Are Patients with Spontaneous CSF Otorrhea and Superior Canal Dehiscence Congenitally Predisposed to Their Disorders?

Shawn M. Stevens, MD¹, Kiefer Hock, MD², Ravi N. Samy, MD³, and Myles L. Pensak, MD⁴

Abstract

Objectives. (1) Compare lateral skull base (LSB) height/thickness in patients with spontaneous cerebrospinal fluid otorrhea (CSF), superior canal dehiscence (SCD), acoustic neuromas (AN), and otosclerosis (OTO). (2) Perform correlations between age, body mass index (BMI), sex, and LSB height/thickness.

Study Design. Case series with chart review.

Setting. Tertiary referral center.

Subjects and Methods. Patients with CSF, SCD, AN, and OTO diagnosed from 2006 to 2016 were included if they had high-definition temporal bone computed tomography (CT) and absence of trauma, radiation, chronic ear disease, and/or congenital anomaly. CT-based measurements included LSB height/thickness and pneumatization rates overlaying the external auditory canal (EAC), tegmen tympani (TgT), perigeniculate region (PG), and internal auditory canal (IAC). LSB height/thickness, age, sex, and BMI were statistically correlated. In total, 256 patients and 493 ears (109 CSF, 115 SCD, 269 AN/OTO) were measured.

Results. Patients with CSF had significantly higher BMIs than the other groups (P < .001). Patients with CSF and SCD had similar radiographic LSB phenotypes at most measured locations. Both groups exhibited a significantly lower LSB height compared to the AN and OTO groups (mean, 3.9-4.2 mm vs 4.9-5.6 mm; P < .001). Patients with CSF and SCD also demonstrated significantly lower pneumatization rates, as low as 17% to 23% overlaying the PG and IAC (P < .001). There were no statistically significant correlations found between age, sex, BMI, and LSB height/thickness at any measurement location in any group.

Conclusions. Patients with CSF and SCD exhibit similar radiographic LSB phenotypes. Age, sex, and BMI do not significantly correlate with LSB height/thickness. These data support the theory that CSF and SCD arise via similar congenital pathoetiologic mechanisms.

Keywords

lateral skull base, tegmen dehiscence, otosclerosis, acoustic neuroma, spontaneous cerebrospinal fluid otorrhea, superior canal dehiscence

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Spontaneous cerebrospinal fluid (CSF) otorrhea and superior canal dehiscence (SCD) syndrome represent 2 disorders of the lateral skull base (LSB) associated with an attenuated tegmen. The pathoetiology of this osseous attenuation remains unclear. Investigators have debated whether a congenital condition, an acquired process, or both is to blame.

Recently, some have begun to suspect that LSB attenuation may be related to aberrant development.¹-⁴ Multiple studies now note that radiographic SCD is common during the first 6 months of life and that LSB height/thickness increases through age 3 years. A small minority of patients will exhibit persistent LSB attenuation and radiographic SCD.³,⁵ These patients also exhibit a high rate of concomitant tegmen dehiscence. This has led some to suggest that

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SCD and spontaneous CSF otorrhea may arise via common mechanisms.\textsuperscript{5-8} Investigators have also described a strong association between spontaneous CSF leaks and obesity (body mass index [BMI] > 30 kg/m\textsuperscript{2}).\textsuperscript{7,9-20} While a direct link between obesity and LSB attenuation has not been established, some theorize that intracranial hypertension (ICH) in obese patients may lead to pressure-induced bony remodeling.\textsuperscript{10,21-24} ICH may arise in obese patients secondary to central venous hypertension,\textsuperscript{25-27} obstructive sleep apnea,\textsuperscript{12,28-31} and/or idiopathic intracranial hypertension.\textsuperscript{12,20,32,33} Proponents of this theory note that patients demonstrate skull base attenuation at most locations of the dura-bone interface.\textsuperscript{10,21,23,34,37} Arguments against the theory point out that some patients with spontaneous CSF leaks and SCD syndrome are not obese.\textsuperscript{10,24} No study currently exists that correlates LSB thickness with intracranial pressure (ICP).

We sought in the present study to develop a large repository of computed tomography (CT)-based LSB measurements. Our primary aim was to determine if distinct patterns of the radiographic LSB phenotype would emerge in patients with spontaneous CSF otorrhea and SCD compared to controls. Our secondary aim was to perform statistical correlations between LSB measures and variables, including age, sex, and BMI. Our hypothesis was that patients with CSF and SCD would have similarly attenuated LSB phenotypes and also demonstrate an inverse correlation between LSB thickness and BMI.

**Methods**

Institutional review board approval (ID2016-4082) was obtained at the University of Cincinnati (UC) College of Medicine.

**Patient Selection and Group Stratification**

A retrospective chart review was conducted from 2006 to 2016 at our single tertiary care center. Using International Classification of Diseases 9/10 codes, all patients with diagnoses of spontaneous CSF otorrhea, SCD, otosclerosis (OTO), and acoustic neuroma (AN) were identified. In this manner, 4 comparison groups were created (OTO, AN, CSF, and SCD). The OTO and AN groups were considered controls and were selected based on the increased likelihood of those patients having undergone temporal bone CTs and the low likelihood of them having concomitant chronic ear disease.

Patients in each comparison group also required the following to be considered for inclusion:

- **CSF otorrhea**: positive β-2 transferrin test
- **AN**: suggestive MRI findings and/or confirmatory tissue diagnosis
- **OTO**: a suggestive preoperative audiometric pattern and a finding of fixed footplate at surgery
- **SCD**: primarily included those patients with a combination of radiographic SCD, core symptoms as described by Minor et al,\textsuperscript{38} and supporting diagnostic evaluations (either vestibular evoked myogenic potentials and electrocochleography) consistent with SCD syndrome

Patients were also stratified to the SCD group if they exhibited radiographic SCD and at least 1 core symptom of SCD syndrome but lacked sufficient supporting evaluations to meet a formal diagnosis. Patients in the CSF, AN, and OTO groups who also demonstrated concomitant radiographic SCD were not dually stratified.

Patients of all ages, sexes, and ethnicities were considered. The primary inclusion criterion, besides group criteria noted above, was the presence of a finely collimated (<1 mm) temporal bone CT scan with coronal reconstructions. Patients with a history of temporal bone trauma, chronic ear disease, intracranial infection, radiation, and congenital anomaly were excluded. Patients who had undergone unilateral otologic/neurotology surgery prior to their temporal bone CT were considered for measurements of their nonoperated ear.

**Imaging and Hardware**

The majority of CT scans were obtained at UC on either a Siemens Somatom Sensation 16 or Siemens Definition 128 CT scanner (Siemens, Munich, Germany). Spatial resolution was rated as accurate to 0.1 to 0.2 mm.

Images were analyzed on standardized computing stations equipped with Intel Core 2 Duo CPUs. Processing speed was 2.3 GHz with 4 GB of available RAM. The stations were all equipped with Lenovo Think Vision 19-inch, square, backlit LED, and flat panel LCD monitors set to a maximum resolution of 1280 × 1024 dpi (Lenovo, Morrisville, North Carolina).

Reformatted images were analyzed via McKessen Radiology Station 12.2 (San Francisco, California). Temporal bone thickness was measured via the partial volume averaging formula (measurement caliper tool) in this software package. The accuracy of this is rated to 0.1 mm. The window level was set to “spine-neuro” to maximize resolution of the bone–soft tissue interface.

**Data Collection and Measurement Protocols**

Clinical data collected included patient sex as well as age and BMI (kg/m\textsuperscript{2}) at the time of the temporal bone CT.

A combination of objective and observational measurements was made on coronal images by 2 independent observers (S.M.S. and K.H.). The localization of measures was initially derived from a standardized and repeatable coronal image (the “reference image”) depicting all of the following simultaneously: the external auditory canal (EAC), the malleus and/or incus, 2 turns of the cochlea, and the internal auditory canal (IAC).

The reference image was chosen as it was felt to contain the greatest density of anatomically repeatable structures within the temporal bone. The structures depicted were also felt to provide the most reliable/relevant landmarks for
placement of the caudal caliper tool when performing LSB height/thickness measures. Starting at the reference image, the following measurements were performed.

**Measurements of LSB height/thickness.** Measurements were made at 4 standardized locations (Figure 1). From lateral to medial, these included the bone overlaying the EAC, the tegmen tympani (TgT), the bone overlaying both the perigeniculate (PG) region, and the IAC. The EAC measurement was derived from the midpoint between the bony-cartilaginous junction and the scutum on a coronal image depicting the largest craniocaudal extent of the EAC. The IAC measurement was made in a similar fashion at the midpoint between the fundus and porus acusticus.

For both the EAC and IAC height measurements, the digital caliper tines were placed caudally at the canal roof (soft tissue/air–bone junction). The vector of each measure was drawn exactly perpendicular to a line tangent to the canal roof at the location of the caudal caliper point. This was taken cephalad and the cranial caliper placed at the intersection of the vector line and the bone-dura junction. In patients with AN, IAC measurements were deferred in cases where the geniculate to the closest visible location of the tegmen-dura interface. If radiologic dehiscence was present, a conventional measure of 0.04 mm was used for that location as this was the minimal allowable measure by the McKesson software. These measures were averaged to provide a relative measure of TgT thickness.

The PG measure was derived from a coronal image just anterior to the reference image at which the labyrinthine and tympanic segments of the facial nerve merged. At this point, a height measurement was performed from the tissue density of the geniculate to the closest visible location of the tegmen-dura interface. If radiologic dehiscence was present, a conventional measure of 0.04 mm was used (Figure 2).

Measurements of left and right ears were averaged at each of the 4 locations (EAC, TgT, PG, and IAC) to create single numerical values for statistical comparison between the comparison groups. This decision was based on a subanalysis demonstrating that left and right LSB height measures did not significantly differ within any of the comparison groups (difference range, 0.16-0.29 mm, left vs right). These data are provided in Supplemental Table SA (available in the online version of the article). In addition, an arbitrary value for LSB height was created and termed the relative skull base height (RSBH). This was the average of the 4 location measurements (bilateral averages). RSBH thus constituted a single continuous variable, allowing statistical comparisons that incorporated all performed measures of the LSB. Intragroup comparisons of RSBH in obese vs nonobese patients were performed.

**Observational measurements.** Skull base pneumatization was tabulated categorically (pneumatized/not pneumatized) at each of the 4 measurement locations. To be considered pneumatizsed, the osseous compartment overlaying the anatomical landmark in question had to clearly demonstrate air density voxels (black color; Figure 3). Patients with any other density pattern (gray) in the osseous compartment were not considered pneumatized.

**Statistical Analysis and Software**

Statistical comparisons and figures were generated via GraphPad Prism 7.0 (GraphPad Software, La Jolla, California). Continuous variables with a normal distribution were summarized by mean ± standard deviation and 95% confidence interval (CI). Those with nonnormal distribution were summarized by median and 95% CI. All continuous variables were tested for normal distribution via the Kolmogorov-Smirnov test. Categorical variables were summarized by frequency/percentage.

Comparisons of outcomes (nominal variables) were performed using Fisher’s exact or χ² test with Yates correction. For continuous variables, comparisons were made using the independent t test and/or analysis of variance (Holm-Sidak’s multiple-comparisons test). A correlation model was used to determine the relationship among continuous variables, including skull base height/thickness measures, age, and BMI. Pearson correlation coefficients were calculated along
with a 2-tailed \( P \) value and 95% CI. A value of \( P < .05 \) was considered indicative of statistical significance.

A final subset analysis was also performed that compared the 4 LSB height measurements (EAC, TgT, PG, and IAC) and RSBH for patients who were obese (BMI \( \geq 30 \) kg/m\(^2\)) with the same measures for patients who were nonobese (BMI <30 kg/m\(^2\)). This analysis was performed on the entire cohort, dichotomized by BMI, irrespective of disease subgrouping.

**Results**

Summary statistics are provided in **Table 1**. In total, 256 patients and 493 ears underwent measurements. For the entire cohort, the age range was 17 to 79 years. The number of patients/ears in each group were similar. The OTO controls were significantly younger (46.5 ± 13.3 years) than each of the other 3 groups (range, 52.0-59.4 years). There were no significant differences in sex distribution. The median BMI of the CSF group (36.8 kg/m\(^2\)) was significantly higher than the other groups.

Subjectively, the OTO and AN controls exhibited similar LSB phenotypes (**Figure 3**) and had the highest/thickest skull bases at each of measurement locations (**Table 1**). They were also more thoroughly pneumatized (**Table 2**). The SCD group exhibited a higher skull base laterally with notable attenuation at the medial measurement locations (TgT, PG, and IAC). The CSF group exhibited an attenuated skull base at all locations (**Table 1**).

Objectively, the OTO controls had significantly higher/thicker skull bases at each of the measurement locations compared to the CSF and SCD groups. Conversely, the CSF group exhibited the lowest/thinnest skull base compared to the OTO and AN controls (**Figure 4**). Height measures for the SCD group were similar to the CSF group medially over the TgT, PG, and IAC. The AN control group, interestingly, was significantly lower/thinner at most locations compared to the OTO group. Compared to the CSF and SCD groups, the AN group was significantly higher/thicker at most locations. Using RSBH as an indicator of skull base attenuation, the lowest/thinnest skull bases were exhibited in the CSF group (3.9 ± 1.5 mm; 95% CI, 3.5-4.3), followed by the SCD group (4.2 ± 1.1 mm; 95% CI, 3.9-4.5), AN group (4.9 ± 1.1 mm; 95% CI, 4.6-5.2), and OTO group (5.6 ± 1.5 mm; 95% CI, 5.3-6.1). A complete listing of intergroup comparisons is provided in **Table 1**.

Pneumatization patterns are described in **Table 2**. The OTO and AN groups had similar pneumatization rates at all locations. The SCD and CSF groups were significantly less pneumatized than the OTO and AN groups at each location. The CSF group had the lowest overall pneumatization rates. The SCD group exhibited the lowest rate of pneumatization of any group at the IAC location (17%).

The results of the correlation analyses for each group are depicted in **Table 2**. None of the groups demonstrated a statistically significantly correlation between either age-RSBH or BMI-RSBH. **Figure 5** and **Figure 6** depict these correlations, respectively, as performed for the entirety of the cohort (which closely mirrored similar intragroup analyses). There was also no significant difference in LSB height measures (including RSBH) between patients who were obese and those who were not (**Table 3**). When RSBH was compared between males and females in each group, no significant differences were detected (**Figure 7**).

Finally, intragroup comparisons of RSBH between obese and nonobese patients are depicted in **Table 2**. There was no significance detected in RSBH between any of the...
Table 1. Intergroup Comparisons of Demographic Variables and Skull Base Measurements.

<table>
<thead>
<tr>
<th></th>
<th>OTO (A)</th>
<th>AN (B)</th>
<th>CSF (C)</th>
<th>SCD (D)</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of patients</td>
<td>60</td>
<td>77</td>
<td>58</td>
<td>61</td>
</tr>
<tr>
<td>No. of ears</td>
<td>120</td>
<td>149</td>
<td>109</td>
<td>115</td>
</tr>
<tr>
<td>Age, mean ± SD (range), y</td>
<td>46.5 ± 13.3 (17-79)</td>
<td>52.8 ± 10.4 (27-73)</td>
<td>59.4 ± 11.3 (28-78)</td>
<td>52.0 ± 13.8 (18-76)</td>
</tr>
<tr>
<td>BMI, median (95% CI), kg/m²</td>
<td>28.1 (27.6-31.3)</td>
<td>29.1 (27.9-30.6)</td>
<td>36.8 (34.3-40.1)</td>
<td>29.1 (27.7-31.1)</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>24</td>
<td>34</td>
<td>17</td>
<td>22</td>
</tr>
<tr>
<td>Female</td>
<td>36</td>
<td>43</td>
<td>41</td>
<td>39</td>
</tr>
<tr>
<td>Lateral skull base height/thickness measurements</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>EAC height, mean ± SD (95% CI), mm</td>
<td>9.8 ± 2.8 (9.1-10.6)</td>
<td>9.3 ± 2.2 (8.7-9.8)</td>
<td>7.1 ± 3.0 (6.3-7.9)</td>
<td>8.2 ± 2.8 (7.4-8.9)</td>
</tr>
<tr>
<td>TgT height, mean ± SD (95% CI), mm</td>
<td>3.1 ± 1.2 (2.8-3.4)</td>
<td>2.4 ± 1.1 (2.1-2.7)</td>
<td>1.7 ± 1.1 (1.5-2.0)</td>
<td>1.6 ± 0.7 (1.4-1.8)</td>
</tr>
<tr>
<td>PG height, mean ± SD (95% CI), mm</td>
<td>4.6 ± 1.8 (4.1-5.1)</td>
<td>3.1 ± 1.7 (2.7-3.6)</td>
<td>2.6 ± 1.8 (2.2-3.2)</td>
<td>3.2 ± 1.3 (2.8-3.5)</td>
</tr>
<tr>
<td>IAC height, mean ± SD (95% CI), mm</td>
<td>5.2 ± 1.6 (4.8-5.6)</td>
<td>4.8 ± 1.4 (4.5-5.2)</td>
<td>4.2 ± 1.5 (3.7-4.6)</td>
<td>3.7 ± 1.3 (3.4-4.1)</td>
</tr>
<tr>
<td>RSBH height, mean ± SD (95% CI), mm</td>
<td>5.6 ± 1.5 (5.2-6.1)</td>
<td>4.9 ± 1.1 (4.6-5.2)</td>
<td>3.9 ± 1.5 (3.5-4.3)</td>
<td>4.2 ± 1.1 (3.8-4.5)</td>
</tr>
</tbody>
</table>

Abbreviations: AN, patients with acoustic neuroma; BMI, body mass index; CI, confidence interval; CSF, patients with spontaneous cerebrospinal fluid otorrhea; EAC, external auditory canal; IAC, internal auditory canal; OTO, control patients with otosclerosis; PG, perigeniculate; RSBH, relative skull base height; SCD, patients with superior canal dehiscence (radiographic syndrome) and no other diagnoses; SD, standard deviation; TgT, tegmen tympani.

*Uppercase letters A to D denote statistical comparisons between groups. P < .05 considered statistically significant (bold values).

Thirty-one patients had formal diagnoses of SCD. Thirty patients had 1 or more core symptoms but lacked enough diagnostic data for a formal SCD syndrome diagnosis.

*A total of 19 patients had measures performed on only 1 ear (0, OTO; 7, SCD; 7, CSF; 5, AN).

Fifty-two patients with AN had a unilateral IAC measure deferred due to tumor extension into the IAC.
## Table 2. Intergroup Correlation Analyses and Skull Base Pneumatization Patterns.a

<table>
<thead>
<tr>
<th>Percentage (No./total No.) of patients with skull base pneumatization by measurement location</th>
<th>OTO (A)</th>
<th>AN (B)</th>
<th>CSF (C)</th>
<th>SCD (D)</th>
<th>Significance</th>
</tr>
</thead>
</table>
| EAC | 98 (117/120) | 96 (143/149) | 68 (74/109) | 83 (96/115) | A-B: \( P = .73 \)  
A-C: \( P < .0001 \)  
A-D: \( P = .0002 \)  
B-C: \( P < .0001 \)  
B-D: \( P = .001 \)  
C-D: \( P = .007 \) |
| TgT | 90 (108/120) | 84 (125/149) | 31 (34/109) | 51 (59/115) | A-B: \( P = .15 \)  
A-C: \( P < .0001 \)  
A-D: \( P < .0001 \)  
B-C: \( P < .0001 \)  
B-D: \( P < .0001 \)  
C-D: \( P = .003 \) |
| PG | 58 (70/120) | 52 (77/149) | 20 (22/109) | 32 (37/115) | A-B: \( P = .32 \)  
A-C: \( P < .0001 \)  
A-D: \( P < .0001 \)  
B-C: \( P < .0001 \)  
B-D: \( P < .0001 \)  
C-D: \( P = .04 \) |
| IAC | 41 (49/120) | 47 (70/149) | 23 (25/109) | 17 (19/115) | A-B: \( P = .33 \)  
A-C: \( P = .005 \)  
A-D: \( P < .0001 \)  
B-C: \( P < .0001 \)  
B-D: \( P < .0001 \)  
C-D: \( P = .24 \) |

### Correlations and comparisons

**Age-RSBH**

<table>
<thead>
<tr>
<th>Pearson (( r ))</th>
<th>95% CI</th>
<th>( P )</th>
</tr>
</thead>
<tbody>
<tr>
<td>EAC</td>
<td>( -0.08 )</td>
<td>( -0.3 ) to ( 0.2 )</td>
</tr>
<tr>
<td>TgT</td>
<td>( 0.06 )</td>
<td>( -0.2 ) to ( 0.3 )</td>
</tr>
<tr>
<td>PG</td>
<td>( 5.4 )</td>
<td>( 4.6 ) to ( 6.2 )</td>
</tr>
<tr>
<td>IAC</td>
<td>( 6.0 )</td>
<td>( 4.9 ) to ( 7.2 )</td>
</tr>
</tbody>
</table>

**BMI-RSBH**

<table>
<thead>
<tr>
<th>Pearson (( r ))</th>
<th>95% CI</th>
<th>( P )</th>
</tr>
</thead>
<tbody>
<tr>
<td>EAC</td>
<td>( -0.07 )</td>
<td>( -0.3 ) to ( 0.2 )</td>
</tr>
<tr>
<td>TgT</td>
<td>( -0.24 )</td>
<td>( -0.4 ) to ( 0.3 )</td>
</tr>
<tr>
<td>PG</td>
<td>( -0.2 )</td>
<td>( -0.4 ) to ( 0.3 )</td>
</tr>
<tr>
<td>IAC</td>
<td>( -0.04 )</td>
<td>( -0.09 ) to ( 0.3 )</td>
</tr>
</tbody>
</table>

**Sex-RSBH, mean ± SD, mm**

<table>
<thead>
<tr>
<th></th>
<th>Male</th>
<th>Female</th>
<th>( P )</th>
</tr>
</thead>
<tbody>
<tr>
<td>EAC</td>
<td>( 6.0 )</td>
<td>( 5.4 )</td>
<td>( .11 )</td>
</tr>
<tr>
<td>TgT</td>
<td>( 4.9 )</td>
<td>( 4.6 )</td>
<td>( .19 )</td>
</tr>
<tr>
<td>PG</td>
<td>( 3.5 )</td>
<td>( 4.0 )</td>
<td>( .18 )</td>
</tr>
<tr>
<td>IAC</td>
<td>( 4.2 )</td>
<td>( 4.1 )</td>
<td>( .78 )</td>
</tr>
</tbody>
</table>

### RSBH: obese patients vs nonobese patients

<table>
<thead>
<tr>
<th></th>
<th>Obese, No.</th>
<th>Nonobese, No.</th>
<th>RSBH, mean ± SD, mm; obese BMI ( \geq 30 ) kg/m(^2) (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>EAC</td>
<td>21</td>
<td>39</td>
<td>( 5.8 ) ± ( 1.4 ) (5.4-6.1)</td>
</tr>
<tr>
<td>TgT</td>
<td>33</td>
<td>44</td>
<td>( 4.8 ) ± ( 1.2 ) (4.3-5.2)</td>
</tr>
<tr>
<td>PG</td>
<td>40</td>
<td>18</td>
<td>( 3.7 ) ± ( 1.3 ) (3.3-4.1)</td>
</tr>
<tr>
<td>IAC</td>
<td>25</td>
<td>36</td>
<td>( 4.5 ) ± ( 1.3 ) (4.2-4.8)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>Obese vs nonobese RSBH, ( P ) value</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>EAC</td>
<td>( .02 )</td>
<td></td>
</tr>
<tr>
<td>TgT</td>
<td>( .002 )</td>
<td></td>
</tr>
<tr>
<td>PG</td>
<td>( .003 )</td>
<td></td>
</tr>
<tr>
<td>IAC</td>
<td>( .03 )</td>
<td></td>
</tr>
</tbody>
</table>

Abbreviations: AN, patients with acoustic neuroma; BMI, body mass index; CI, confidence interval; CSF, patients with spontaneous cerebrospinal fluid otorrhea; EAC, external auditory canal; IAC, internal auditory canal; OTO, control patients with otosclerosis; PG, perigeniculate; RSBH, relative skull base height; SCD, patients with superior canal dehiscence (radiographic syndrome) and no other diagnoses; SD, standard deviation; TgT, tegmen tympani; —, no statistical comparisons.

*aCorrelations between continuous variables demonstrated via Pearson coefficient (\( r \)), 95% CI, and \( P \) value. Uppercase letters A to D denote statistical comparisons between groups. \( P < .05 \) considered statistically significant.*
subgroups with the exception of the SCD group, where obese patients were found to have significantly higher/thicker skull bases compared to nonobese patients ($P = .03$).

**Discussion**

In review of these data, the study hypothesis was only partially supported. As anticipated, the SCD and CSF groups exhibited similar patterns of radiographic LSB attenuation, which were unique compared to patients with OTO and AN (Table 1, Figure 4). The CSF group exhibited the most attenuated and poorly pneumatized LSB of any group. Patients with SCD exhibited similar attenuation to the patients with CSF at the medial measurement locations but had less attenuation and better pneumatization laterally over the EAC.

Contrary to our expectations, no statistical correlation was detected between BMI and LSB height/thickness in any of the comparison groups. In addition, obese patients in the individual groups exhibited no difference in LSB attenuation compared to nonobese patients (Table 2). This was especially surprising in the CSF group, where elevated BMI is a commonly reported finding, including within the present investigation.7,9,10,12-14,18,20 These findings were further underscored when similar LSB height measures were detected for the cohort as a whole (regardless of presenting diagnosis; Table 3).

This lack of correlation is consistent with prior reporting from 2 smaller studies involving lateral skull base measures.8,10 One potential explanation for this may be that BMI is a poor measure for the theorized pathologic process at work. As some have theorized that obesity-related ICH is responsible for skull base remodeling, a better variable for the purposes of our statistical correlations may have been intracranial pressure.

Unfortunately, intracranial pressure can currently only be measured via lumbar puncture with opening pressure (LP OP). Given the limitations of our retrospective study design, the relatively high morbidity of LP, and the relative infrequency with which the LP OP is performed, obtaining such data was not possible for this investigation. New technologies are currently in development that may allow for noninvasive ICP measurements.39 Future study designs may incorporate this technology or could prospectively perform LP to support/refute the findings reported here.

When the data from this investigation are considered in aggregate, 2 notable observations emerge. First, the similarities in radiographic phenotype observed between patients with CSF and SCD would suggest a common pathoetiologic mechanism for LSB attenuation in both disorders. This has been postulated previously by others.6-8 Allen et al,7 in particular, noted that the prevalence of SCD may be 30 times higher in patients with spontaneous CSF otorrhea than what has been reported for the general population.5 In addition, multiple investigators have described a high rate of concomitant tegmen dehiscence (up to 76%) in patients with SCD syndrome.1-5,37

Second, our inability to detect a statistical link between obesity and LSB attenuation would argue against an acquired mechanism and instead favor a congenital one. Such a mechanism has been suggested previously in patients with SCD syndrome.1-5,37 The present study, to date, is the largest investigation to provide evidence in support of a congenital attenuation theory in patients with CSF. However, the data do not explain why the obesity rate is consistently high in these patients compared to patients with SCD syndrome.
Considering the currently available literature and the present data, we would propose a theoretical 2-hit hypothesis for the pathoetiology of spontaneous CSF otorrhea. The first hit would be the congenital predisposition of patients to an attenuated LSB. Based upon histologic studies by Carey et al\textsuperscript{5} in 2000 and subsequent investigations, the prevalence of this phenomenon could be as low as 0.5% to 1.9%.\textsuperscript{4} The second hit would occur when patients with a congenital LSB attenuation become obese later in life and develop secondary ICH. With a thin and/or dehiscent tegmen and hydrodynamic strain on their leptomeninges, these patients would theoretically be at elevated risk for eventual dural compromise, possible encephalocele formation, and subsequent leak formation.

This hypothesis would explain why the incidence of spontaneous CSF otorrhea is relatively very low despite a domestic obesity rate approaching 35%.\textsuperscript{13,40} It could also explain why most patients with nonobese SCD syndrome with concomitant skull base dehiscence fail to develop CSF otorrhea.\textsuperscript{5-8,37} This hypothesis would not explain why nonobese patients on occasion can develop spontaneous CSF otorrhea.

This study has a number of imitations, including its retrospective design and relatively small size for a population study. In addition, the comparison groups were chosen based on known diagnoses rather than random sampling, so selection bias may have influenced the results. This was difficult to avoid given that the study design required high-definition temporal bone CTs, which are not randomly performed. Finally, the study included few pediatric patients (age <18 years) due to the nature of the disorders investigated and our practice makeup.

One additional consideration is that the present study design did not incorporate an assessment of interrater agreement. We decided to forgo this analysis based on the fact that such analyses have been previously performed by our group and others for similar measurement protocols to those employed here.\textsuperscript{4,10} These prior analyses have shown good to very good interrater agreement.

### Conclusion

Patients with SCD and spontaneous CSF otorrhea have distinct radiographic LSB phenotypes compared to patients with OTO and AN. Patients with the former disorders have highly attenuated and poorly pneumatized skull bases overlying key structures of temporal bone anatomy. No correlation was detected between age, sex, BMI, and LSB height among any of the comparison groups. When taken together, these findings support a theory of congenital lateral skull base attenuation.

### Acknowledgments

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**Table 3. Comparison of Skull Base Height Measures between Obese and Nonobese Patients.**

<table>
<thead>
<tr>
<th></th>
<th>Obese Patients</th>
<th>Nonobese Patients</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of patients</td>
<td>119</td>
<td>136</td>
<td></td>
</tr>
<tr>
<td>No. of ears</td>
<td>227</td>
<td>264</td>
<td></td>
</tr>
<tr>
<td>Age, mean ± SD (95% CI), y</td>
<td>53.9 ± 11.4 (52-57)</td>
<td>51.6 ± 14.1 (47-56)</td>
<td>.14</td>
</tr>
<tr>
<td>Sex, No.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>47</td>
<td>49</td>
<td>.61</td>
</tr>
<tr>
<td>Female</td>
<td>72</td>
<td>87</td>
<td></td>
</tr>
<tr>
<td>EAC height, mean ± SD (95% CI), mm</td>
<td>8.5 ± 3.1 (7.9-9.1)</td>
<td>8.9 ± 2.7 (8.5-9.4)</td>
<td>.22</td>
</tr>
<tr>
<td>TgT height, mean ± SD (95% CI), mm</td>
<td>2.2 ± 1.3 (1.9-2.4)</td>
<td>2.2 ± 1.2 (1.9-2.4)</td>
<td>.71</td>
</tr>
<tr>
<td>PG height, mean ± SD (95% CI), mm</td>
<td>3.2 ± 1.7 (2.8-3.5)</td>
<td>3.3 ± 1.9 (2.9-3.7)</td>
<td>.51</td>
</tr>
<tr>
<td>IAC height, mean ± SD (95% CI), mm</td>
<td>4.4 ± 1.5 (4.1-4.6)</td>
<td>4.5 ± 1.6 (4.2-4.8)</td>
<td>.44</td>
</tr>
<tr>
<td>RSBH height, mean ± SD (95% CI), mm</td>
<td>4.5 ± 1.4 (4.3-4.8)</td>
<td>4.7 ± 1.5 (4.5-4.9)</td>
<td>.29</td>
</tr>
</tbody>
</table>

Abbreviations: CI, confidence interval; EAC, external auditory canal; IAC, internal auditory canal; PG, perigeniculate; RSBH, relative skull base height; SD, standard deviation; TgT, tegmen tympani.
Author Contributions

Shawn M. Stevens, conception, design, acquisition, analysis, interpretation of data; drafting manuscript; final approval for publication; accountable for accuracy/originality; Kiefer Hock, acquisition, analysis, interpretation of data; drafting manuscript; final approval for publication; accountable for accuracy/originality; Ravi N. Samy, design, analysis, drafting, final approval for publication; accountable for accuracy/originality; Myles L. Pensak, design, analysis, drafting, final approval for publication; accountable for accuracy/originality.

Disclosures

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Supplemental Material

Additional supporting information is available in the online version of the article.

References


