Review

EAONO/JOS Joint Consensus Statements on the Definitions, Classification and Staging of Middle Ear Cholesteatoma

Matthew Yung, Tetsuya Tono, Ewa Olszewska, Yutaka Yamamoto, Holger Sudhoff, Masafumi Sakagami, Jef Mulder, Hiromi Kojima, Armağan İncesulu, Franco Trabalzini, Nuri Özgirgin

The European Academy of Otology and Neurotology (EAONO) has previously published a consensus document on the definitions and classification of cholesteatoma. It was based on the Delphi consensus methodology involving the broad EAONO membership. At the same time, the Japanese Otological Society (JOS) had been working independently on the “Classification and Staging of Cholesteatoma.” EAONO and JOS then decided to collaborate and produce a joint consensus document. The EAONO/JOS joint consensus on “Definitions, Classification and Staging of Middle Ear Cholesteatoma” was formally presented at the 10th International Conference on Cholesteatoma and Ear Surgery in Edinburgh, June 5–8, 2016. The international otology community who attended the consensus session was given the chance to debate and give their support or disapproval. The statements on the “Definitions of Cholesteatoma” received 89% approval. The “Classification of Cholesteatoma” received almost universal approval (98%). The “EAONO/JOS Staging System on Middle Ear Cholesteatoma” had a majority of approval (75%). Some international otologists wanted to see more prognostic factors being incorporated in the staging system. In response to this, the EAONO/JOS steering group plans to set up an “International Otology Outcome Working Group” to work on a minimum common otology data set that the international otology community can use to evaluate their surgical outcome. This will generate a large database and help identify relevant prognostic factors that can be incorporated into the staging system in future revisions.

KEYWORDS: Definitions, classification, staging, cholesteatoma

The aims of the European Academy of Otology and Neurotology/Japan Otological Society (EAONO/JOS) Joint Consensus Statements on Definition, Classification and Staging are as follows:

1. The definitions provide terminologies in the description of cholesteatoma.
2. The classification categorized cholesteatoma into distinct categories to facilitate the comparison of surgical outcomes across reports.
3. The staging system reflects the severity of the cholesteatoma, the difficulty to achieve complete removal, and the subsequent restoration of normal function.

The authors wish to present the final consensus first, followed by an explanation of the methodology on how the EAONO/JOS consensus was reached by the steering group.

The clinical classification of middle ear mucosa is summarized in Figure 1.
Definitions and Statements on Cholesteatoma

1. Cholesteatoma is a mass formed by the keratinizing squamous epithelium in the tympanic cavity and/or mastoid and subepithelial connective tissue and by the progressive accumulation of keratin debris with/without a surrounding inflammatory reaction.

2. Cholesteatoma consists of matrix (keratinizing squamous epithelium), perimatrix (varying thickness of the subepithelial connective tissue), and keratin debris.

3. The pathophysiology of cholesteatoma is not completely understood.

4. Recurrent infections and inflammatory reactions at the subepithelial connective tissue of cholesteatoma contribute to bone resorption in the adjacent area.

5. Cholesteatoma is diagnosed with a detailed otologic history, physical examination by otomicroscopy, and endoscopy with or without imaging.

6. Cholesteatoma is classified into two general categories: congenital and acquired.

7. Acquired cholesteatoma is characterized by clinical symptoms/signs that are the result of growth with/without destruction of the adjacent structures:
   - with or without tympanic membrane retraction and/or perforation,
   - with or without otorrhea,
   - with or without hearing deterioration,
   and/or CT/MRI findings (soft tissue masses, focal areas of bony erosion of the middle ear, and mastoid)

8. A retraction pocket can develop into acquired cholesteatoma when it loses its ability of self-cleaning and starts the accumulation of keratin debris.

9. Acquired cholesteatoma is not present at birth.

10. Acquired cholesteatoma might develop from a retraction pocket of the pars flaccida, pars tensa, or both and from basal cell invasion through the basilar membrane and could be a sequela of the dysfunction of middle ear pressure regulation. Acquired cholesteatoma can also develop secondary to tympanic membrane perforation as a result of previous chronic otitis media, trauma, or iatrogenic causes.

11. Congenital cholesteatoma is typically an expanding cystic mass with keratinizing squamous epithelium located medial to the intact tympanic membrane, is assumed to be present at birth, but is usually diagnosed during infancy or in early childhood in patients with no prior history of otorrhea, perforation, or previous ear surgery.

12. A history of previous bouts of otitis media or an effusion does not exclude congenital cholesteatoma.

13. Congenital cholesteatoma is usually located at the anterosuperior quadrant of the middle ear. However, it may be located at the posterosuperior quadrant or other locations.

14. The clinical presentation of congenital cholesteatoma is determined by the location and extent of the lesion. It may be characterized by
   - a white mass medial to an intact tympanic membrane,
   - hearing loss when enlarged to fill the middle ear or erodes the ossicles,
   - extremely rarely with pain,
   and/or CT/MRI findings (usually as a round soft tissue mass at the anterosuperior quadrant, the posterosuperior quadrant, or other locations)

15. Cholesteatoma recidivism includes both residual and recurrent cholesteatoma. It is essential to differentiate them.

16. Residual cholesteatoma results from the incomplete surgical removal of the cholesteatoma matrix.

17. Recurrent cholesteatoma results from the reformation of the retraction pocket after a complete previous surgical cholesteatoma removal.

18. Cholesteatoma is classified into acquired, congenital, and unclassifiable (cholesteatoma whose origin cannot be accurately determined).

Acquired cholesteatoma is further subclassified into

1. retraction pocket cholesteatoma
   a) pars flaccida (attic cholesteatoma)
   b) pars tensa cholesteatoma
   c) combination of pars flaccida and pars tensa cholesteatoma

2. non-retraction pocket cholesteatoma
   a) cholesteatoma secondary to tympanic perforation (the so-called secondary acquired cholesteatoma)
   b) cholesteatoma following trauma and/or otologic procedures

Post-surgical cholesteatoma may be residual or recurrent, although these are not mutually exclusive.
Staging of Middle Ear Cholesteatoma

1. Divisions of the middle ear space (STAM system)
   In order to simplify the extent of cholesteatoma, the middle ear and mastoid space are divided into four sites: difficult access sites (S), tympanic cavity (T), attic (A), and mastoid (M). The difficult access sites (S) includes S1, the supratubal recess (also called the anterior epitympanum or protympanum) and S2, the sinus tympani. The posterior border of the attic is the posterior end of the incus short process or the fossa incudis. The mastoid includes the antrum and mastoid cells.

   Divisions of the middle ear space using the STAM system is illustrated in Figure 2.

2. The EAONO/JOS staging system applies to four types of middle ear cholesteatoma
   (Pars flaccida cholesteatoma, pars tensa cholesteatoma, congenital cholesteatoma, and cholesteatoma secondary to a tensa perforation)

   Stage I: Cholesteatoma localized in the primary site*
   * The site of cholesteatoma origin, i.e., the attic (A) for pars flaccida cholesteatoma; the tympanic cavity (T) for pars tensa cholesteatoma, congenital cholesteatoma, and cholesteatoma secondary to a tensa perforation

   Stage II: Cholesteatoma involving two or more sites

   Stage III: Cholesteatoma with extracranial complications or pathologic conditions including
   - Facial palsy,
   - Labyrinthine fistula: with conditions at risk of membranous labyrinth,
   - Labyrinthitis,
   - Postauricular abscess or fistula,
   - Zygomatic abscess,
   - Neck abscess,
Canal wall destruction: more than half the length of the bony ear canal, Destruction of the tegmen: with a defect that requires surgical repair, and Adhesive otitis: total adhesion of the pars tensa.

Stage IV: Cholesteatoma with intracranial complications including Purulent meningitis, Epidural abscess, Subdural abscess, Brain abscess, Sinus thrombosis, and Brain herniation into the mastoid cavity.

The staging system does not apply to petrous bone cholesteatoma.

3. Staging systems for respective cholesteatoma types
1) Pars flaccida cholesteatoma (attic cholesteatoma)
   Stage I: Cholesteatoma localized in the attic
   Stage II: Cholesteatoma involving two or more sites
   Stage III: Cholesteatoma with extracranial complications
   Stage IV: Cholesteatoma with intracranial complications

2) Pars tensa cholesteatoma, cholesteatoma secondary to a tensa perforation, and congenital cholesteatoma
   Stage I: Cholesteatoma localized in the tympanic cavity
   Stage II: Cholesteatoma involving two or more sites
   Stage III: Cholesteatoma with extracranial complications
   Stage IV: Cholesteatoma with intracranial complications

Background on the Collaboration Between EAONO and JOS on the Definitions, Staging, and Classification of Middle Ear Cholesteatoma
The European Academy of Otolaryngology and Neurotology (EAONO) has previously published a document on the definitions and classification of cholesteatoma. They were published in 2015 and are summarized in Appendix 1. The statements were based on the Delphi consensus methodology involving the broad EAONO membership. At the same time, the Japan Otological Society (JOS) had been working independently on the “Classification and Staging of Cholesteatoma.” Its recommendations were formulated by the JOS steering board alone and are summarized in Appendix 2.

The respective steering group of EAONO and JOS decided to work together to produce a single consensus document on the “Definitions, Classification, and Staging of Middle Ear Cholesteatoma” to globalize the system. The first EAONO/JOS steering group meeting was held in 2015 at the 30th Politzer Society Meeting in Niigata. The final version of the “Joint EAONO/JOS Consensus on the Definitions, Classification, and Staging of Middle Ear Cholesteatoma” was the end product of many rounds of discussions and refinements over a 12-month period.

Formulation of a Joint EAONO/JOS Consensus on the Definitions, Classification, and Staging of Middle Ear Cholesteatoma
a. Methodology
   Six European otologists of the original EAONO steering group (Matthew Yung, Ewa Olszewska, Nuri Özgirgin, Holger Sudhoff, Jef Mulder, and Armağan İncesulu) and four Japanese otologists of the original JOS steering group (Tetsuya Tono, Masafumi Sakagami, Yutaka Yamamoto, and Hiromi Kojima) participated in the joint EAONO/JOS steering group to work on the consensus project. Collectively, these 10 members produced the first draft of the document by consensus (Draft 1).

b. Consensus among steering group members (Draft 1):
1. Definitions of Cholesteatoma-The definitions provide terminologies in the description of cholesteatoma. Except for some minor changes in the narratives, the original EAONO statements on definitions of cholesteatoma were adopted. These changes include:
   - The revised EAONO/JOS statement “Congenital cholesteatoma is usually located at the anterosuperior quadrant of the middle ear. However, it may be located at the posterosuperior quadrant or other locations” is an amendment to the original EAONO statement to reflect the fact that many congenital cholesteatomas in Japan were found at the posterosuperior quadrant.
   - The term “chronic otitis media with or without cholesteatoma” in the original 2015 EAONO document was dropped from the joint consensus as the term is not universally accepted.

2. Classification of Middle Ear Cholesteatoma-The classification categorized cholesteatoma into distinct categories to facilitate the comparison of surgical outcome across reports. The classification proposed originally by EAONO and JOS independently were compared, modified, and merged:
   - The terms “primary acquired” and “secondary acquired” were dropped as they are historical terms and are confusing. In the joint EAONO/JOS classification, acquired cholesteatoma was divided into retraction pocket cholesteatoma and non-retraction pocket cholesteatoma.
   - The joint EAONO/JOS classification applies only to “Middle Ear Cholesteatoma” as the inclusion of petrous cholesteatoma makes the classification and staging system too complex.
   - Cholesteatoma was classified as “congenital,” “acquired,” and “unclassifiable.” The last category was not present in the original 2015 EAONO classification. In certain large or open cholesteatomas, it may not be possible to ascertain whether they are “congenital” or “acquired.”
   - “Suspected congenital cholesteatoma” from the original JOS classification was dropped.

3. Staging of Middle Ear Cholesteatoma-The staging system reflects the severity of the cholesteatoma, the difficulty to achieve complete removal, and the subsequent restoration of the normal function. The EAONO/JOS steering group modified the original JOS staging system and adopted the new version as the joint EAONO/JOS staging system.
   - “Retraction pocket” was dropped from the original JOS staging system because it is not cholesteatoma by definition.
   - Stages 1 and 2 are based on sites of cholesteatoma involvement. Stage 2 represents the involvement of multiple sites.
   - The original sites of protympanum, tympanic cavity, attic, and mastoid proposed by JOS (symbolized as PTAM as illustrated in Figure 3) were changed to STAM (S1: supratubal recess, S2: sinus tympanum, tympanic cavity, attic, and mastoid) in the joint EAONO/JOS staging system.
   - Stage 3 represents extracranial extension, and stage 4 represents intracranial extension. These extensions are specified in the joint EAONO/JOS staging system.
International Feedback of the Proposed EAONO/JOS Consensus
The 10th International Conference on Cholesteatoma and Ear Surgery, June 5–8, 2016 (Chole2016) provided the opportunity for the EAONO/JOS steering group to gauge the international acceptance of the proposed EAONO/JOS “Definitions, Classification, and Staging of Middle Ear Cholesteatoma.” Over 1000 delegates from 54 countries attended Chole2016, with 23 national otology societies presenting mini-symposia. The EAONO/JOS steering group went through several rounds of international feedback assist in producing the final version.

a. One month before Chole2016, the draft EAONO/JOS consensus document was sent to the presidents and/or the representatives of various national otology societies. Specific comments were received from the British Society of Otology, American Otological Society, Australian Otological Society, German HNO, and Canadian Otological Society. They were mostly in agreement with the EAONO/JOS proposal and only minor adjustments were made in response to these comments (Draft 2).

b. Draft 2 of the EAONO/JOS consensus document was formally presented at a consensus session at Chole2016 (Staging and Classification of Cholesteatoma). The delegates present at the consensus session were given the chance to debate and comment on the definitions, classification, and staging of the proposed document section by section. Their feedback was recorded, considered, and refinement was made to the document (Draft 3).

c. As it took a few days for the EAONO/JOS steering group to produce Draft 3 in response to the comments received at Chole2016, the delegates were invited to provide follow up feedback later on. Those agreed to be contacted again had their ID code (on the conference badge) scanned. Draft 3 was then sent to each international delegate together with a standardized feedback form electronically. Their approval/disapproval of Draft 3 and the reasons for disapproval were recorded.

d. Analysis of international feedback on the “Definitions of Cholesteatoma” (Table 1).

Altogether, 47 international delegates provided follow up feedback on Draft 3. Of these, 3 were trainee otolaryngologists. Their responses were, therefore, excluded from the analysis.

Eighty-nine percent of the international delegates gave their approval to the statements on definition. Five (5) comments were given as the reason for disapproval:

1. Reason given by one UK delegate: On Terminology-commented that the title should be specified as “Middle Ear Cholesteatoma;” The EAONO/JOS steering group agreed and made the change as suggested.

2. Reason given by one Australian delegate: On Terminology-the term “middle ear and mastoid” in Statement 1 should be changed to “tympanic cavity and mastoid.” This was thought to be reasonable and was amended accordingly.

3. No reason given from another Australian delegate.

4. Reason given by one Polish delegate: On Terminology-the term “middle ear and mastoid” in Statement 1 should be changed to “tympanic cavity and mastoid.” This was thought to be reasonable and was amended accordingly.

5. Reason given by one Brazilian delegate: Two of the statements in Draft 3 were repetitive and the delegate recommended one of them to be deleted. The EAONO/JOS agreed and deleted one of the statements.

All the above amendments were regarded as minor and the EAONO/JOS steering group felt that they did not change the essence of the “Definitions of Middle Ear Cholesteatoma.”

e. Analysis of international feedback on the “Classification of Cholesteatoma” (Table 2).

It was very encouraging to see 98% of the international delegates gave their approval on the “Classification of Middle Ear Cholesteatoma.” The single comment provided by an Australian delegate that led to the disapproval was:

1. Advised relegating “cholesteatoma secondary to perforation” to “others” as it is rare. EAONO/JOS decided against making this change.
f. Analysis of international feedback on the “Staging of Cholesteatoma” (Table 3).

The EAONO/JOS Staging System on Middle Ear Cholesteatoma received most comments during the consensus session at Chole2016. The debate was mainly on whether it should be simple but easy to use, or more complex to include more prognostic factors. It was, therefore, not surprising that it received less consensus compared to the sections on definitions and classification. Nevertheless, 75% of the international delegates approved the staging system. There were 11 delegates who did not approve the proposed consensus on staging. Their comments were summarized into several themes:

1. The proposed EAONO/JOS staging system was thought by some to be too simplistic. Several responders suggested a TNM style staging system to incorporate other prognostic factors that may influence surgical outcome (Netherlands, 1; UK, 1; Switzerland, 1; Norway, 1; and Algeria, 1). Several other responders suggested increasing the number of stages, i.e., more than 4 stages to accommodate more prognostic factors (UK, 1; Italy, 1; South Africa, 1).

2. On the other hand, one responder (Australia, 1) proposed an alternative staging system that was even simpler than the EAONO/JOS staging system. This was at odds with the others who wanted a more complex system.

3. One responder (Bulgaria, 1) recommended changing the term “tensa perforation” to “tympanic perforation” to include pars flaccida as well. This was felt to be reasonable and the change was made accordingly.

4. One responder suggested incorporating petrous cholesteatoma back into the system (Australia, 1). The steering group did not make the change as it made the staging system even more complicated.

Table 2. International comments on the EAONO/JOS Classification of Cholesteatoma at Chole 2016 (44 responses)

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Table 3. International comments on the EAONO/JOS Staging of Cholesteatoma at Chole 2016 (44 responses)

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<td>Total</td>
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<td>Total = 33 (75%)</td>
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Figure 3. Divisions of the middle ear space using the PTAM system
about its over-simplicity. Five out of eight recommended a TNM style
system to incorporate other parameters such as ossicular status,
mucosal status, and pneumatization of the mastoid cells. Three out
of eight recommended increasing the number of stages within the
system to incorporate extra parameters. However, these responders
could not agree as to which parameters should be included as there
is a lack of evidence or consensus in the literature. The EAONO/JOS
steering group felt that a more complex staging system may result in
even more controversy. Therefore, the staging system was kept sim-
ple at this stage and other prognostic factors may be incorporated in
the future only if they are supported by evidence.

The method in reaching the final version of the EAONO/JOS consen-
sus document is summarized in Figure 4.

**Plan for the future**
The “EAONO/JOS Consensus on Definitions of Middle Ear Choleste-
atomata” received 89% international approval. Minor alterations were
made that did not alter the essence of the document. The final “EAO-
NO/JOS Consensus Document on the Classification of Middle Ear Cho-
lesteatoma” received almost universal international approval (98%). The “EAONO/JOS Staging System on Middle Ear Cholesteatoma” had
a majority of international approval (75%). Some international otol-
ogists wanted to see more prognostic factors incorporated into the
staging system. In response to this criticism, the EAONO/JOS steer-
ing group plans to set up an “International Otology Outcome Work-
ning Group” under the auspices of the Politzer Society. The aim of that
group is to agree on a minimum common otology data set that the
international otology community can use to evaluate their surgical
outcomes. The steering group will facilitate multi-center studies with
a large database to identify relevant prognostic factors that could be
incorporated into a future revised EAONO/JOS staging system. Such
parameters will then be based on evidence and not on personal opin-
ion or sentiment.

**Peer-review:** Externally peer-reviewed.

**Author Contributions:** Concept – M.Y., T.T., E.O., Y.Y., H.S., M.S., J.M., H.K., A.I.,
F.T., N.Ö.; Design – M.Y., T.T., E.O., H.S., J.M., H.K., N.Ö.; Supervision – M.Y., T.T.,
N.Ö.; Resources - M.Y.; F.T., N.Ö.; Data Collection and/or Processing - M.Y., T.T.,
E.O., Y.Y., H.S., M.S., J.M., N.Ö.; Analysis and/or Interpretation - M.Y., T.T., E.O.,
Y.Y., H.S., M.S., J.M., N.Ö.; Literature Search – E.O.; Writing Manuscript – M.Y.,

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REFERENCES


