as minimally invasive approach.

c) The advantages over alternative techniques with applicable references to previous studies

L50-53 Compared to the excellent but straight-line view with limited illumination in the microscopic approach, the endoscopic approach provides a panoramic view combined with high resolution, high magnification and the ability to use angled lenses.

d) A description of the context of the technique in the wider body of literature

L57-66 Traditional microscopic approaches might require a canal wall down (CWD) technique with excessive temporal bone drilling for improved visualization and complete removal of the cholesteatoma[6]. A less invasive alternative for limited cholesteatoma is the canal wall up (CWU) technique, although the limited visualization is often associated with a higher rate of residual cholesteatoma[7]. Endoscopes were therefore incorporated as adjunct in canal wall up surgery to reduce the residual rate of cholesteatoma after CWU surgery[1,8]. Proceeding from this, the transcanal exclusive endoscopic approach has emerged as a possible alternative approach in cholesteatoma surgery as minimally invasive approach. This

resulted in excellent results in limited cholesteatoma with comparable rate of residual cholesteatoma compared to the traditional CWD technique[9–11].

e) Information to help readers to determine whether the method is appropriate for their application

L51-55 …endoscopic approach provides a panoramic view combined with high resolution, high magnification and the ability to use angled lenses. The technique experiences increasing interest, despite the loss of binocular vision and two handed working possibility[3]. As a consequence of the one-handed technique, safe and sufficient hemostasis is required…

L64-66 This resulted in excellent results in limited cholesteatoma with comparable rate of residual cholesteatoma compared to the traditional CWD technique.

4. Please include an ethics statement before the numbered protocol steps, indicating that the protocol follows the guidelines of your institution's human research ethics committee.

L73-74 The protocol follows the guidelines of the local institution's human research ethics committee and was approved by the local institutional review board (KEK-BE 2019-00555).

5. Please ensure that all text in the protocol section is written in the imperative tense as if telling someone how to do the technique (e.g., "Do this," "Ensure that," etc.). The actions should be described in the imperative tense in complete sentences wherever possible. Avoid usage of phrases such as "could be," "should be," and "would be" throughout the Protocol. Any text that cannot be written in the imperative tense may be added as a "Note." However, notes should be concise and used sparingly. Please include all safety procedures and use of hoods, etc.

Done as suggested.

6. Please ensure that the Protocol contains only action items that direct the reader to do something.

Done as suggested.

7. Please note that your protocol will be used to generate the script for the video and must contain everything that you would like shown in the video. Please add more details to your protocol steps. Please ensure you answer the "how" question, i.e., how is the step performed? Alternatively, add references to published material specifying how to perform the protocol action. Please add more specific details (e.g. button clicks for software actions, numerical values for settings, etc) to your protocol steps. There should be enough detail in each step to supplement the actions seen in the video so that viewers can easily replicate the protocol.

Done as suggested.

8. Line 78-79: Is the endoscope screen adjusted manually? Please specify

The information was added in L82: manual adjustment…

9. Line 80: How is the facial nerve monitoring checked?

The information was added in L85: checking impedances and performing a tap test…

10. Line 81: Please specify the surgical site? How is the povidone-iodine solution applied?

The information was added in L87-88: Disinfection of the auricle and retroauricular region with swabs soaked in povidone-iodine solution.

11. Line 82: How is the sterile draping done?

The information was added in L90: with sterile blankets.

12. Line 83: How is the EAC cleaned and rinsed with Ringer solution? Is any instrument/ surgical used?

The information was added in L92: with blunt syringe…

13. Line 84-85: How is white balancing performed? How is the anti-fog solution applied?

The information was added in L94-95: with white gauze and apply drops of anti-fog solution…

14. Line 89-91: Please add more details to the step. Is the dilution 1: 200 or 1 :200,000? Please correct. How much volume is injected in each of the four quadrants? Injection volume in the vascular strip?

Diluted epinephrine 1:200.000 was used. The injection volume was added for each side L102-105.

15. Line 92: How is the tympanic membrane inspected? Please ensure to include all the details required to replicate the experiment elsewhere.

The phrasing was revised to Inspection of the tympanic membrane and attic region with 0° endoscope L107.

16. Line 93-96: How is the hemostasis applied using cautery?

The phrasing was revised to Hemostasis is applied by electrocoagulation using cautery L111.

17. Line 101: How is this performed?

The phrasing was revised to Perform limited atticotomy using unpowered instruments, bone drilling or ultrasonic devices by stepwise removal of the lateral portion of the attic and evaluate the extent of cholesteatoma infiltration L125-127.

18. Line 107-120: Please revise the lines as actionable steps.

Done as suggested in L133-154.

19. Line 132: how is the tissue harvested? Add more details.

More details were added in L174-175.

20. Line 134: How is the scutum reconstructed? How is underlay tympanoplasty performed?

More details were added in L177-182.

21. Line 143-146: How is the flap repositioned? Any suturing done? Is there any specific size of silicone or silk strips used?

The phrasing was revised to:

Reposition the tympanomeatal flap and adapt it to the EAC curvature without sutures in L196.

Splint the tympanic membrane with silicone or silk strips of adequate size for defect coverage in L198-199.

22. Please include a one-line space between each protocol step and then highlight up to 3 pages of the Protocol (including headings and spacing) that identifies the essential steps of the protocol for the video, i.e., the steps that should be visualized to tell the most cohesive story of the Protocol. Remember that non-highlighted Protocol steps will remain in the manuscript, and therefore will still be available to the reader.

Done as suggested.

23. Please consider including some figures to better explain the surgical procedure.

We have considered including figures, however, we believe that the video illustrates the individual surgical steps more clearly.

24. As we are a methods journal, please revise the Discussion to explicitly cover the following in detail in 3-6 paragraphs with citations:
a) Critical steps within the protocol

L233-235 However, single-handed surgery requires habituation and particular care has to be taken to avoid damage to surrounding structures directly or indirectly during attico- and antrotomy with powered instruments.

b) Any modifications and troubleshooting of the technique

L263-267 With the technique of a transcanal endoscopic retrograde mastoidectomy, even the removal of cholesteatoma extensions into the antrum in a sclerotic mastoid can be achieved by an exclusive endoscopic transcanal approach[20,21]. However, extensive cholesteatoma formation inside the mastoid or severe hemorrhage might require a switch to a microscopic retroauricular approach.

c) Any limitations of the technique

L255-259 Nevertheless, inaccessibility of cholesteatoma extending deep into the mastoid remains one of the limiting factors in the success of the transcanal exclusive endoscopic approach. Despite the use of angled optics, complete endoscopic explorability is not always feasible, especially in the case of more excavated retrotympanal regions[18].

d) The significance with respect to existing methods

L236-254 Since the first description of exclusive endoscopic cholesteatoma surgery for limited cholesteatoma by Tarabichi in 1997[2], several studies have been published reporting its successful application in cases of limited attic cholesteatoma. Tarabichi presented in 2004 a cohort of 73 procedures in 69 cases, who all received transcanal exclusive endoscopic cholesteatoma removal, showing 5 cases of recurrence in a mean follow up periode of 43 months[9]. In 2008, Barakate and Botrill presented 68 procedures of endoscopic cholesteatoma surgery in 66 cases, all of them receiving a second look procedure within a mean of 16 months[14]. In the second look procedure 10 ears revealed residual disease and 4 ears presented a recurrence. Migirov et al. demonstrated no residual disease in 18 patients after exclusive endoscopic cholesteatoma eradication after more than 1 year[10]. In 2013 Marchioni et al. reported on 146 patients with attic cholestatoma and 120 patients undergoing an exclusive endoscopic approach, 26 patients underwent an endoscopic approach combined with mastoidectomy[11]. Thereof, 7 patients presented with residual cholesteatoma, with no case having limited attic cholesteatoma in the beginning. Thus, the rate of residual and recurrent cholesteatoma of 6.4% after endoscopic assisted or exclusive endoscopic removal seems to be comparable to the rate after most CWD procedures with 0 - 13.2%, while using a minimally invasive approach[7,15]. In addition, direct comparison of endoscopic with microscopic techniques revealed significantly better middle ear structural visibility, reduced pain scores and faster wound healing as further advantages of an endoscopic minimally-invasive approach[16,17].

e) Any future applications of the technique

L277-279 Therefore, the application of endoscopic cholesteatoma surgery with improved technical devices and chemically or physically assisted dissection is promising to further evolve the minimally invasive approach und reduce the rate of residual disease.

25. Please ensure that the references appear as the following: [Lastname, F.I., LastName, F.I., LastName, F.I. Article Title. Source. Volume (Issue), FirstPage – LastPage (YEAR).] For more than 6 authors, list only the first author then et al. Title case and italicize journal titles and book titles in the references. Do not use any abbreviations. Article titles should start with a capital letter and end with a period and

should appear exactly as they were published in the original work, without any abbreviations or truncations.

Done as suggested.

26. Please ensure that the Table of Materials includes all the supplies (reagents, chemicals, instruments, equipment, software, etc.) used in the study. Please sort the table in alphabetical order.

Table of Materials was arranged in alphabetical order.

Reviewers' comments:

Reviewer #1:

Manuscript Summary:

This manuscript illustrates a detailed step-by-step protocols for the exclusive endoscopic removal of epitympanic cholesteatoma.

Major Concerns:

1. The authors claimed that different techniques for cholesteatoma dissection and bone removal for epitympanectomy were introduced. However, some essential techniques such as the underwater technique and scutum reconstruction methods need more detailed description.

Thank you for this comment. Underwater technique and scutum reconstruction were described in more detail in L141-145 and L177-178.

2. The indications for the endoscopic cholesteatoma surgery also need to be demonstrated. This may be important for the audiences, especially for exclusive endoscopic cholesteatoma surgery. Moreover, intra-operative complications and the treatment methods need to be introduced, which are vital for the surgeons.

Thank you for this recommendation. The information was added in L254-259 and L265-267.

Minor Concerns:

None.

Reviewer #2:

Manuscript Summary:

Overall the manuscript is well written.

Thank you very much for your appreciation.

Minor Concerns:

In Protocol section:

Line 92 I think it is better to mention inspection of tympanic membrane and attic region as well, rather than just tympanic membrane only.

Done as suggested.

Line 95 As you have mentioned about the ways of hemostasis using bipolar/monopolar, hemostasis can also be controlled using RF cautery.
Amended as suggested.

Line 102 to 104, Along with the careful evaluation of anterior epitympanum, careful dissection of cholesteatoma involving the middle ear, Incudostapedial, and the stapedial area is also required especially in cases where the ossicular chain is intact.
Thank you for this comment. The information was supplemented in L122-123.

Techniques of atticotomy:
Atticotomy can be done by drill, curette, piezo as mentioned in the manuscript. But, it can also be done using a chisel and hammer and by using the ultrasonic bone curette (UBC). This would be better to mention in the protocol or in discussion as one of the aims of this manuscript is to mention different techniques of cholesteatoma dissection.
Thank you for this recommendation. The phrasing ultrasonic device was used instead of piezoelectric devices and chisel and hammer were added in L136-137.

5.1. Harvest a large piece of tragal cartilage with perichondrium on both sides for scutum and possible ossicular chain or tympanic membrane reconstruction ---> not clear statement
also not mentioned about the graft temporalis fascia
Done as suggested. The phrasing was revised in L174-182.