

Peer Review File

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Reviewer A

Methods: A cross-sectional study was performed on electronic medical records from.

ATTENTION: the title talks about retrospective review in the cross sectional study method deciding how to set up the study.

Reply: Thank you for your response, the methods have been edited to describe a retrospective review study (Page 2, Lines 23-25)

Changes in the text:

Methods: A retrospective review was performed on electronic medical records from 2012 to 2021 were searched for the diagnosis of ES. Demographics, symptomology, medical and surgical treatments, and clinical course data were collected and analyzed.

Conclusion: they do not give any important information for the literature.

Reply: Thank you for your comment, the conclusion has been edited to highlight the contribution to the literature (Pages 15-16, Lines 322-327).

Changes in the text:

In contrast to previous literature, patients in this study with ES were not more likely to have a history of tonsillectomy and the length of the styloid process did not correlate with symptomatology. Therefore, careful correlation of symptoms with imaging as well as assessment of response to attempted interventions assists in appropriate diagnosis. Surgical treatment seems to have low morbidity and may be effective in improving clinical symptoms in the short term, within three months of surgery.

Reviewer B

In this paper the author presents the results of a retrospective case series on patients (n=47) treated for Eagle syndrome in a single center from 2012 to 2021. They conclude that ES is not necessarily related to a history of tonsillectomy and surgery is effective in improving symptoms.

The paper is well written and quite easy to understand. English is fine. Image and tables are essential to comprehension.

Several methodological issues have to be addressed:

- absence of a quality checklist (see STROBE statement)

Reply: Thank you for your comment. The STROBE assessment quality checklist has been added as a supplemental figure.

Changes in the text:

Supplemental Figure 1: Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) Assessment

- absence of data regarding the concordance between the laterality of the radiological elongation and symptoms for unilateral cases.

Reply: Thank you for this suggestion. An analysis has been conducted on symptom laterality and radiological findings and the results are now found in Table 2. The manuscript has been edited to account for the findings (Page 8, Lines 146-148; Page 14 Lines 285-291).

Changes in the text:

Laterality of radiological findings (styloid elongation and stylohyoid ligament calcification) did not correlate with laterality of symptoms as shown in **Table 2**.

Interestingly, there was no significant correlation between laterality of symptoms and laterality of the styloid process abnormality seen on imaging in our cohort. This means that some patients that had unilateral pathology experienced bilateral symptoms or some with bilateral pathology experienced unilateral symptoms. While those with bilateral pathology and unilateral symptoms may be explained by more severe involvement on the symptomatic side, unilateral pathology with bilateral symptoms, while less frequent, may be explained by compression or irritation of surrounding nerves or muscles and the mechanisms of referred pain and central sensitization.(25)

- the case presented at line 233 clearly shows a jugular variant of ES. Authors are suggested to revise current literature about and integrate (see for example [10.3390/diagnostics13020298](https://doi.org/10.3390/diagnostics13020298))

Reply: Thank you for your reply. The two cases of vascular ES described in our results were further classified based on the literature and were expanded on in the discussion. (Page 11, Lines 218-222; Page 13, Lines 266-273)

Changes in the text:

The second patient presented with recurrent headaches, tinnitus, peripheral paresthesia, and mild residual right leg weakness following a stroke one month prior to presentation. CT angiography revealed elongated styloid processes with compression of bilateral jugular veins, worse on the left side, classifying it as a Type II vascular ES.(19)

Two patients included in our study had features suggestive of vascular ES. One patient exhibited compression of the internal jugular vein by an elongated styloid process which has been reported in the literature and is classified as a Type II vascular ES.(19, 23, 24) The second patient demonstrated an elongated styloid process in close proximity to the mid-internal carotid artery which has been defined as a Type I vascular ES.(19) Both forms of vascular ES are rare with limited data on surgical outcomes in the literature. While our patient with Type I ES was lost to

follow-up, the patient with Type II ES did not demonstrate improvement in symptoms following surgical intervention.

- improvement in symptoms needs to be better defined in Methods section (no/partial/significant see Table 2)

Reply: Thank you for the suggestion. We understand that symptom improvement required more specific definition, the manuscript was adjusted as such. Furthermore, the limitations of our methodology due to the retrospective nature of the study was added as well. (Page 6, Lines 98-101; Page 15, Lines 303-306).

Changes in the text:

Symptom improvement was judged to be significant, partial or none based on patient report at follow up evaluation. Significant improvement was defined as complete or nearly complete resolution of symptoms and partial improvement was defined as a noticeable alleviation in symptoms but still present.

Limitations of this study are inherent to those of retrospective reviews, including relying on the available data in the electronic medical record. However, records from outside institutions were accessed through CareEverywhere whenever possible. Our data extraction of symptom improvement relied on language reported in the patient chart.

- authors should be more cautious in conclusion when stating that "Surgical treatment has low morbidity and is effective in improving clinical symptoms". The short follow up and unclear patient's assessment prevent from such an inference.

Reply: We appreciate that the language used in our conclusion was too assertive given the results of our study. The conclusion was edited to provide softer language about surgical outcomes based on our results. (Page 16, Lines 322-327)

Changes in the text:

In contrast to previous literature, patients in this study with ES were not more likely to have a history of tonsillectomy and the length of the styloid process did not correlate with symptomatology. Therefore, careful correlation of symptoms with imaging as well as assessment of response to attempted interventions assists in appropriate diagnosis. Surgical treatment seems to have low morbidity and may be effective in improving clinical symptoms in the short term, within three months of surgery.

Reviewer C

I recommend the authors the following:

All post-operative complications must be tabled and classified into trans-oral vs transcervical.

Reply: Thank you for the suggestion. Post-operative complications, classified by

surgical approach, have now been outlined in Table 4.

Changes in the text:

Frequency of complications compared between the two surgical approaches was not significantly different and is summarized in **Table 4**.

The authors must classify the Eagle syndrome Patients regarding the BMJ classifications (<http://dx.doi.org/10.1136/bcr-2022-249558>) and subdivide to which type of Eagle syndrome had transoral vs transcervical.

Reply: We appreciate this reviewer's suggestion. The two cases of vascular ES described in our results were further classified based on the literature and were expanded on in the discussion. Transcervical and transoral approaches for styloidectomy is specified in the text (Page 11, Lines 213-224; Page 13, Lines 266-273)

Changes in the text:

Two patients presented with symptomology suggestive of vascular ES. The first patient presented with Horner's syndrome and a prior history of possible carotid artery dissection. CT imaging demonstrated an elongated styloid process near his mid-internal carotid artery which has been previously classified as a Type I vascular ES.(19) The patient underwent a unilateral transcervical styloidectomy; however, follow-up data was unavailable as the patient returned home to a foreign country shortly after surgery. The second patient presented with recurrent headaches, tinnitus, peripheral paresthesia, and mild residual right leg weakness following a stroke one month prior to presentation. CT angiography revealed elongated styloid processes with compression of bilateral jugular veins, worse on the left side, classifying it as a Type II vascular ES.(19) Patient underwent bilateral transoral styloidectomy and had post-operative bleeding with a high INR attributable to the patient taking warfarin for antiphospholipid syndrome. He did not note improvement in symptoms in follow up visit after surgery.

Two patients included in our study had features suggestive of vascular ES. One patient exhibited compression of the internal jugular vein by an elongated styloid process which has been reported in the literature and is classified as a Type II vascular ES.(19, 23, 24) The second patient demonstrated an elongated styloid process in close proximity to the mid-internal carotid artery which has been defined as a Type I vascular ES.(19) Both forms of vascular ES are rare with limited data on surgical outcomes in the literature. While our patient with Type I ES was lost to follow-up, the patient with Type II ES did not demonstrate improvement in symptoms.

The authors must explain why they operated on asymptomatic Eagle syndrome.

Reply: Thank you for your comment and we apologize for the confusion. Patients with asymptomatic ES did not undergo surgery. We appreciate that the text may not have clearly explained this and has been edited (Page 9, Lines 177-178).

Changes in the text:

The results of surgical treatment and outcomes for patients with ES are summarized in **Table 3**. None of the asymptomatic patients underwent surgery.

The usual pattern of Eagle syndrome diagnosis is that patients had been going around different specialities before having a confirmed diagnosis, how the authors were able to pinpoint the diagnosis immediately, as at least half of the patients usually had been going around different specialities.

Reply: We appreciate this comment, this is true, ES patients often see multiple providers before arriving at a diagnosis. Diagnoses were based on the culmination of past history and evaluation provided at our tertiary care center, where the charts for this study were reviewed. All patients included in our analysis were clinically diagnosed prior to our review. No specific ICD code exists for ES, therefore we used a broad initial search followed by chart review to narrow down the patients based on clinical diagnosis. We appreciate that this may not be clear in the manuscript and the text was thus edited (Page 5, Lines 80-91)

Changes in the text:

Electronic medical records from 2012 to 2021 that contained relevant diagnoses during patient visits were collected and analyzed. Because ES is not an International Classification of Diagnosis (ICD) condition, similar diagnoses of Eagle symptomology were used to search records including those recommended by the American Academy of Otolaryngology.⁽¹⁷⁾ The following ICD 10 codes, and their corresponding ICD 9 codes, were used for the initial search: M24.20 (Disorder of ligament, unspecified site), J02.9 (Acute pharyngitis, unspecified), R13.10 (Dysphagia, unspecified), G50.1 (Atypical facial pain), R07.0 (Pain in throat), M54.2 (Cervicalgia), R13.19 (Other dysphagia), M62.89 (Other specified disorders of muscle), M89.8X8 (Other specified disorders of bone, other site). Patient were included during chart review if a clinical diagnosis of ES was made by the treating physician using standard criteria of styloid process measuring ≥ 3 cm and/or calcification of the stylohyoid ligament with symptoms reasonably attributable to the syndrome.

HD photos of 3-D reconstructions of all different types of Eagle Syndrome patients pre and post-intervention must be provided

Reply: Thank you for your suggestion. The 3D reconstructions were not part of the methodology for our study in evaluation of ES or measurement of the styloid process, which was conducted on 2D images. The 3D reconstructions provided were merely used as a visual representation of the difference between styloid process elongation and stylohyoid ligament calcification. We are happy to remove the 3D reconstruction figures if the presence of the figure may lead to confusion. Furthermore, post-operative CT scans for ES were not routinely performed at our institution and are thus not available. The text has been edited to more clearly outline the purpose of the figures (Page 5, Lines 88-95).

Changes to the text:

Patient were included during chart review if a clinical diagnosis of ES was made

using standard criteria (styloid process measuring ≥ 3 cm and/or calcification of the stylohyoid ligament with symptoms reasonably attributable to the syndrome). Example 3D reconstructions of styloid elongation and stylohyoid ligament calcification made using Horos open-source software (version 3.3.6) are shown in **Figure 1**. In patients with isolated styloid elongation, the length was measured by two raters (RW, AO) on 2D sagittal sections of neck CT imaging using Impax software (AFGA Corporation, Mortsels, Belgium).