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Measuring the density of the fissula antefenestram and the section of the basal turn of the cochlea: Are they useful in the radiological diagnosis of otosclerosis?

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ABSTRACT

Introduction: The role of objective parameters in terms of improvement of the accuracy of high-resolution computed tomography (HRCT) of the temporal bone in the diagnosis of otosclerosis remains unclear.
Objectives: To investigate the relationship between the density of the fissula antefenestram (FAF) and of the width of the transversal section of the basal turn of the cochlea (BTC), and the diagnosis of otosclerosis.
Methods: This is a retrospective study in which preoperative HRCT data from ears of patients submitted to stapedotomy due to otosclerosis (case group) were evaluated. For the control group, normal hearing ears having undergone HRCT for other purposes were included. Case and control HRCT images were objectively assessed by an experienced blinded radiologist. During this evaluation, measurements of the relative radiological density of the FAF and of the transversal section of the BTC were obtained. The results were compared between the groups. Also, a receiver operating characteristic curve was created and the area under the curve (AUC) was calculated for each variable. Significance level was set at .05.
Results: 40 ears were included in each group. Case ears presented reduced values for the relative radiological density on the FAF (p-value<0.0001). Moreover, ears with otosclerosis (p-value: 0.022) presented lower transversal section of the BTC. The AUC for these variables reached 0.929 and 0.646, respectively.
Conclusions: Otosclerotic ears present reduced radiological density on the FAF and narrower BTC. The relative density of the FAF also shows a great diagnostic power in the context of this disease.

1. Introduction

Otosclerosis is a focal bone disease affecting the otic capsule. It is a prevalent cause of hearing loss and, less frequently, of other audiovestibular symptoms among adults(T. C. Lee et al., 2009; Vicente et al., 2006). The diagnosis is often clinical, and supported by audiometric and tympanometric evaluation. Usually, a conductive or mixed hearing loss with absent stapedial reflexes is observed in otosclerotic ears.

High-resolution computed tomography (HRCT) of the temporal bone frequently shows suggestive findings in suspected cases(Vicente et al., 2006). Thus, the HRCT might be needed in particular cases for differential diagnosis.(Wolfovitz and Luntz, 2018). However, the routine use of CT imaging with diagnostic purposes is a matter of discussion, despite the increasing accuracy reported with the most recent techniques(McElveen Jr and Kutz Jr, 2018). Moreover, even though the use of algorithms including analysis of objective radiological parameters is increasingly recognized as beneficial to the diagnostic performance of the HRCT in the context of otosclerosis, this field has been poorly explored. This is mostly due to persistent doubts about which variables should be used and the diagnostic value of each of them. Two of the parameters which

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might be promising in this scenario are the radiological density of the *fissula antefenestram* (FAF) and the dimensions of the basal turn of the cochlea (BTC).

This study aims to investigate the presence of alterations in the radiological density of the FAF and in the transversal section of the BTC in the HRCT scans of otosclerotic ears and to discuss the eventual diagnostic value of each of these parameters.

2. Material and methods

This is a retrospective study wherein medical records from patients with surgically-confirmed otosclerosis treated in a tertiary otolaryngology department between 2018 and 2020 were evaluated. In brief, audiometric, radiological and general data were obtained from ears eligible to the case group. For controls, general and radiological data from adult patients with normal audiometry and stapedial reflexes were collected. These data were examined, computed and analysed for each ear individually. The study was approved by the Institutional Ethics Committee (*CAAEs: 11483219.1.0000.0096*).

For case group, ears from adults who underwent stapedotomy in order to treat hearing loss secondary to suspected otosclerotic stapes fixation were enrolled. All the ears were operated by the same surgeon, in the same institution, and under the same surgical technique. Otosclerotic stapes fixation was confirmed intraoperatively. Ears from patients whose HRCT scans were not obtained in the same institution, under the same protocol of imaging acquisition and processing, or in less than three months prior to the surgical procedure were excluded. Yet, ears from patients that did not undergo primary stapedotomy as the unique treatment for otosclerosis were also withdrawn from analysis. These included ears for which alternative diagnoses were set intraoperatively, those submitted to reoperations, and those whose procedures included surgical techniques or tools which are not part of the standard technique described ahead.

Ears from adult individuals with normal audiometry and tympanometry, both performed in the same institution of the study, were allocated in the control group. Besides, to be included in the sample, they had to have their HRCT also performed in the same clinic of the case group, following the same imaging protocol, and in no more than three months from the date of their audiological evaluation.

Ears from case group were submitted to stapedotomy under local anesthesia and sedation. The procedure was performed under microscopic view, using a transcanal approach, and without drills. Fenestration of the footplate was performed using a manual microperforator, namely without the need of drilling or laser, and also after confirming the stapes fixation and removal of the suprastructure. The prosthesis of choice was a 6 mm-diameter polytetrafluoroethylene piston, whose length was tailored during surgery for each patient according to the distance between the footplate and the long crus of the incus.

The HRCT scan images were obtained with a 256-channel scanner in a square matrix of 512x512 pixels. The images had a slice thickness of 1 mm and were considered and assessed for each side separately. After acquisition, they were reformatted in axial, coronal and oblique planes in a postprocessing workstation. The body of data was recorded and encrypted before transferring it to the radiologist. To allow blind evaluation, a random number was assigned to each HRCT scan. The correlation between each number with the corresponding ear was kept in the possession only of the lead researcher until the end of the data collection. Imaging data was assessed using the RadiAnt DICOM Viewer (version 2020.1).

Disease foci were considered in the presence of abnormal hypodense areas (otospongiotic or active focus) or volumetric and/or contour abnormalities affecting the structures of the otic capsule (otosclerotic or inactive focus). According to the overall evaluation of the HRCT scan of each individual, the radiologist deemed it as compatible or incompatible with otosclerosis. After, two objective parameters was assessed in a systematic fashion. These parameters are described in detail as follows:

a. Relative radiological density of the *fissula antefenestram*

The absolute density of the *fissula antefenestram* was obtained by inserting a region of interest (ROI) onto this area, with an approximate dimension of 0.01 cm^2, in an axial section, and in the plane of the oval window (Fig. 1A). Then, another ROI with the same dimensional features was used to acquire the absolute density of the most posterior high-density portion of the zygomatic arch of the same ear, also in an axial view (Fig. 1B). The ratio between these two values determined the relative radiological density of the FAF.

b. Transversal section of the basal turn of the cochlea

For this variable, an axial view in the plane of the mediolateral axis of the BTC was obtained. After, the largest anteroposterior section of this structure was measured, as depicted by Fig. 2A.

For each variable, the results were gathered and compared according to the allocation group. The data was summarized and firstly described using mean and standard deviation (sd).

To test the samples for normality, the Shapiro-Wilk test was used. After, for inferential analysis of categorical variables, the chi-square and the Fisher's exact test were employed, whereas the T-test and Mann-Whitney test were used when the variables were numerical. Moreover, to investigate the diagnostic power of each variable, a receiver operating characteristic (ROC) curve was created by plotting the true-positive rate against the false-positive rate at various threshold settings. The area under the curve (AUC) was then calculated to estimate how well each parameter could distinguish otosclerotic ears from unaffected ones.

The significance level was set at 0.05 and the tests were bilateral. For statistical analysis, the software R (version 4.0.2) was used. The study flow chart is shown in Fig. 3.

3. Results

89 patients had their medical records evaluated, of which 40 were eligible for the study. None of them underwent bilateral stapedotomy during the study, and the final case group sample comprised 40 ears. 20 subjects met the control group criteria. As they had their both ears individually assessed, the control group contained also 40 ears.

Among case ears, 30 (75%) belonged to female individuals and the mean age of the patients was 40.1 (sd: 10.4) years-old. Twenty-six (65%) ears from case group were from the left side. For the control group, also 30 ears were from women, and the mean age was 44.9 (dp: 11.53) years-old. No significant difference between case and control groups was observed when comparing then according to sex (p-value:1, chi-square test), age (p-value: 0.057, Mann-Whitney test), or side of the ear (p-value: 0.17, chi-square test).

Within the case group, 36 (90%) ears showed findings compatible with otosclerosis during the radiological assessment. None of the control ears showed signs of disease upon the blind analysis.

a. Relative density of the *fissula antefenestram*

Among case ears, the mean relative radiological density of the FAF was 0.77 (sd: 0.32) and, for the control group, this value

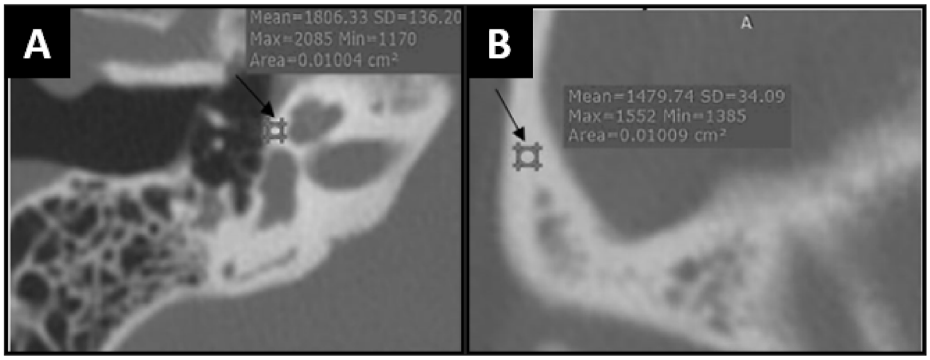

Fig. 1. HRCT scan images of the right temporal bone showing the measurements of the radiological density of a region of interest of 0.01 cm^2 (black arrows). A: in the plane of the oval window, for the antefenestral measurement. B: in the plane of the zigomatic arch, for the most posterior high-density area of this bone.

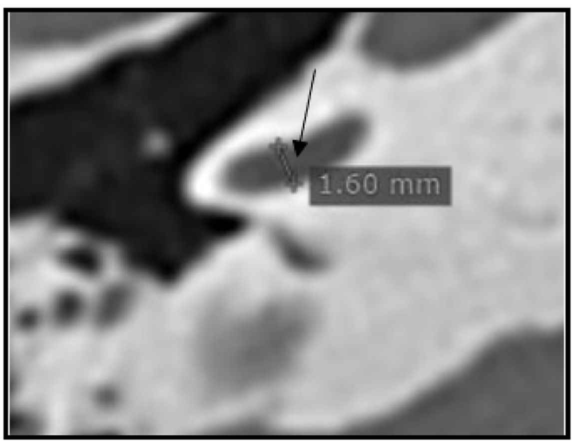

Fig. 2. Axial section of a HRCT scan of the temporal bone showing the measurement of the transversal basal turn of the cochlea (black arrow).

reached 1.35 (sd: 0.17). There was a significant difference between the results obtained for this variable according to the group of allocation (p-value <0.001, Mann-Whitney test, Fig. 4A). Thirty-seven (92.5%) ears with otosclerosis showed lower relative density of the FAF than that obtained on average for controls.

b. Transversal section of the basal turn of the cochlea

The mean width of the transversal section of the BTC was 1.76 (sd: 0.21) mm for the case group, whereas for the control group it reached 1.89 (sd: 0.26) mm. Again, the results obtained for the ears with otosclerosis were significantly inferior (p-value: 0.022, T-test, Fig. 4B) than those found among controls.

Fig. 5 shows the ROC curves for both the relative density of the FAF and the transversal section of the BTC. The area under the curve for the use of the density of the FAF as a discriminating tool was 0.929, while this value reached 0.646 for the use of the transversal section of the BTC.

4. Discussion

An increasing number of studies have aimed to investigate the use of imaging in otosclerosis. HRCT is the method of choice in the evaluation of structural abnormalities of the temporal bone in

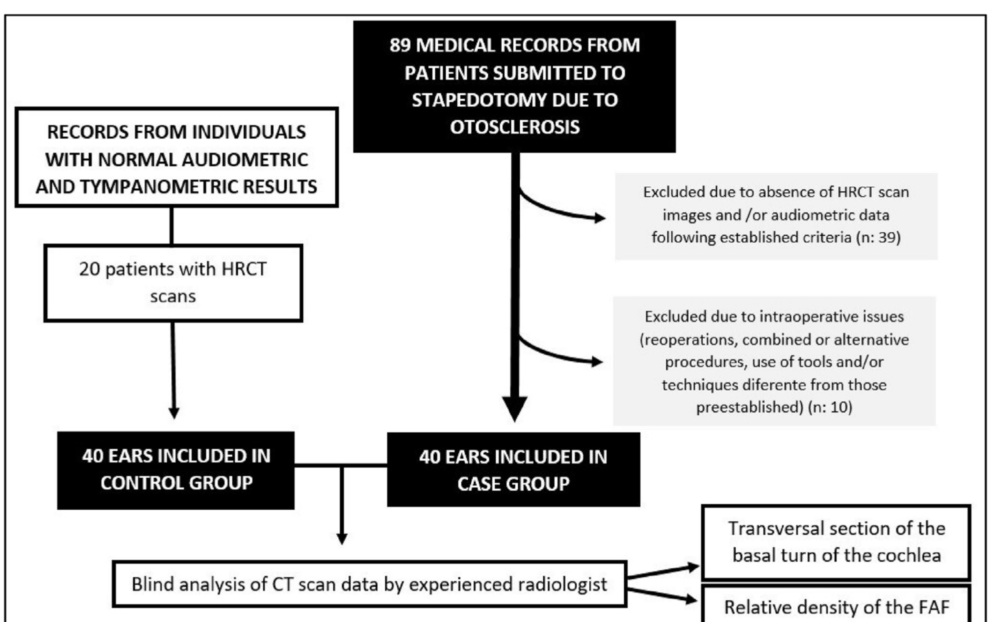

Fig. 3. Study flow chart. Legend: n: number; HRCT: high-resolution computed tomography; CT: computed tomography; FAF: fissula antefenestram.

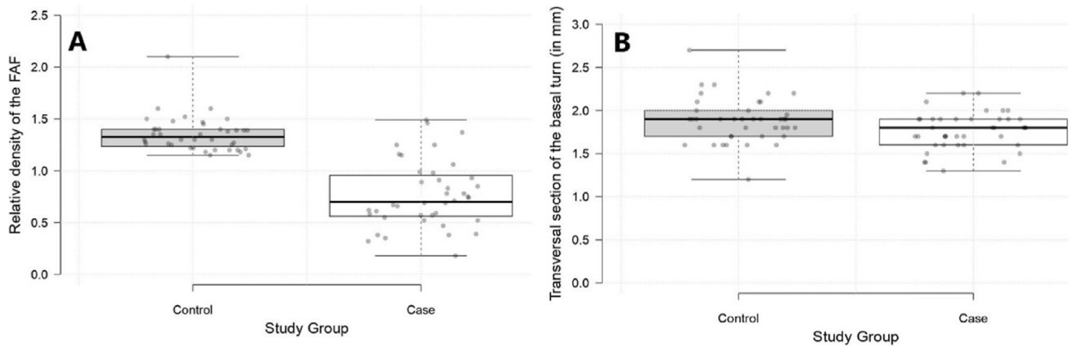

Fig. 4. Distribution of the results obtained for each variable of the study, according to the allocation group. A: relative density of the *fissula antefenestram*. B: Transversal section of the basal turn of the cochlea. Legend: mm: millimeters; FAF: *fissula antefenestram.*

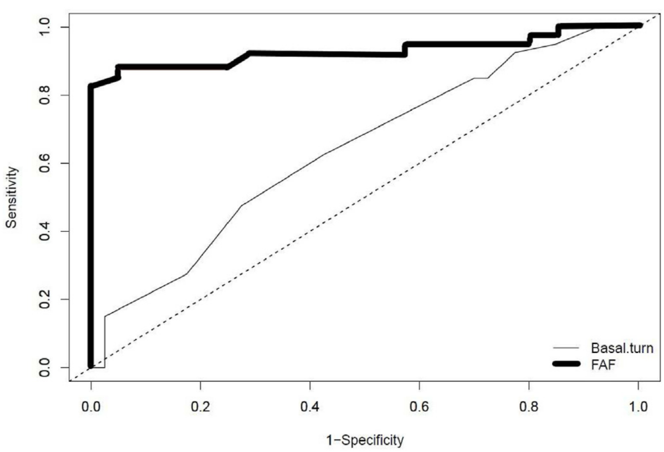

Fig. 5. ROC curves showing the diagnostic ability of the transversal section of the basal turn of the cochlea and for the relative density of the FAF to discriminate individuals with otosclerosis using HRCT scans. Legend: FAF: fissula antefenestram.

conductive hearing losses, for instance in cases suspected for osteodystrophy (Goh et al., 2002; Mansour et al., 2011; Sziklai et al., 2009). The exact value of HRCT in otosclerosis is still a matter of debate, and patients with typical findings are seldom submitted to radiological assessment prior to surgery (Chole and McKenna, 2001; Mansour et al., 2011; Marx et al., 2011).

In the otospongiotic phase, the disease foci are seen as zones of diminished lucency within the otic capsule. These foci are typically found in the FAF in the fenestral type of the disease (T.-L. Lee et al., 2009; Vicente et al., 2006). Those with retrofenestral disease show perilabyrinthine radiolucent foci, at times distinctively surrounding the cochlea, which leads to a "double-ring" aspect in CT scans. In the otosclerotic phase, the increased density of the inactive foci hinders their identification, incurring in higher false-negative rates. In this phase, the irregularities of bone contours and volumetric changes are key to the diagnosis (T.-L. Lee et al., 2009; Naumann et al., 2005; Vicente et al., 2006). Nonetheless, the hypothetical lower sensitivity of HRCT in inactive otosclerosis seems to be less important than predicted, as the disease tends to be multifocal, with concurrent active and inactive foci in the same patient (Chole and McKenna, 2001; Karosi et al., 2012; Mafee et al., 1985). False-negatives could also be due to the ankylosis or fibrotic changes limited to the annular ligament, which are thought to often occur in the most initial phases of the condition (Cherukupally et al., 1998).

In this study, among ears with confirmed otosclerosis, 90% showed compatible HRCT findings. This percentage reflects the high sensitivity of this method in the context of the study. Also, 100% of controls were accurately identified, as none of them showed signs of otosclerosis in the HRCT scans. Taken together, these data reassure the high accuracy of HRCT for evaluation of otosclerosis in candidates for surgery – which is in agreement with the most recent literature. A broad systematic review demonstrated that, with the most recent techniques, HRCT might present great sensitivity and specificity, both over 90% (Virk et al., 2013). Accordingly, a review on this subject has also shown that, although having shown great variability across the studies, the HRCT scan sensitivity in otosclerosis could reach up to 95%(Wegner et al., 2015).

Ears with otosclerosis have significantly shown lower relative densities of the FAF and reduced dimensions of the BTC. These findings might reflect morphological alterations linked to the pathophysiology of the disease, and could be useful when evaluating a CT scan of a suspected case.

As for the use of densitometric assessment in HRCT scans of otosclerotic ears, Kutlar et al. have demonstrated that patients with the disease showed lower densities of the FAF, but not of other sites within the temporal bone, when compared to healthy individuals (Kutlar et al., 2014). On the other hand, Kawase et al., when evaluating 24 ears with the disease, showed lower radiological densities not only for the FAF, but also for the anterior wall of the internal acoustic canal (Kawase et al., 2006). Grayeli et al. made a prospective analysis of 10 patients with otosclerosis which revealed lower radiological densities in the FAF and in the surroundings of the posterior semicircular canal (Grayeli et al., 2004). Also consistent with these authors, the present study has demonstrated that the use of the radiological density of the FAF in patients with the disease might help distinguish them from healthy controls, as they present significantly reduced local lucency.

In this regard, 92.5% of the ears with otosclerosis have shown relative densities inferior to 1.35 – the average value obtained in the control group. Half (2/4) of the ears in case group which were considered as normal by the radiologist have demonstrated reduced values for the relative density of the FAF. Thus, the routine use of this measurement could, for example, have raised suspicion for otosclerosis in cases which seemed unaltered at a first glance. Only 2.37% (1/36) of the correctly-diagnosed affected ears region showed increased relative density of the FAF. In these very particular cases, the routine use of the parameter could be a confounding factor. In brief, one could considerate that the systematic measurement of the relative density of the FAF corroborates most of the diagnoses and, in borderline situations, it could enhance the HRCT scan diagnostic performance. The use of a relative variable, namely the ratio between the density of the region of interest and that of a control site, seems beneficial to diminish inter-subject variability, and therefore increase the external validity of the analysis. This has been previously suggested in the literature (Yamashita et al., 2014, 2017).

The BTC is a frequent site of involvement in retrofenestral otosclerosis. Due to the surrounding bone abnormalities, a reduction of the lumen of this structure is often described. Indeed, the presence of this finding in HRCT scans is one of the parameters used in the Rotteveel Classification for the disease (Rotteveel et al., 2004). However, few studies have investigated the consistent effect of otosclerosis in the dimensions of the lumen of the BTC. In fact, it could be a more usual finding in otosclerosis than previously thought and, as such, it could be function as a radiological marker of the disease.

In consonance with this hypothesis, in the present study, the transversal section of the BTC were significantly narrower among ears with otosclerosis. Therefore, the disease might frequently lead to a constriction of this structure – which could possibly help explain the sensorineural hearing loss observed during its course. Also, during HRCT investigations of suspected cases, finding a more constricted basal turn could contribute, along with other findings, to establish a diagnosis. Considering the mean value of 1.89 mm found for controls, in the case group 70% of the ears presented narrower basal turns than the paired healthy sample.

Although both parameters of the study are significantly reduced in otosclerotic ears, the individual diagnostic power of them seem to differ. When using ROC curves to analyze how they behave in distinguishing control from case ears, the relative density of the FAF showed an outstanding performance, with high true-positive along with reduced false-positive rates in some of the plotted thresholds. This is confirmed with the very high AUC (92.9%), which could be understood as the chance of a randomly individual with otosclerosis having a test result indicating greater suspicion for the condition than a random healthy subject. On the other hand, the AUC for the width of the transversal section of the BTC reached 64.6%, an indicator that the performance of this variable as a single diagnostic tool is fairly poor.

This study has several limitations that should be considered when analysing the results. First, it is retrospective and dependent upon the analysis of medical records, which are prone to inconsistencies and errors. The attempt to gather a comparable sample with the use of strict inclusion criteria aimed to reduce heterogeneities which could incur in selection and/or measurement biases. However, an important collateral effect is the considerable sample loss. Secondly, when selecting case ears, only those submitted to surgery were included. Thus, the results are valid within this context, and one must avoid extrapolations. It means, for example, that the differences seen between case ears and controls might be pertinent only when significant clinical otosclerosis is present. For very initial conditions, with smaller airbone gaps, the conclusions of this work could be less relevant. Yet, this study did not aim to investigate the reproducibility or concordance of the techniques used to obtain the results. To at least partially overcome this limitation, the measurements were described and made in an objective and simple fashion.

Prospective investigations involving larger samples could be carried out to confirm the results obtained. It should be highlighted that the use of objective measurements to achieve better preoperative diagnostic accuracy in otosclerosis is a potential field in radiology and it might, in near future, include also artificial intelligence. Hence, the combined use of several objective parameters related to the temporal bone – and known to be commonly altered in otosclerotic ears, could help creating algorithms aimed to enhance the performance of diagnostic HRCT scans.

5. Conclusions

Ears from subjects with otosclerosis present reduced values for the relative radiological density of the FAF and for the width of the transversal section of the BTC. These variables reflect the pathophysiology of the disease and might help differentiate affected individuals from normal subjects. In this sense, the relative density of the FAF has a high diagnostic power, and performs very satisfactorily even when used as a single investigation tool.

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