The Laryngoscope

Prevalence of Ventilation Blockages in Patients Affected by Attic Pathology: A Case-Control Study

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Objectives/Hypothesis: Using a retrospective video evaluation of exclusive endoscopic middle ear procedures, we analyzed the different anatomical and pathological findings between patients with attic disease or cholesteatoma and patients without attic disease.

Study Design: A case-control study based on a retrospective chart review in a tertiary university referral center.

Methods: Videos from endoscopic middle ear procedures carried out between February 2007 and August 2012 were reviewed. We analyzed and compared two groups of patients who underwent surgery in our university hospital: patients with selective attic disease (e.g., non–self-cleaning attic selective retraction pockets or attic cholesteatoma) were compared with subjects without attic disease (e.g., chronic middle ear disease, congenital cholesteatoma, or secondary cholesteatoma).

Results: In total, 152 patients were included in the study. Of these, 102 were affected by primary acquired cholesteatoma (84/102) or severe pars flaccida retraction pockets (18/102), whereas 50 cases were controls. A blockage of the isthmus was present in almost all cases (98/102) compared with a lower prevalence in controls (3/50) ($P<.0001$). Similarly, a complete tensor fold was identified in 99/102 patients compared to controls (9/46; data were not available in four controls) ($P=.001$).

Conclusions: Selective epitympanic dysventilation occurred when a blockage of the isthmus was present and associated with a complete tensor fold, causing ventilatory separation between the epitympanum and mesotympanum. This mechanism could be the basis for a selective decrease in pressure in the attic, with the subsequent development of attic retraction pockets and cholesteatoma even in subjects with a normally functioning eustachian tube.

Key Words: Attic cholesteatoma, cholesteatoma pathogenesis, middle ear surgery, ventilation blockages, endoscopic surgery.

Level of Evidence: 3b

***Laryngoscope*, 123:2845–2853, 2013**

INTRODUCTION

Generally, three separate types of cholesteatoma have been identified based on different etiologies: congenital, primary acquired, and secondary acquired.

Congenital cholesteatomas arise as a consequence of squamous epithelium trapped within the temporal bone during embryogenesis, whereas secondary acquired cholesteatomas occur as a direct consequence of some type of injury to the tympanic membrane.[1] Primary acquired cholesteatomas, the most frequent type, arise as a result of tympanic membrane retraction. The classic primary acquired cholesteatoma develops from progressively deeper medial retraction of the pars flaccida into the epitympanum.

Several theories have been described[2–4] for the pathogenesis of primary acquired cholesteatoma, in particular, attic cholesteatoma: the retraction theory,[2] with retraction of Shrapnell's membrane as a result of chronic dysfunction of the eustachian tube; papillary proliferation theory,[3] with inflammation leading to the proliferation of epithelial cones in the basal layers of the keratinizing epithelium of Shrapnell's membrane; immigration theory,[4] with an ingrowth of squamous epithelium through a preexisting peripheral perforation; and metaplasia theory, with metaplasia of the inflamed middle ear epithelium into keratinizing squamous epithelium.

In the authors' opinion, a number of theories have been postulated without considering the anatomical and physiological mechanisms related to middle ear ventilation. In our experience, it is fundamental to relate the pathogenesis of attic cholesteatoma to middle ear ventilation routes.

Aeration of the tympanic cavity, mastoid cells, and anatomic pathways for middle ear ventilation have been studied since the end of the 19th century, starting with the work of Prussak in 1867.[5] Palva and colleagues[6,7] were the first to focus on ventilation patterns and their implications for middle ear disease and recently described the anatomy of the epitympanic diaphragm first postulated by Chatellier and Lemoine in 1946.[8]

In our previous study,[9] we focused on epitympanic size in patients affected by limited attic cholesteatoma, and we observed that the anterior epitympanic recess

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Editor's Note: This Manuscript was accepted for publication March 28, 2013.

The authors have no funding, financial relationships, or conflicts of interest to disclose.

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DOI: 10.1002/lary.24165

(AER) in an affected ear is smaller than in a nonaffected one. The blockage of the tympanic isthmus could create a selective negative pressure in the atticomastoid spaces. Subsequently, we reported[10] the importance of obtaining an unobstructed intraoperative view of the epitympanic diaphragm and the utility of tensor fold excision to obtain direct ventilation of the upper unit, preventing the development of a retraction pocket or recurrence of attic cholesteatoma.

Over a period of time, we have found that the intraoperative evaluation of middle ear anatomy allows us to clearly understand the middle ear ventilation routes and visualize the presence of anatomic blockages of middle ear ventilation trajectories.[11,12] These blockages might provoke a sectorial dysventilation of the middle ear creating a selective epitympanic dysventilation[12] consisting of the contemporaneous presence of an attic retraction pocket or cholesteatoma, normal eustachian tube function, complete epitympanic diaphragm, and isthmus blockage.

Using a retrospective video evaluation of exclusive endoscopic middle ear procedures, the aim of this study was to analyze the different anatomical and pathological findings between patients with attic disease or cholesteatoma and patients without attic disease.

MATERIALS AND METHODS

During August 2012 and September 2012, videos from endoscopic middle ear procedures carried out between February 2007 and August 2012 and stored in our database were reviewed retrospectively.

We analyzed and compared two groups of patients who underwent surgery in our university hospital: patients with selective attic disease (e.g., non–self-cleaning attic selective retraction pockets or attic cholesteatoma) were compared with subjects without attic diseases (e.g., chronic middle ear disease, congenital cholesteatoma, or secondary cholesteatoma).

The study group and control group were composed on the basis of inclusion and exclusion criteria.

Study Group

Inclusion criteria. Videos of surgical procedures on patients affected by selective attic disease (attic retraction pocket or attic cholesteatoma) with normal aspect of the eardrum (pars tensa) and who underwent an endoscopic procedure were selected, included in the study group, and analyzed.

Exclusion criteria. Videos of surgical procedures on patients with retraction of the pars tensa, with or without attic involvement, chronic middle ear diseases, congenital cholesteatoma, secondary cholesteatoma, or middle ear neoplasms were excluded from the study group.

Control Group

Inclusion criteria. Videos of surgical procedures on patients without any attic diseases and who underwent an endoscopic procedure were included in the control group and analyzed.

Exclusion criteria. Patients with diseases of the attic (retraction or attic cholesteatoma) were excluded.

In each group, we analyzed the following anatomical conditions: 1) the anatomical condition of the mucosa in the mesotympanic and protympanic compartments of the middle ear and the anatomical condition of the attic mucosa, 2) the epitympanic diaphragm (with a description of the anatomy of the isthmus and the tensor fold), and 3) the presence of mucosal fold or granulation tissue blocking the isthmus.

Armamentarium

The instrumentation consisted of 3-mm diameter, wide angle (15-cm length), 0° and 45° sinuscopes (Karl Storz, Tuttlingen, Germany). The video equipment comprised a three-chip video camera (Karl Storz) and 20-in high-definition monitor; all procedures were recorded digitally on a hard disk (AIDA system; Karl Storz).

Surgical Approach

In the study, we included all of the surgical procedures where we were able to perform a transcanal lateral approach to the tympanic isthmus and tensor fold with endoscopic view. The 3-mm diameter, 0° and 45° endoscopes were used to analyze the anatomy of the isthmus (the anterior and posterior isthmus of Proctor). Different procedures were performed based on the extent of disease.

Transcanal exclusive endoscopic approach. This approach was performed when the disease was limited to the attic or to the mesotympanum without mastoid involvement.

Endoscopic/microscopic combined surgery. This approach was performed in subjects affected by middle ear cholesteatoma with mastoid involvement. In all of these cases, a transcanal endoscopic approach was used to remove the disease from the tympanic cavity, with a microscopic mastoidectomy to remove the disease from the mastoid cells.

Endoscopic assisted surgery. In this case, a traditional microscopic canal wall down or canal wall up procedure was selected where a previous endoscopic analysis of the isthmus and tensor fold had been performed before the microscopic steps.

In all of these surgical procedures, during the surgical approach to the middle ear, an endoscope was introduced into the middle ear, and the tympanic isthmus and tensor fold were consecutively examined to aid our understanding of the epitympanic diaphragm of the upper unit in all of our patients (Fig. 1).

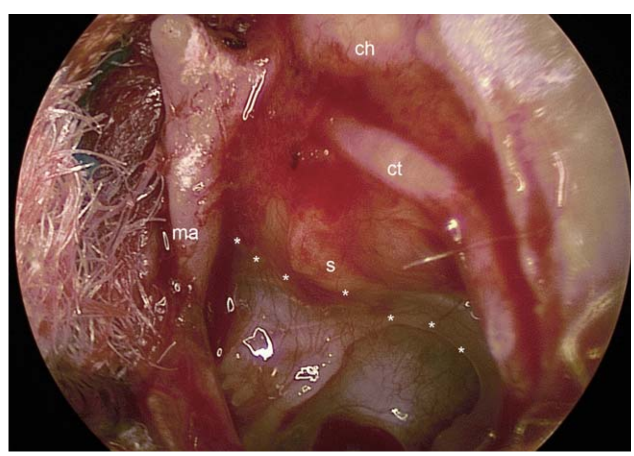

Fig. 1. Study group, left ear. Endoscopic view during surgical approach to the isthmus in a subject affected by attic cholesteatoma. A mucosal web (asterisks) is seen blocking the isthmus and separating the mesotympanum from the epitympanum. ch = cholesteatoma; ct = chorda tympani; ma = malleus; s = stapes. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

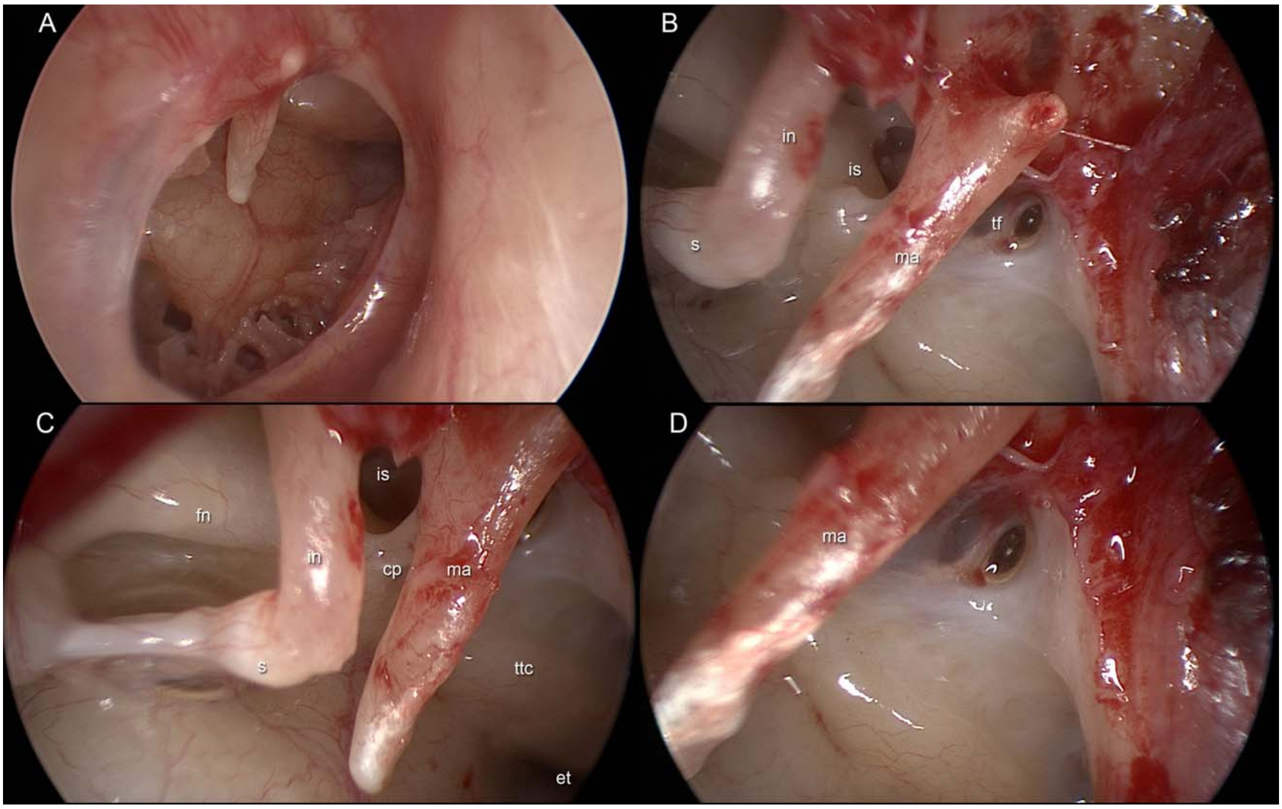

Fig. 2. Control group, right ear. (A) Endoscopic view of the isthmus and tensor fold in a subject with eardrum perforation. (B) A 45° endoscope is used to detect the conformation of the isthmus and the inferior edge of the tensor fold. (C) An open isthmus with a good connection between the attic and mesotympanum seen endoscopically. (D) Inferior approach to the tensor fold. In this patient, a complete tensor fold is detected. cp = cochleariform process; et = eustachian tube; fn = facial nerve; in = incus; is = isthmus; ma = malleus; s = stapes, tf = tensor fold; ttc = tensor tendon canal. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

We defined the isthmus area as the connecting space between the attic compartments and the mesotympanic compartments represented by the large tympanic opening between the medial part of the posterior incudal ligament posteriorly and the tensor tendon anteriorly. We analyzed the two portions of this anatomical space: 1) Proctor's anterior isthmus, defined as the space between the incudostapedial joint and the cochleariform process with the tensor tendon, was analyzed with 0° and 45° endoscopes; and 2) Proctor's posterior isthmus, defined as the space between the pyramidal process and the short process of the incus, was analyzed with a 45° endoscope.

The tensor fold was examined by two different endoscopic procedures.

Endoscopic inferior approach. A 45° endoscope was inserted into the protympanic region anteriorly with respect to the malleus; the eustachian tube opening and supratubal recess were detected. At this point, the inferior edge of the tensor fold was exposed endoscopically and examined (Fig. 2).

Endoscopic superior approach. When required, an anterior atticotomy was performed exposing the anterior epitympanic space anteriorly with respect to the head of the malleus; the superior edge of the tensor fold was exposed and analyzed.

We described the conformation of this mucosal fold and defined a complete tensor fold when it showed a complete conformation, separating the anterior epitympanic space from the protympanum. We defined an incomplete tensor fold when it showed a tissue defect, permitting a communication zone between the anterior epitympanic space and the protympanum.

Statistical Analysis

Fisher exact test was used to identify statistically significant differences between cases and controls. SPSS 18.0 software (IBM SPSS, Armonk, NY) was used for analysis.

RESULTS

We analyzed 270 patients who underwent endoscopic ear surgery between February 2007 and August 2012. In total, 152 patients were included in the study (102 males, 47 females, three cadavers). Of these, 102 patients were affected by primary acquired cholesteatoma (84/102) or severe pars flaccida retraction pockets (18/102), whereas 50 cases were controls (27 chronic otitis, six acquired cholesteatomas from previous surgical operations, five stapes surgery, three cadaveric dissections, four cochlear implants, and five others (e.g., middle ear carcinoid tumor, vestibular nerve neuroma).

In case patients, 38 were treated by combined microscopic/endoscopic approaches, whereas 64 were treated by an exclusive endoscopic technique. In 36/102, the pathology involved only the attic, 7/102 involved the attic and mesotympanum, 30/102 had antral involvement, and 29/102 had mastoid involvement. A blockage of the isthmus was present in almost all cases (98/102) (Figs. 3–5), with a lower prevalence in controls (3/50)

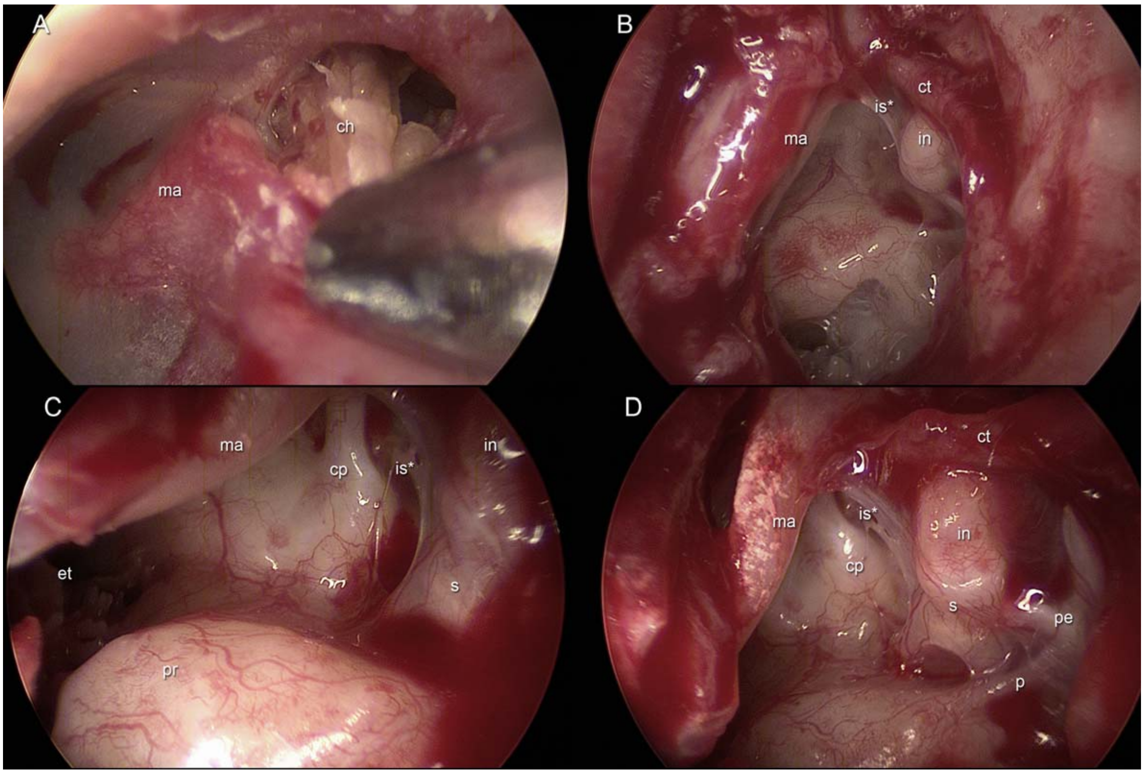

Fig. 3. Study group, left ear. (A) Attic cholesteatoma is detected endoscopically. (B) After tympanomeatal flap elevation, a 0° endoscope is used to check the isthmus; a mucosal web is found between the incudostapedial joint and the malleus. (C, D) a 45° endoscope is used to check the isthmus area. In this subject, the mucosal fold is lying between the cochleariform process and the incudostapedial joint blocking the isthmus and separating the mesotympanum (well aerated) from the epitympanum (where the cholesteatoma is located). ch = cholesteatoma; cp = cochleariform process; ct = chorda tympani; et = eustachian tube; in = incus; is* = blockage of the isthmus; ma = malleus; p = ponticulus; pe = pyramidal eminence; pr = promontory; s = stapes. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

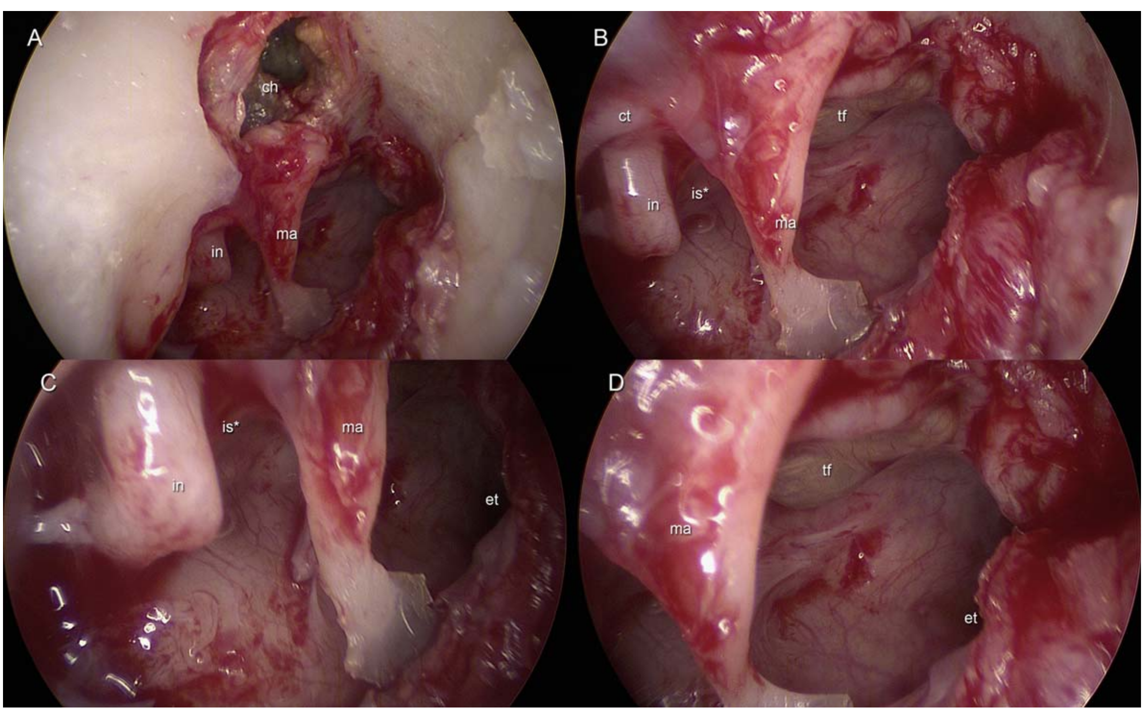

Fig. 4. Study group, right ear. (A) Subject affected by attic cholesteatoma seen during the endoscopic approach. (B) A 45° endoscope is used to observe the condition of the isthmus and the inferior edge of the tensor fold. In this subject, a mucosal fold is seen blocking the isthmus and associated with a complete tensor fold. (C) Endoscopic magnification of the isthmus blockage. (D) Endoscopic magnification of the complete tensor fold. ch = cholesteatoma; ct = chorda tympani; et = eustachian tube; in = incus; is* = blockage of the isthmus; ma = malleus; tf = tensor fold. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

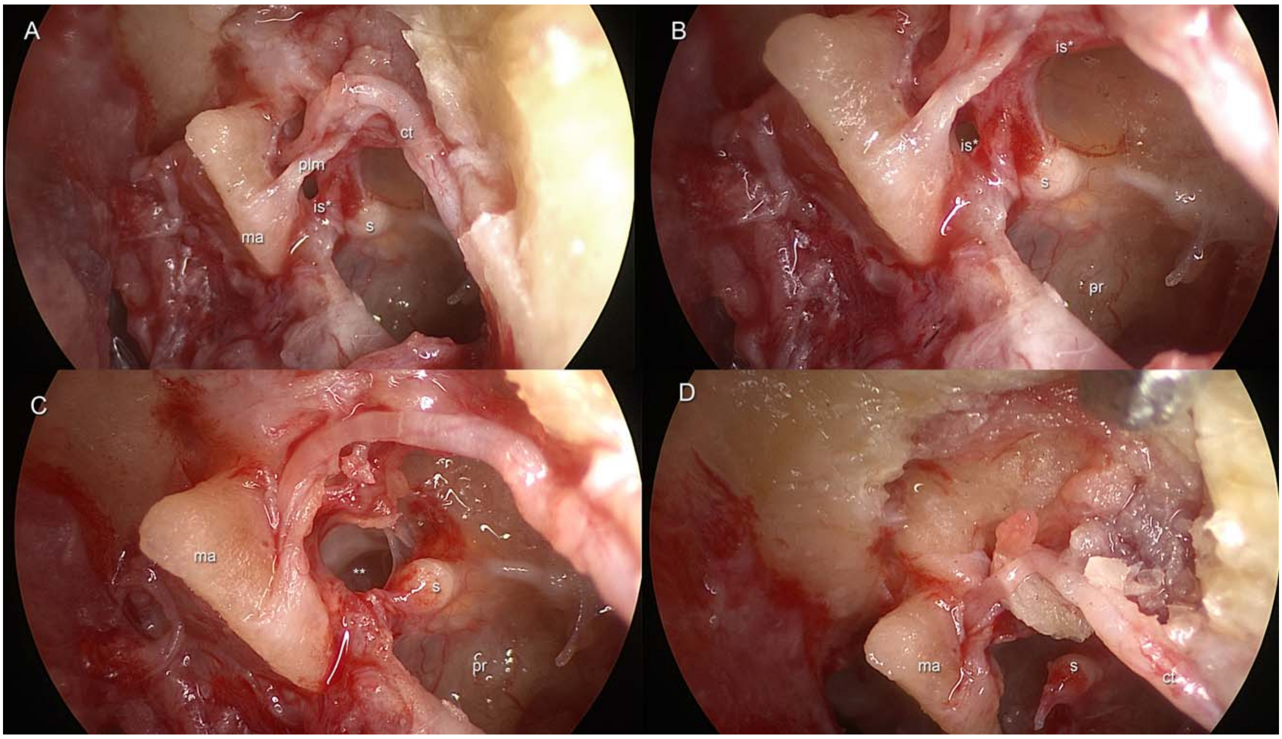

Fig. 5. Study group, left ear. (A, B) An inflammatory web blocking the isthmus is visible endoscopically in a subject with attic retraction cholesteatoma. The long process of the incus is eroded. (C) The inflammatory web is removed, and a well-ventilated mucosa is seen across the web (**). (D) Cholesteatoma and granulation tissue are present in the attic. ct = chorda tympani; is* = blockage of the isthmus; ma = malleus; plm = posterior ligament of the malleus; pr = promontory; s = stapes. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

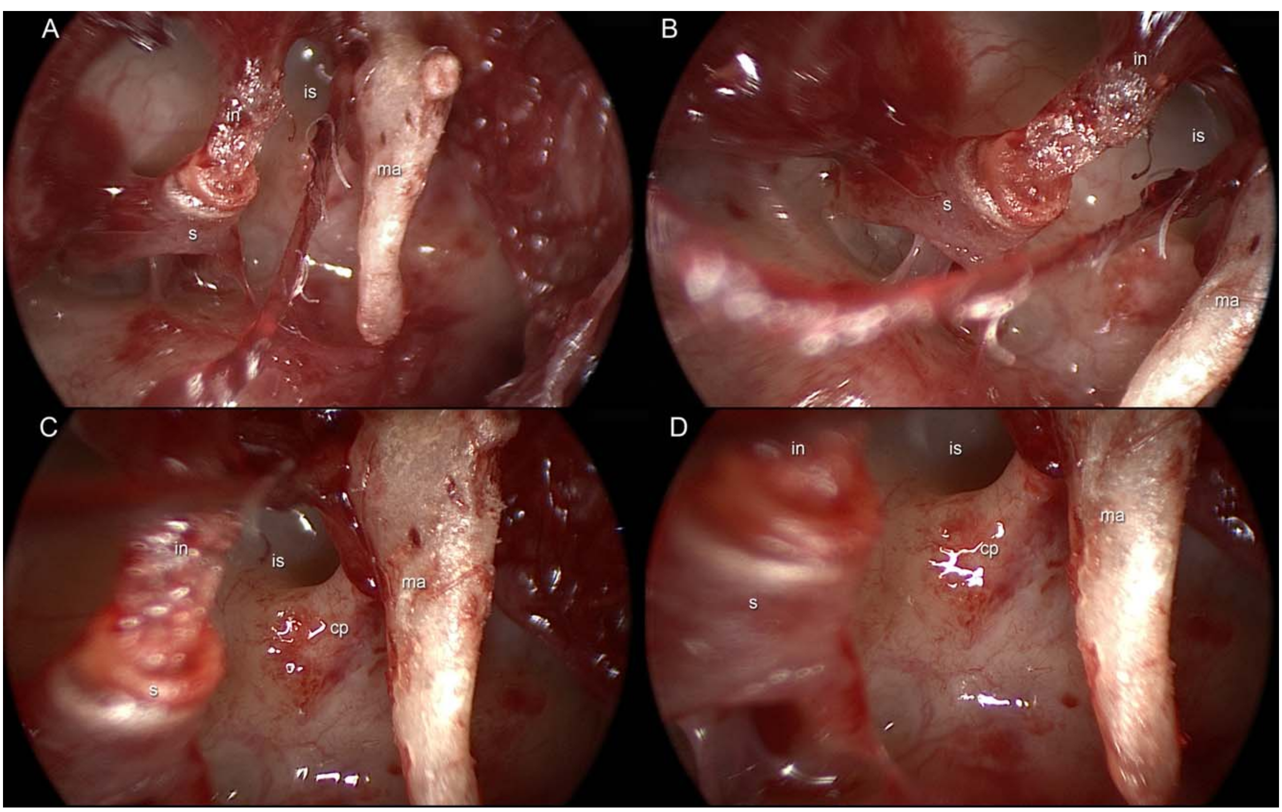

Fig. 6. Control group, right ear. (A–D) Endoscopic view of the isthmus in a subject with no attic problems. The posterior and anterior isthmus are opened showing a good connection between the medial attic and mesotympanum (C, D). cp = cochleariform process; in = incus; is = isthmus; ma = malleus; s = stapes. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

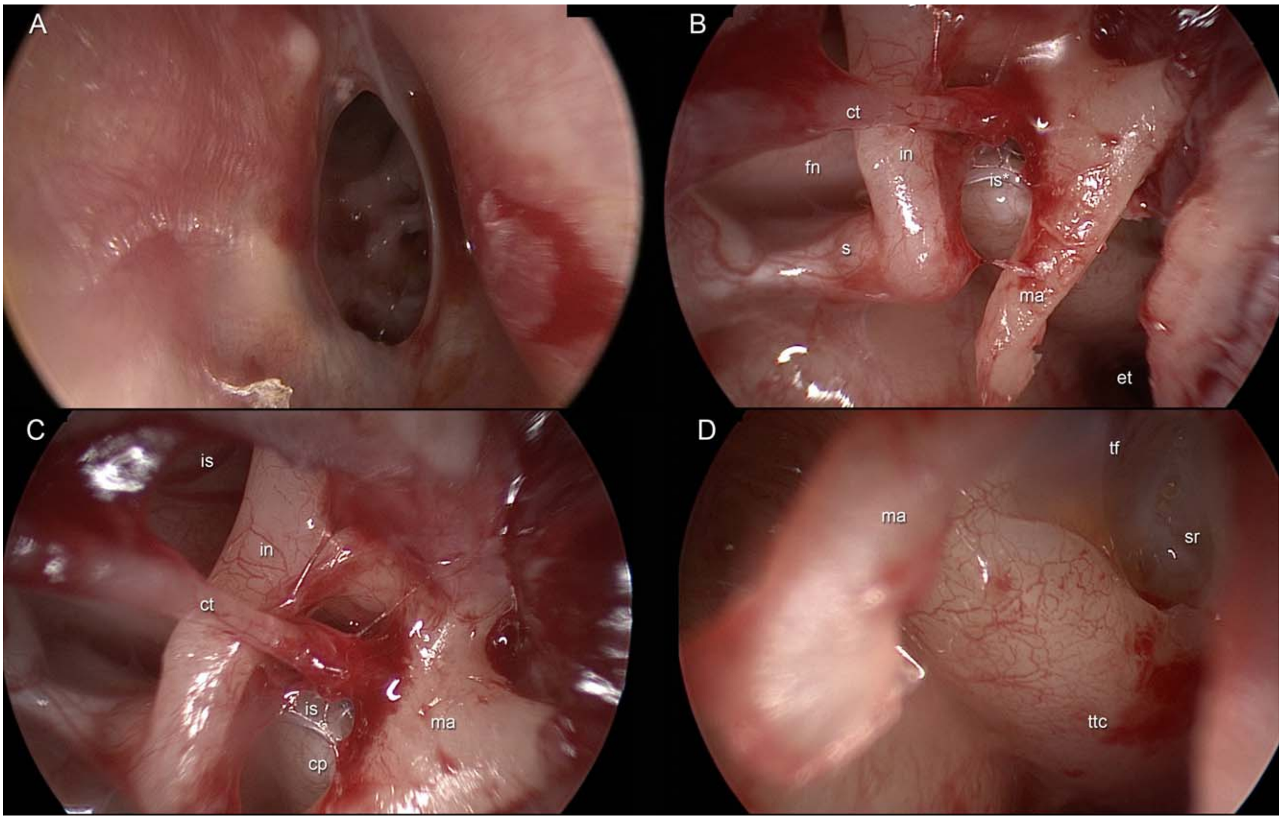

Fig. 7. Control group, right ear. (A) Subject with perforation of the eardrum. (B) A mucosal web is seen on the isthmus partially blocking this anatomical area. (C) The posterior isthmus is opened. (D) The inferior edge of the tensor fold is detected endoscopically. A complete conformation is seen in this subject. cp = cochleariform process; ct = chorda tympani; et = eustachian tube; fn = facial nerve; in = incus; is = isthmus; is* = blockage of the isthmus; ma = malleus; s = stapes; sr = supratubal recess; tf = tensor fold; ttc = tensor tendon canal. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

(Figs. 2, 6, and 7) (Table I) ($P < .0001$). Similarly, a complete tensor fold was identified in almost all patients (99/102), compared to controls (9/46; data were not available in four controls) (Table II) ($P = .001$). In only 2/50 controls, an isthmus blockage was identified associated with a complete tensor fold, whereas in the remaining controls, there was at least one ventilation route to the epitympanic compartment. Of the 3/102 cases with a blockage of the isthmus associated with an incomplete tensor fold, in at least one case a vertical fold was identified. In the case group, no patient was identified with both an unblocked isthmus and an incomplete tensor fold.

DISCUSSION

From an anatomical and ventilatory point of view, the middle ear is divided into two compartments by the epitympanic diaphragm, which consists of three malleal ligamental folds (the anterior, lateral, and posterior), the posterior incudal ligamental fold, and two purely membranous folds (the tensor fold and the lateral incudomalleal fold) together with the malleus and incus[7,8] (Fig. 8). All epitympanic compartments receive their aeration via the large tympanic isthmus between the medial part of the posterior incudal ligament and the tensor tendon.

The aeration pathway from the eustachian tube leads directly to the mesotympanic and hypotympanic spaces, whereas the epitympanum is away from the direct air stream and is only aerated through the tympanic isthmus, not including any possible auxiliary pathways.

Acquired cholesteatoma is morphologically characterized by epithelial cell proliferation and granulation tissue formation. Unfortunately, despite many studies, our understanding of the mechanisms underlying the

TABLE I.
Isthmus Block on Cases and Controls.

	Free	Blocked
Cases	4	98
Controls	47	3

$P < .0001$ (Fisher exact test).

TABLE II.
Tensor Fold Type on Cases and Controls.

	Incomplete	Complete
Cases	3	99
Controls	9	37

$P = .001$ (Fisher exact test). Data were not available for four controls.

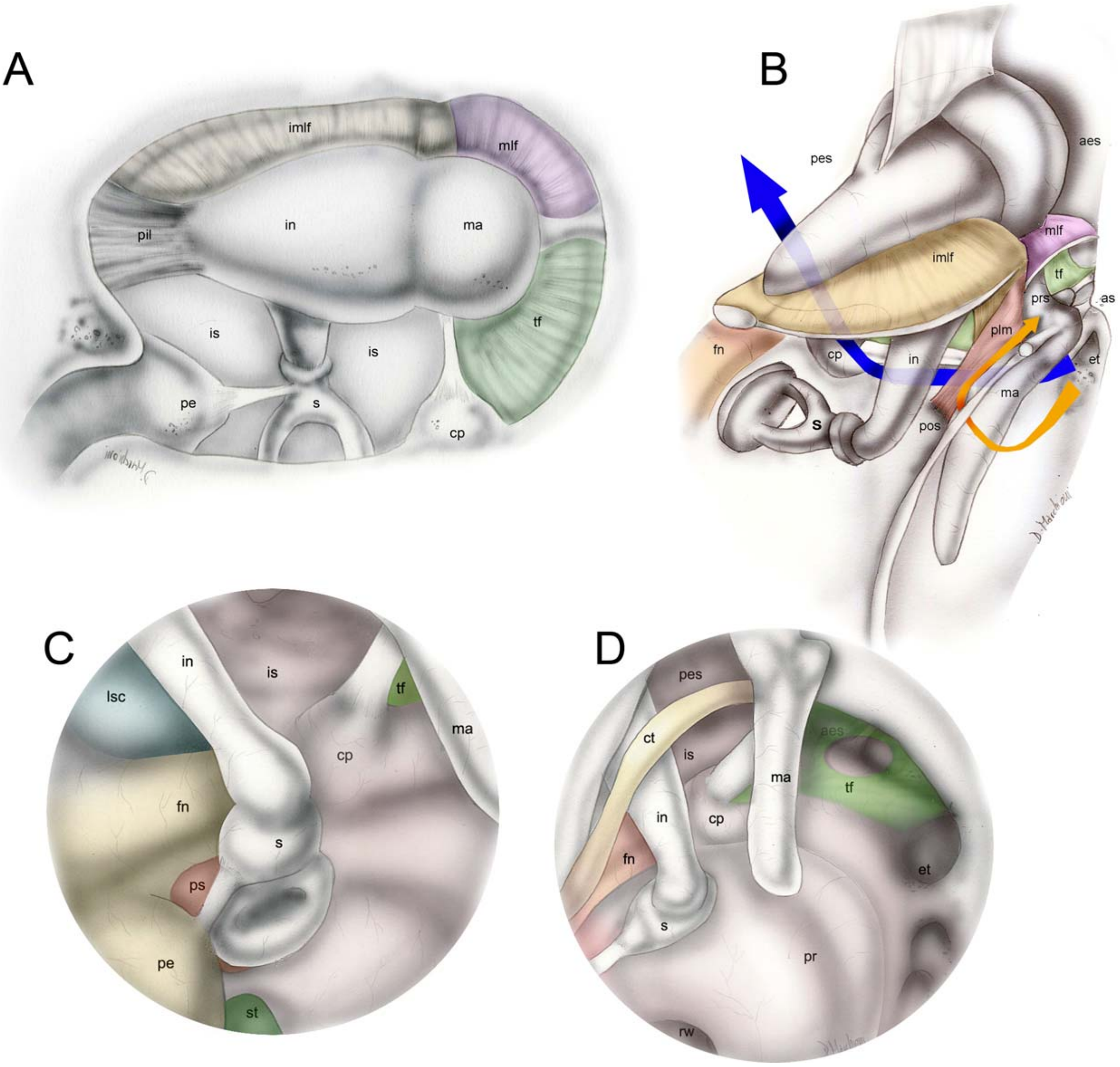

Fig. 8. Schematic drawing representing the epitympanic diaphragm and the main ventilation routes of the middle ear, view from above (A) and anterior to posterior view (B). The blue arrow represents the main aeration pathway from the eustachian tube to the epitympanum and mastoid through the isthmus, and the orange arrow represents the aeration pathway from the eustachian tube to Prussak's space through the posterior pouch. (C) Schematic drawing representing the endoscopic view of the tympanic isthmus using a 45° endoscope. (D) Schematic drawing representing the endoscopic view of the tensor fold using a 45° endoscope. In this case, an incomplete tensor fold is represented. aes = anterior epitympanic space; as = anterior spine; cp = cochleariform process; ct = chorda tympani; et = eustachian tube; fn = facial nerve; imlf = incudomalleal lateral fold; in = incus; is = isthmus; ma = malleus; mlf = malleolar lateral fold; pe = pyramidal eminence; pes = posterior epitympanic space; pil = posterior ligament of incus; plm = posterior ligament of malleus; pos = posterior spine; pr = promontory; prs = Prussak's space; ps = posterior sinus; rw = round window; s = stapes; st = sinus tympani; tf = tensor fold. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

pathogenesis of cholesteatoma is limited. Several theories for the genesis of cholesteatoma formation have been proposed in the literature.[2–4] The most accepted theory currently is the retraction pocket theory. This was postulated by Bezold in 1890,[2] He proposed that a retraction of Shrapnell's membrane as a result of chronic dysfunction of the eustachian tube might progress into formation of an attic cholesteatoma**.**

Recently, an habitual sniffing theory has been described and postulated under the heading of retraction theory.[13] Habitual sniffing associated with a closing failure of the eustachian tube is believed to be closely related to the etiology of retraction-type cholesteatoma. It seems that such sniffing induces a high negative pressure in the middle ear and may sometimes promote the development of cholesteatoma or its recurrence after surgery.

These theories have been postulated without consideration of the anatomical and physiological mechanisms related to middle ear ventilation.

Until now, previous studies have been based on cadaveric dissections or on animal models, because of

Fig. 9. Right ear. Schematic drawing representing the selective epitympanic dysventilation syndrome. (A) Granulation tissue is visible blocking the anterior isthmus. The mesotympanic spaces are normally ventilated (orange arrow) due to normal functioning of the eustachian tube; instead the attic space is dysventilated (red color). This condition could be the basis for the decrease in pressure in the attic with consequent attic retraction pocket development (B). dr = eardrum; fn = facial nerve; in = incus; is* = blockage of isthmus; ma = malleus; prs = Prussak's space; s = stapes; tf = tensor fold. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

the difficulty of studying subjects affected by attic cholesteatoma. With the introduction of the endoscope during middle ear surgery, it became possible to study the anatomical variations and the ventilatory pathways of pathological patients, due to the magnification of critical areas such as the tensor fold and tympanic isthmus.

In previous studies on this topic,[10] an isthmus blockage in association with a complete tensor fold was found in the majority of patients affected by attic retraction/cholesteatoma. For this reason, a selective attic dysventilation was postulated. The present study also confirmed that an isthmus blockage was present in more than 96% of patients with attic disease, compared to 6% in the control group (patients without attic disease). Similar results were found for a complete tensor fold, which was present in more than 96% of patients compared to 19% in the control group.

Based on the emerging data obtained, subjects affected by attic cholesteatoma identified endoscopically presented a concomitant condition of an isthmus blockage with complete tensor and incudomalleal folds. This condition represents a selective epitympanic dysventilation syndrome.[12,14]

When a blocked isthmus was found in subjects with a complete tensor fold, there was a complete separation between the mesotympanic compartments and epitympanic/mastoid compartments, creating a selective dysventilation in these latter compartments. This event might also be present in subjects with a normally functioning eustachian tube, creating two different aeration conditions between the attic/mastoid and mesotympanum. In fact, in these subjects, the mesotympanum could have good ventilation due to the normal functioning of the eustachian tube, whereas the attic and mastoid could have poor ventilation despite the normal functioning of the eustachian

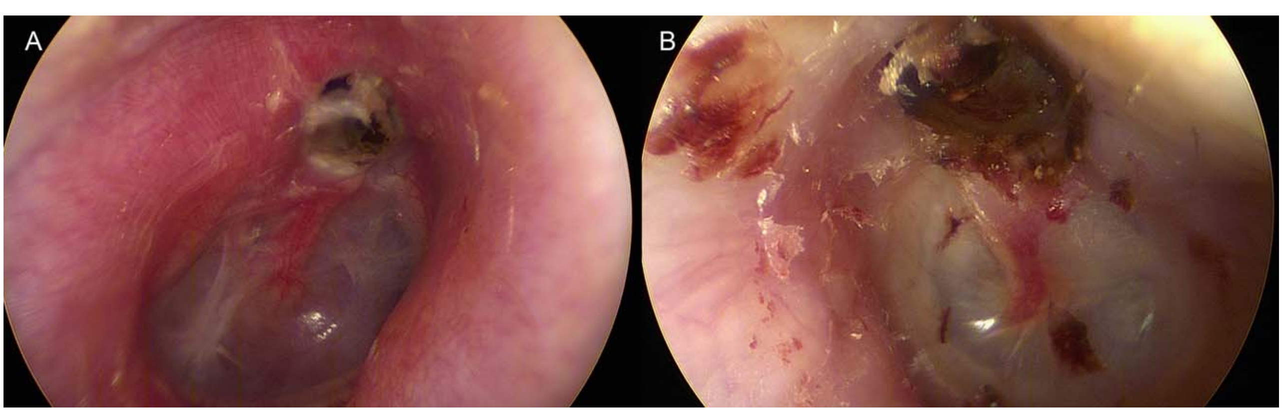

Fig. 10. Study groups. (A) A classical morphology of attic cholesteatoma. (B) A normal position of the eardrum is seen with the presence of cholesteatoma in the attic. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

tube but due to the blocked isthmus. Over time, a decrease in pressure could have occurred in the epitympanic compartments, and consequently, a retraction of the pars flaccida could have occurred in the attic (Fig. 9).

This mechanism might be the basis of the genesis of attic cholesteatoma in accordance with retraction theory. In addition, this scenario could explain the classical morphology of attic cholesteatoma, where an attic retraction with scutum erosion is usually associated with a normal position of the eardrum (pars tensa), and with supposedly good ventilation of the mesotympanic compartments (Fig. 10).

The findings of this study are in close agreement with the currently most accepted retraction pocket theory postulated by Bezold in 1890,[2] but the retraction might be occurring as a result of the ventilatory separation between the mesotympanic and epitympanic spaces, even in the presence of a normally functioning eustachian tube.

CONCLUSION

On the basis of our previous experience and this work, a new theory for the genesis of attic cholesteatoma has been postulated. Selective epitympanic dysventilation occurs when a blockage of the isthmus is present and associated with a complete tensor fold, causing a ventilatory separation between the epitympanum and mesotympanum. This mechanism could be the basis for a selective decrease in the pressure in the attic, with the subsequent development of attic retraction pockets and cholesteatoma even in subjects with a normally functioning eustachian tube.

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