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Interaction effect of tegmen tympani and superior semicircular canal statuses on the thickness of the roof of the glenoid fossa: a cross-sectional descriptive study.

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Abstract

Purpose Homogeneous development of temporal bone structures is explained by their ontogenic origin; tegmen tympani (TT) and superior semicircular canal (SSC) are related with the glenoid fossa at the temporomandibular joint (TMJ). Therefore, our objective was to determine a possible relationship between TT status (dehiscence or integrity) and the roof of the glenoid fossa (RGF) thickness; SSC status has also been considered.

Methods This cross-sectional descriptive study was conducted in 2 tertiary hospitals on 95 patients (109 ears) presenting hypoacusia, facial palsy, vertigo, tinnitus, and other single or combined symptoms, and submitted to a thin-section multidetector-row computed axial tomography (CT) scan.

Results A significant interaction effect of TT x SSC statuses on RGF thickness was found (p= 0.049). A significant difference in RGF thickness was found only for SSC integrity status between TT integrity and TT dehiscence (p = 0.004). The TT dehiscence increased the risk for RGF dehiscence 12.047 times (p = 0.002).

Conclusions There is an interaction effect of the statuses of both TT and SSC on the thickness of the RGF, instead of an independent effect of the TT status. When RGF dehiscence is found, TT and SSC statuses should be assessed, in order to discard associated dehiscences.

Keywords Temporal bone; Positron-emission tomography; Statistics; Cross-sectional studies; Anatomy.

Introduction

Homogeneous development of temporal bone structures is explained by their ontogenic origin. Structures of middle cranial fossa, such as tegmen tympani (TT) and superior semicircular canal (SSC), are related with the glenoid fossa at the temporomandibular joint (TMJ).

Friedland and Michel [3] and Rizk et al. [14] referred to a statistically significant decrease in the thickness of the middle cranial fossa and its different components in situations involving temporal bone defect. The relationship between TT and SSC statuses (dehiscence or integrity) was previously described [18]. In a recent work, Crovetto-Martínez et al. [1] found a relationship between the thickness of the roof of the glenoid fossa (RGF) and the thickness of the bone covering the superior semicircular canal (SSC); the thinning or thickening of both structures was similar, and the association of SSC dehiscence with RGF thinning or dehiscence was frequently observed.

The aim of the present work was to determine if there is a relationship between TT status (dehiscence or integrity) and RGF thickness tacking into account the SSC status.

Methods

Study population

The present study was performed in two University Hospitals in North-eastern Spain between January 2012 and December 2017. For this cross-sectional descriptive study, a computed axial tomography (CT) scan of the temporal bone was performed in patients who presented hypoacusia, facial palsy, vertigo, tinnitus, and other single or combined symptoms (inclusion criteria). Patients were excluded from this study if the measures of the temporal bone could not be carried out due to technically inaccurate radiological studies. One experienced senior radiologist per participant hospital studied the CT scans. The sample size was determined by the number of patients that met the inclusion criteria presented in the participant Hospitals during the study period. A total of 95 patients were studied (190 ears); TTD status (tegmen timpani dehiscence) was detected in 57/95 (60%) patients, 36/95 (37.89%) patients showed SSCD status (superior semicircular canal dehiscence) and RGFD status (roof of the glenoid fossa dehiscence) occurred in 15/95 (15.79%) patients. A detailed distribution of SSC, TT, and RGF statuses for the 95 studied patients are shown in Table 1.

Study design

Both right and left sides were separately evaluated in every individual that meets the inclusion conditions. Women accounted for 60% (57/95) of the sample. The mean age of the patients in the present work was 55.96 years (standard deviation, SD = 12.52 years); age ranged from 18 to 82 years, and 79/95 (83.2%) of the patients were older than 45 years.

Variables and measurements

A multislice helical computed tomography CT equipment (Philips Brillance 6) produced 0.5 mm axial collimation and 0.1 mm spatial resolution images; the scanner characteristics and the validations of the measurements were described elsewhere (3 and 4). The TT and SSC statuses were evaluated as previously described [18]. The RGF thickness at the TMJ was measured according to Crovetto-Martínez et al. [1]. For TT, SSC and RGF, statuses were codified as D (dehiscence: measurement = 0 mm) or I (integrity).

For statistical analysis, both unilateral and bilateral dehiscence statuses were included as dehiscence individual status. Therefore, when dehiscence was detected on any of the sides (right or left) or even on both of them, individual status was categorized as dehiscence (RGFD, TTD, and SSCD); otherwise, individual status was integrity (RGFI, TTI, and SSC: roof of the glenoid fossa integrity, tegmen timpani integrity and semicircular superior canal integrity). In each studied patient, the average of both sides for RGF minimum thickness was calculated [ARGF = (right RGF minimum thickness + left RGF minimum thickness)/2].

Statistical analysis

Statistical analysis was undertaken using the SPSS software v.22 (SPSS Inc., Chicago, IL, USA). The mean and SD was calculated for ARGF. Effects of sex and age on ARGF were analysed using the general linear model (GLM), where sex was considered a fixed effect and age was introduced as a covariate. Association between SSC and RGF statuses was studied using Fisher's exact test. A 2x2 two-way ANOVA was applied to investigate the effects of both the TT and SSC individual statuses (fixed factors, independent variables) on ARGF (dependent variable)[6]; p < 0.050 was considered to be statistically significant. Analyses of single main effects for both TT and SSC individual statuses were performed with statistical significance receiving a Bonferroni adjustment as being accepted at the p < 0.025 level. Partial eta squared (partial η^2) measures the proportion of the total variance in a dependent variable that is associated with the membership of different groups defined by an independent variable; in this measure, the effects of other independent variables and interactions are partialled out [13]. Observed power for α =0.050 has been estimated for every test. A binomial logistic regression was performed to ascertain the effects of TT and SSC individual statuses (independent

variables) on the likelihood that a patient shows RGTD (dependent variable) [10]. The model was built using the Wald method; significance levels for partial correlations to enter and to be removed were $\alpha \le 0.05$ and $\alpha \ge 0.10$, respectively. The stepwise procedure ends when no variables comply with the entry/removal conditions. Nagelkerke R^2 means the proportion of variance in the dependent variable associated with the independent variables. Results

Figure 1 shows the CT image from a patient showing both TT and RGF dehiscence statuses.

In the present work, a significant difference for ARGF was found between men and women (0.90 \pm 0.673 mm vs. 0.60 ± 0.423 mm, respectively; p = 0.013; power=0.711); no significant effect of age was found (p = 0.443; power=0.119).

Table 2 shows the means and SDs for ARGF in the function of TT and SSC individual statuses. The two-way ANOVA detected a significant interaction effect of TT x SSC individual statuses on ARGF mean (F (1, 91) = 3.997; p = 0.049; partial $\eta^2 = 0.042$; power=0.507). Therefore, the effect of one independent variable on ARGF is different depending on the status of the other independent variable.

The analysis of single main effects for TT individual status indicated a statistically significant difference in mean ARGF for SSCI status between TTI and TTD statuses (F(1,91) = 8.808; p = 0.004; partial η^2 = 0.088; power=0.836), but not such a significant difference between TTI and TTD statuses was found for SSCD (F(1,91) = 1.083; p = 0.301; power=0.178). As can be seen in Table 2, for SSCI status, mean ARGF was lower for TTD status than for TTI status.

In the analysis of single main effects for SSC individual status, no significant difference was found for TTD individual status between SSCI and SSCD individual statuses (F(1,91) = 0.002; p = 0.964; power=0.050). Because Bonferroni adjustment was applied, the limit for significance in this kind of comparison is p=0.050/2=0.025; therefore, no significant difference was detected for TTI individual status between SSCI and SSCD individual statuses (F (1, 91) = 4.620; *p* = 0.034; power=0.566).

A binomial logistic regression was performed to ascertain the effects of TT and SSC individual statuses on the likelihood that patients show RGFD individual status. The final logistic regression model was statistically significant (χ^2 (1) = 10.071; p = 0.002). The model explains 17.3% (Nagelkerke R²) of the variance in RGF individual status. Of the two independent variables, only TT individual status was statistically significant.

Individuals showing TTD individual status had a 12.047 times higher odds ratio (OR) to exhibit RGFD status than patients with TTI individual status (see Table 3).

Discussion

The discovery of the SSC dehiscence syndrome has led to new research on temporal bone structures. In the present work, we showed the interaction effect of TT and SSC statuses on RGF thickness, instead of supporting an independent effect of the TT status. As shown in Table 2, the effect of TTD individual status on ARGF is very similar for both SSCI and SSCD statuses and produces a decrease in RGF thickness with respect to the normal situation (TTI and SSCI individual statuses). The lowest ARGF mean was observed for TTI and SSCD individual statuses, but no significant differences were found when compared to the remaining TT and SSC individual statuses.

This situation could be due to the scarcity of individuals showing TTI and SSCD individual statuses (only 2); therefore, this constitutes a limitation of the present work. However, the decrease in RGF thickness was quantitatively important for these two patients, pointing again to the interaction between TT and SSC individual statuses on ARGF mean; the effect of SSC individual status on ARGF depends on the TT individual status.

The patients with TTI and SSCD individual statuses have been infrequently found in CT studies. As previously stated in Spanish patients [1], SSC pattern was significantly associated with TT status; the risk for TTD increased 12 times and 20 times for papyraceous (<0.6mm) and SSCD patterns, respectively. On the other hand, the risk for TTD also increased with age (4.1% per year).

The characteristics of these two patients (named A and B) were as follows:

-A: 51-year-old man, bilateral RGFD (ARGF = 0 mm), TTI, right unilateral SSCD (left SSC thickness = 0.8 mm; categorized as normal pattern).

-B: 61-year-old woman, RGFI (right RGF thickness = 0.4 mm; left RGF thickness = 0.3 mm; ARGF = 0.35 mm), TTI, unilateral left SSCD (right SSC= = 0.5 mm; categorized as papyraceous pattern).

As can be seen, the great difference in ARGF between patients A and B caused the mean ARGF for this type of individual to be very low (mean ARGF for TTI and SSCD individual status = (0 + 0.35)/2 = 0.175 mm).

Both individuals A and B would be expected to show TTD status, especially B, on the basis of her age and SSC pattern. Therefore, the probability of getting a higher number of patients showing TTI and SSCD individual statuses by increasing sampling is low.

Our final model for binomial logistic regression did not include SSC status because this independent variable did not reach the limit to enter into the model, as described in the statistical methods. However, we could state a tendency to an association between SSC and RGF statuses; in the present work, 9/36 (25%) patients with SSCD individual status also showed RGFD individual status, versus only 6/59 (10.17%) patients with SSCI individual status also showing RGFD individual status (Fisher's exact test, unilateral p = 0.053; power<0.01). This result, very close to the limit for significance (p < 0.050), would be explained by the low number of patients with SSCD that we found.

The global mean of ARGF in the present work was 0.719 mm (SD = 0.554 mm); similar values, in the interval 0.7 mm (SD = 0.12mm)–0.85 mm (SD = 0.31 mm), were previously described [7, 9, 17], using CT techniques. Honda et al. [4] did not find significant effects of sex and age on RGF thickness.

Kurtz et al. [8] described an association between SSCD and TMJ pathology. Crovetto-Martinez et al. [1] found a significant correlation between the thickness of both the bone overlying the SSC and RGF (p < 0.001). As Crovetto- Martínez et al. [1] explained, they increased the recruitment of SSCD patients in an attempt to secure a large number of patients with this characteristic. On the other hand, these authors did not consider TT individual status, nor the interaction of TT x SCC individual statuses, as we did, constituting a novel aspect of the present work.

In terms of the found interaction effect of TT x SSC statuses on ARGF, a series of previous works pointed to several explanations. Rodriguez-Vazquez et al. [15] described the TT as the key region linking the TMJ development to SSC development; this relationship was based on the disco-malleolar ligament. Park et al. [12] observed that the otic capsule was significantly thinner for patients showing SSCD status. Rizk et al. [14] confirmed that SSCD patients showed a tinning of the cranial bone with the floor shape of the middle cranial fossa noticeably more marked than for individuals that were not selected. De Jong et al. [2] demonstrated that SSCD was associated with both decreased volume and density of the temporal bone, which might explain the relationships found between lesser RGF thickness and SSCD status.

From the point of view of embryological development, the TMJ and the ear show complex relationships. The roof of the TMJ is developed from the temporal blastema, which forms the glenoid fossa with

its roof [11]. As described by Horna et al. [5], the TT ontogenetic development occurs by means of two expansions: the external or lateral expansion, from temporal blastema, with membranous ossification, and the internal or medial expansion, which derives from the otic capsule, called the "tegmental process" by Tóth et al. [16], with cartilaginous or endochondral ossification. Both expansions progressively approach to join in the petrosquamous suture.

Dehiscence of TT is an important finding; TTD means a direct communication between middle ear and epidural space so that a mild pathology as acute medial otitis would derive in a brain abscess or meningitis. On the other hand, SSCD causes many deceptive symptoms and signs as transmission hearing loss (THL), which can lead us to perform unnecessary and even dangerous operations for the patients, and also can cause a vertigodizziness picture, incapacitating for the patient and difficult to diagnose. In fact, a middle and inner ear CT is usually performed before surgery on suspicion of otosclerosis, in order to rule out this pathology. For these reasons, when RGFD is found in a patient, TT and SSC statuses should be assessed, in order to discard associated dehiscences, either asymptomatic or not.

Conclusions

In conclusion, this work provided evidence of an interaction of the statuses of both TT and SSC on the thickness of the RGF, instead of supporting an independent effect of the TT status. Dehiscence status of RGF causes few clinical manifestations. Arthralgia and chewing pain causes by RGFD are annoying to the patient but they are not indicative of a serious problem. However, we have found an association of RFGD with TTD and SSCD within a malformative context in the development of the skull base of the middle fossa.

Author's contribution

Protocol/project development: JW, AIC, MAC.

Data collection and management: JW, JJF, MAC, RC, AW, LVM.

Data analysis: JW, MTT.

Manuscript writing/edition: JW, AIC, JJF, AW, RC, LVM, MAC, MTT.

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Compliance with ethical standards

Conflict of interest The author declare taht they have no conflict of interest.

Research involving Human Participants and Informed consent The present study was performed following the guidelines of the Helsinki Declaration of 1983. All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional research committees. A signed informed consent was obtained from every participating patient, and patients were completely anonymized by researchers. All authors ensure that submissions are HIPAA-compliant. Researchers followed every mandatory (health and safety) procedures.

References

1. Crovetto-Martinez R , Vargas C , Lecumberri I , Bilbao A , Crovetto M, Whyte J (2018) Radiologic correlation between the thickness of the roof of the glenoid fossa and that of the bony covering of the superior semicircular canal. Oral Surg Oral Med Oral Pathol Oral Radiol 125:358-363. https://doi.org/10.1016/j.oooo.2017.12.008

2. De Jong MA, Carpenter DJ, Kaylie DM, Piker EG, Frank-Ito DO (2017) Temporal bone anatomy characteristics in superior semicircular canal dehiscence. J Otol 12:185-191. https://doi.org/10.1016/j.joto.2017.08.003

3. Friedland DR, Michel MA (2006) Cranial thickness in superior canal dehiscence syndrome: implications for canal resurfacing surgery. Otol Neurotol 27: 346-354.

4. Honda K , Kawashima S , Kashima M , Sawada K , Shinoda K, Sugisaki M (2005) Relationship between sex, age, and the minimum thickness of the roof of the glenoid fossa in normal temporomandibular joints. Clin Anat 18: 23-26. https://doi.org/10.1002/ca.20054

5. Horna J, Gamboa J, Jorda JV, Olaizola F (1990) Embriología del oído. In: Olaizola F (ed) Malformaciones genéticas del oído y su tratamiento, Ed. Garsi, España, pp. 19-30.

6. Iversen GR, Norpoth H (1987) Analysis of variance. Sage Publications, Inc., UK.

7. Kijima N, Honda K, Kuroki Y, Sakabe J, Ejima K, Nakajima I (2007) Relationship between patient characteristics, mandibular head morphology and thickness of the roof of the glenoid fossa in symptomatic temporomandibular joints. Dentomaxillofac Radiol 36: 277-281. https://doi.org/ 10.1259/dmfr/56344782

8. Kurt H, Orhan K, Aksoy S, Kursun S, Akbulut N, Bilecenoglu, B (2014) Evaluation of the superior semicircular canal morphology using cone beam computed tomography: a possible correlation for temporomandibular Joint symptoms. Oral Surg Oral Med Oral Pathol Oral Radiol 117: 280-288. https://doi.org/ 10.1016/j.0000.2014.01.011

9. Matsumoto K, Honda K, Sawada K, Tomita T, Araki M, (2006) The thickness of the roof of the glenoid fossa in the temporomandibular joint: relationship to the MRI findings. Dentomaxillofac Radiol 35:357-364. https://doi.org/ 10.1259/dmfr/30011413

10. Menard S (2010) Logistic regression: From introductory to advanced concepts and applications. SAGE Publications, Inc., UK.

 Mérida-Velasco JR, Rodríguez-Vázquez FJ, Mérida-Velasco JA, Sánchez-Montesinos I, Espin-Ferra J,
 Jiménez-Collado J (1999) Development of the human temporomandibular joint. Anat Rec 255 :120-133. https://doi.org/ 10.1002/(SICI)1097-0185(19990501)255:1<20::AID-AR4>3.0.CO;2-N

12. Park JH, Kang SI, Choi HS, Lee SY, Kim JS, Koo JW (2015) Thickness of the bony otic capsule: etiopathogenetic perspectivas on superior canal dehiscence syndrome. Audiol Neurootol 20 : 243-250. https://doi.org/ doi: 10.1159/000371810

13. Richardson JTE (2011) Eta squared and partial eta squared as measures of effect size in educational research. Educ Res Rev 6:135-147. https://doi.org/10.1016/j.edurev.2010.12.001

14. Rizk HG, Hatch JL, Stevens SM, Lampert PR, Meyer TA (2006) Lateral skull base attenuation in superior semicircular canal dehiscence and spontaneous cerebrospinal fluid otorrhea. Otolaryngol Head Neck Surg 155: 641-648. https://doi.org/10.1177/0194599816651261

15. Rodriguez-Vazquez JF, Murakami G, Verdugo-Lopez S, Abe SI, Fujimiya M (2011) Closure of the middle ear with special reference to the development of the tegmen tympani of the temporal bone. J Anat 218: 690-698. https://doi.org/10.1111/j.1469-7580.2011.01378.x

16. Tóth M, Helling K ,Baska G, Mann W (2007) Localization of congenital tegmen tympani defects. Otol Neurotol 28 : 1120-1123.

17. Tsuruta A , Yamada K , Hanada K , Hosogai A , Tanaka R , Koyama J , Hayashi T (2003) Thickness of the roof of the glenoid fossa and condylar bone change: a CT study. Dentomaxillofac Radiol 32: 217-221. https://doi.org/10.1259/dmfr/15476586

18. Whyte J, Tejedor MT, Fraile JJ, Cisneros A, Crovetto R, Monteagudo LV, Whyte A, Crovetto MA (2016) Association between tegmen tympani status and superior semicircular canal pattern. Otol Neurotol 37: 66-69. https://doi.org/10.1097/MAO.00000000000918

Figure caption:

Fig. 1 CT image from a patient showing bot TT (white arrow) and RGF (black arrow) dehiscence statuses.

Figure legends:

 Table 1 Distribution of superior semicircular canal (SSC), tegmen tympani (TT), and roof of the glenoid fossa

 (RGF) statuses (I: Integrity; D: Dehiscence) for the 95 studied patients.

Table 2 Means and SDs (mm) for average roof of the glenoid fossa (ARGF) thickness in the function of tegmen tympani (TT) and superior semicircular canal (SSC) individual statuses (I: Integrity; D:Dehiscence). ^{a,b:} Values within a row with different superscripts differ significantly at p < 0.025.

Table 3 Binary logistic regression model, showing the effects of tegmen tympani (TT) individual status on the probability of dehiscence of the roof of the glenoid fossa (RGFD).



Table

SSC status	TT status	RGF status					
55°C Suitus		RGFI (n=80)	Unilateral RFGD (n=9)	Bilateral RFGD (n=6)			
SSCI	TTI	36/80 (45.00%)	0/9 (0%)	0/6 (0%)			
	Unilateral TTD	2/80 (2.50%)	2/9 (22.22%)	0/6 (0%)			
	Bilateral TTD	15/80 (18.75%)	2/9 (22.22%)	2/6 (33.33%)			
Unilateral SSCD	TTI	1/80 (1.25%)	0/9 (0%)	1/6 (16.67%)			
	Unilateral TTD	13/80 (16.25%)	1/9 (11.12%)	0/6 (0%)			
	Bilateral TTD	3/80 (3.75%)	2/9 (22.22%)	2/6 (33.33%)			
Bilateral SSCD	TTI	0/80 (0%)	0/9 (0%)	0/6 (0%)			
	Unilateral TTD	4/80 (5.00%)	0/9 (0%)	0/6 (0%)			
	Bilateral TTD	6/80 (7.50%)	2/9 (22.22%)	1/6 (16.67%)			

	TT individual status				
		TTI	TTD		
SSC individual status	n	ARGF Mean ± SD (mm)	n ARGF Mean ± SD (mm)		
SSCI	36	0.98 ± 0.494^{a}	23	0.57 ± 0.444^{b}	
SSCD	2	0.17±0.247ª	34	$0.57{\pm}0.590^{a}$	

	В	SE	Wald	df	р	Odds ratio (OR)	95% CI for OR	
							Lower	Upper
TT individual status	2.489	1.059	5.552	1	0.019	12.047	1.511	96.023
Constant	-3.611	1.013	12.696	1	< 0.001	0.027		