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The bone mineral density of the lateral skull base and its relation to obesity and spontaneous CSF leaks

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Abstract

Objective: Evaluate the bone mineral density (BMD) of the lateral skull base by thin sliced CT scans. Determine the BMD and its relation in patients who are obese or who have spontaneous CSF leaks.

Study Design: Blinded retrospective case control series.

Setting: Tertiary care university setting.

Patients: A control group consisting of age and gender matched non-obese patients were compared to obese and CSF leak patients

Interventions: Three blinded reviewers measured the BMD at multiple locations along the lateral skull base using thin sliced high-resolution CT scans. Additional BMD measurements were obtained from the temporal bone squamosal and otic capsule. The BMD was compared between the groups.

Main outcome measure: Lateral skull base BMD in patients who are obese or have CSF leaks as compared to non-obese controls.

Results: Sixty-five (n= 65) patients were included in the study. The control group (n=21) had a median density along the tegmen of 499.4 (178.8) HU, obese (n=26) had an average HU of 559.5 (207.2) and CSF leak group (n=18) had an average 472.9 (154.9), respectively (p=0.35). The BMD in the temporal bone squamosa (p=0.07) was not significantly different, however the otic capsule was denser in the CSF leak group (p=0.01) compared to the control group or the obese group. The intraclass correlation coefficient of the CT reviewers' measurements were moderate to strong (k=0.69–0.99).

Conclusion: There appears to be no difference between the BMD of the lateral skull base as it relates to obesity or spontaneous CSF leaks compared to normal weight controls. These findings suggest the BMD does not have a significant role in the development of lateral skull base thinning or dehiscence leading to CSF leaks.

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Introduction

Computed tomography (CT) is widely used to delineate cross-sectional anatomy and the diagnostic capabilities of CT are also expanding including evaluating bone mineral density (BMD). The gold standard for testing the BMD has long been the DEXA scan and its implications for osteoporosis.¹ However, CT-attenuation values as measured by Hounsfield units (HU) have been used as a reliable alternative to DEXA scans for BMD.²⁻³ Aside from measuring thickness, CT's may be used to measure areas and volumes.⁴

CT is particularly helpful when evaluating the detailed bony anatomy, especially that of the lateral skull base. Several authors have used CT for studying patients with cerebrospinal fluid (CSF) leaks.⁵ It has been shown that patients with spontaneous lateral skull base CSF leaks and/or encephaloceles are more likely to have thin skull bases when compared to non-obese patients.⁶⁻⁷ These studies have utilized CT scans to measure the thickness of the skull base at specific locations along the tegmen tympani and tegmen mastoideum. Other studies have looked at thickness of the squamosa of the temporal bone which is also thinner in patients with CSF leaks.⁸ Most studies have shown an association with obesity and thinning lateral skull base.^{6-7, 9} Further, the role of obesity has been shown to decrease overall bone health by altering various aspects of bone metabolism and there is evidence that the cortical bone in obese individuals maybe more dense as compared to normal weight individuals; however, this increase in density may not reflect greater bone strength.¹⁰⁻¹¹ Takahashi, et al, recently demonstrated that regional bone density differences occur within the temporal bone throughout development but this has not been studied in terms of obesity or potential for CSF leaks.¹² However, to date, there have been no studies looking at the BMD of the lateral skull base and its relation to obesity and CSF leaks. With the current rising epidemic of obesity in the US, we expect to see more patients with obesity related skull base complications including CSF leaks and encephaloceles. The aim of this study is to measure the BMD along with area of the lateral skull base in patients who are obese or have CSF leaks and compare them to healthy controls.

Methods

Approval was obtained from the Institutional Review Board.

Group Selection

We conducted a retrospective review of patients undergoing evaluation and/or treatment at our institution from July 2007 to May 2017. Three groups of patients were identified utilizing two departmental databases. The first group (control group) was comprised of normal weight or non-obese patients whose BMI was less than 30. The second group of patients (obese group) was comprised of patients whose BMI was greater than 30. These two groups were compiled from our cochlear implant database at our institution. These patients had preoperative CT scans that were high resolution and had thin cuts from which we could obtain measurements of the skull base which will be discussed further. The third group of patients (CSF leaks) was obtained using our skull base surgical records database. This database contains all patients who have undergone a skull base procedure and is maintained by the operating surgeons. This database is divided into procedures including

CSF leak repairs. These records were manually reviewed. These groups were then age and gender matched. All three groups met the same inclusion and exclusion criteria for the study. Inclusion criteria were: age over 18 years and a dedicated preoperative CT scan of the temporal bones that included axial and coronal sections with a slice thickness less than or equal to 0.75 mm. Exclusion criteria were prior skull base or mastoid surgery, temporal bone trauma, or incomplete demographic information including height and/or weight. Chronic middle ear or mastoid disease was not an exclusion criterion. Demographic data collected included: age, gender, BMI, ethnicity, and smoking status.

Imaging and Hardware

The analyzed temporal bone CT scans had to have maximum slice thickness of less than 0.75mm. The CT scans that were obtained at our institution were performed using either a Siemens Somatom Sensation 16 or a Siemens Definition 128 (Siemens Medical Solutions, Malvern, Pennsylvania). Spatial resolution was rated as accurate to 0.1 to 0.2 mm per protocol. The CT slice thickness of images obtained at our institution were 0.6 mm. The images had to have both axial and coronal views. Software-reformatted images were analyzed via the proprietary digital radiology imaging system AGFA Impax 6 (AGFA Impax, Mortsel, Belgium). The images were viewed on ThinkVision™ monitors with the resolution of 1920 by 1080 pixels. The control group and the obese group had their scans obtained at our institution as part of their preoperative cochlear implant assessment. The CSF leak group scans were obtained from multiple radiology centers and referral centers; however, if the slice thickness of the CT was greater than 0.75 mm these patients were excluded from the study.

CT Measurements

The measurements were performed in a blinded fashion by three individuals: second year neurotology fellow, fourth-year medical student, and clinical research fellow. To assess the measurements, all the reviewers went through five cases together and then were asked to independently measure relevant structures thus, allowing the measurement of intra- and inter-rater reliability. Prior to obtaining the measurements, the blinded reviewers were given a tutorial regarding radiology software and how to use the measuring calipers and HU average measurement device. The reviewers were asked to obtain measurements of HU in the following locations. First, the pars squamosa of the temporal bone at the level of the optic canals using axial images. Second, the otic capsule measured around the basal turn of the cochlea using axial images. Third, the majority of the lateral skull base was measured in the coronal plane. Sequential CT slices were measured beginning at the first appearance of the head of the malleus and ending at the posterior semicircular canal. These specific beginning and ending measurements were chosen based on prior studies that have measured the thickness of the skull base at these specific areas.⁶⁻⁷ Further the pneumatization patterns of the mastoid cavity are variable and these specific beginning and ending points provided the CT reviewers standardization. The measurements of the lateral skull included at a minimum of 17 measurements per side and a maximum of 23 measurements per side. Both the HU and total surface area were measured at this location. (figure 1) The surface area was recorded based on the assumption that a greater surface area with less dense bone would be significant in patients with CSF leaks

Statistics

Data analyses were performed with SPSS 24.0 (SPSS Inc., IBM Corp., Armonk NY), SigmaPlot 12.5 (Systat Software, Inc., San Jose, CA), and MedCalc 18.2.1 (Ostend, Belgium). Categorical variables were summarized by frequency and percentage. Continuous variables were summarized by mean standard deviation (SD) and range where appropriate. All continuous variables were assessed for normality using the Kolmogorov–Smirnov test. Comparisons of baseline characteristics and outcomes (categorical variables) were performed using a Fisher's exact test or Chi Square test. For continuous variables, comparisons between two groups were done with an independent t-test or a Mann–Whitney rank-sum test. A One-Way ANOVA or ANOVA on Ranks was used to compare mean values among three groups (control, CSF leak, and obesity). If there is a significant difference, then a Duncan's (normal distribution) or Dunn's (non-normal distribution) post hoc was used to determine statistical significant between groups. Finally, intraclass correlation coefficient (k) was used as an index for the reliability of different CT reviewers averaged together. Given the different levels of training of the CT reviewers, the intraclass correlation coefficient helps to determine that the CT reviewers were making similar measurements of the skull base. The intraclass correlation coefficient is an index for the reliability of different raters' averaged together. The k value can be interpreted as follows: <0.20, poor; 0.21–0.40, fair; 0.41–0.60, moderate; 0.61–0.80, good; 0.81–1.00, very good. A p value of <0.05 was considered to indicate a statistically significant difference for all statistical tests.

Results

Originally, the study started with 90 patients with 28 in each group, but after applying the exclusion criteria including incomplete data, low resolution or poor quality CT scans, or prior surgery, there were 65 patients included in the study. There were 21, 18 and 26 patients in the control group, CSF leak group, and obese group, respectively. The average age for the patients for all 3 groups were 61.5 for the control group, 60.3 for the obese group and 55.0 for the CSF leak group. There was no significant difference in average age between groups ($p=0.27$). The average BMI for the control was 23.3 and 33.9 for the CSF leak group ($p=0.00$). The obesity group BMI average was 35.1. There was no significant difference between the groups in terms of race and smoking status ($p=0.34$, 0.43 respectively) (see table 1). There was predominance of females in the study; $n=55$ (males $n=10$). There were two patients in the CSF leak group who were previously diagnosed with idiopathic intracranial hypertension (IIH).

Each patient had both temporal bones measured bringing the total number of ears or temporal bones measured to $n=130$. The number of images or slices measured per patient per side ranged from 19 to 25 beginning from the malleus (anterior limit) to the posterior semicircular canal (posterior limit) for the lateral skull base, pars squamosa and otic capsule thus a minimum of 38 measurements per patient were recorded. The control group's median HU for the skull base was 499.4 (SD 178.8), CSF leak group's average was 472.9 (SD 154.9), and the obese group's average was 599.5 (SD 207.2). There was no statistically significant difference amongst the three groups ($p=0.35$). The average area of the skull base in the control group was 0.21 cm², CSF leak group 0.19 cm² and obese group 0.20 cm².

These measurements were not significantly different between groups ($p = 0.18$). Similarly, single measurements of the temporal bone squamosa were performed. The median HU for the squamosa was 1254.1 (183.0) for the control group, 1157.40 (160.6) for the CSF leak group, and 1207.5 (170.7) for the obese group with no statistical difference ($p=0.07$). The median HU for the otic was 1768.6 (69.8) for the control group, 1821.2 (111.4) for the CSF leak group, and 1744 (6.8) for the obese group. This was statistically significant for the CSF leak group having a greater density ($p=0.01$) Results are summarized in table 2

A subset analysis of the CSF group was performed by comparing the side with the CSF leak to the unaffected side. There were 12 CSF leaks on the right side and 6 on the left side. There was no difference in the BMD of the lateral skull base, pars squamosal or the otic capsule ($p=0.63$, $p=0.66$, and $p=0.44$; respectively).

The intraclass correlation coefficient of the all reviewers when comparing HU of the skull base, squamosal, and otic capsule ranged from $k=0.41$ to $k=0.99$ indicating moderate to strong correlation. Results are summarized in table 2

Discussion

Previous studies have shown that thinning of the skull base is more common in patients with CSF leaks and in patients who are obese. Previous work by Stevens et al, concluded that another process independent of obesity was contributing to thin skull bases in patients with CSF leaks.⁷ They hypothesized that this may be related to hormones playing a role in bony metabolism or a congenital predisposition. Similarly, Rizk et al showed that patients with superior semicircular dehiscence with an average BMI lower than 30, had a thickness of the lateral skull base that was less than obese controls.⁶ They concluded that obese patients may have increased BMD, but that this increase in BMD does not translate to greater strength. However, they did not specifically measure BMD in that study. Other studies have concluded similar results as well using measurements of the pars squamosa of the temporal bone and comparing it to the zygomatic arch. They inferred that the thinning of the squamosa was reflected by global thinning of the entire calvarium including the lateral skull base.⁸ However, they were unable to measure the lateral skull base directly. Given the prior studies' conclusions, the aims of this study were to explore the relation between spontaneous CSF leaks of the lateral skull base and BMD, and to determine if obesity contributes to the BMD of the lateral skull base.

As cited earlier, CT scans are sensitive and specific (greater than 90%) for diagnosing osteoporosis and decreased bone mineral density of vertebral bodies by utilizing HU measurements.² Further, the correlation between HU and bone mineral density is well established.³ Our CT reviewers took continuous measurements along the skull to encompass the majority of the tegmen tympani and the tegmen mastoideum. The prior studies took specific measurements of certain areas of the tegmen tympani and tegmen mastoideum; which was 12 measurements per patient.⁶⁻⁷ In contrast, our reviewers recorded a minimum of 38 measurements per patient including 34 measurements along the various aspects of the tegmen. By capturing the majority of the skull base we were attempting to determine if there was a more global problem related to the BMD leading to CSF leaks.

Interestingly, we did not find a significant difference in the average HU amongst the three groups in the lateral skull base, or temporal squamosa. This leads us to conclude that while the skull bases maybe thin in both patients with CSF leaks or who are obese, the underlying BMD is not affected in either circumstance. This suggests that other pathophysiologic processes must be occurring that lead to thinning and ultimately causing spontaneous CSF leak and or encephaloceles.

A prior study has measured the BMD of the otic capsule and the average density was 1772.3 HU.¹³ The averages of our study groups were similar to that study in that the average HU for all patients in our study was 1784 (HU) however, we found that the otic capsule was statistically significant for patients in the CSF leak group having a denser otic capsule. In a study by Takahasi et al, they have shown that the various regions of the temporal bone have different bone mineralization patterns. In particular, the otic capsule was consistent through birth to adulthood in terms of its HU, whereas the middle fossa had the lowest bone mineral density.¹² These findings may suggest that there may be certain hereditary, congenital or acquired changes leading to a wider variability in the densities in certain regions of the temporal bone such as the otic capsule as compared to the tegmen in patients with CSF leaks. This is the first study to report this finding of a denser otic capsule in this patient population.

A number of skull base disorders have been associated with idiopathic intracranial hypertension (IIH); including superior canal dehiscence syndrome (SCDS), sigmoid sinus dehiscence/diverticulum, anterior/lateral skull base dehiscence, encephalocele and spontaneous CSF leaks.^{9,14} The leading hypothesis for the common mechanism behind these disorders involves chronic bone resorption where over pressurized dura, cerebral venous sinuses and/or arachnoid granulations contact the skull base.¹⁴ While this study did not specifically address patients with IIH, we did not find that obesity, which is a risk factor for IIH, contributed to bone mineral demineralization. There were only two patients within the CSF group that were diagnosed with IIH, but this number would likely be higher had routine lumbar punctures for opening pressure following CSF leak repair been performed. The role of IIH and its effects on bone needs further research but we agree with prevailing hypotheses and treatments aimed at lowering intracranial hypertension. It has also been shown that morbid obesity leads to a decrease in cortical bone density, in long bones and vertebra but this has not been found in other non-weight bearing bones.¹⁰ There is also evidence which shows that obesity may alter the bony architecture via adipokines or cytokines that lead to a decrease in bone strength without altering the BMD.¹⁵⁻¹⁶ The pathophysiology of bone health and obesity remains an active area of research.¹¹

This current study also examined the area of the lateral skull base from the anterior measurement of the malleus to the posterior measurement of the posterior semicircular canal. There was no significant difference in the total area of the tegmen tympani or tegmen mastoideum for the three groups. There are currently no studies addressing the pneumatization of the mastoid cavity or surface area of the lateral skull as it relates to obesity or CSF leaks. It seems logical; however, that a greater surface area of the skull base along and/or a more pneumatized mastoid cavity would be factors in contributing to the development of CSF leaks in individuals with a predisposition. This has been demonstrated

in recent data that have shown in anterior skull base CSF leaks that increased pneumatization of the sphenoid sinus along with increased BMI were associated with spontaneous CSF leaks.¹⁷

There are some limitations of this study. While the CT reviewers were blinded to patient data, there are certain characteristics of the scans of patients with CSF leaks including unilateral mastoid opacification and focal thinning or dehiscence of the tegmen. Also, we looked globally at the skull base. CSF leaks may occur in specific areas of bone mineral resorption that we did not specifically measure. The majority of scans were performed at our institution with slice thickness of 0.6 mm. The remaining scans were from outside facilities with variable slice thickness ranging from 0.6 to 0.75 mm. The scans that were not from our institution were predominately found within the CSF leak group which could be a potential source of bias for our CT reviewers.

Conclusions

This is the first study to look at BMD of the lateral skull as measured by CT scan and its relation to CSF leaks and obesity. There appears to be no correlation between the BMD of the lateral skull base or the pars squamosa in patients who are obese or who have spontaneous CSF leaks as compared to normal weight patients. Patients with CSF leaks had a significantly denser otic capsule as compared to the other two groups. These findings also suggest the BMD does not have a significant role in the development of lateral skull base thinning or dehiscence leading to CSF leaks, and that other pathophysiologic mechanisms are likely leading to thinning of the skull base.

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Figure 1: Skull base density measurements

Upper left – coronal image of the area and density measured in a control patient. Upper right – coronal image of the area and density measured in a CSF leak patient. Lower left – axial image showing the measurement around the otic capsule. Lower right – Bilateral squamosa density measurements.

Table 1.

Patient demographics.

	Control	CSF Leak	Obese	<i>p</i> value
<u>N</u>	21	18	26	
Age	61.5 (22 to 88)	60.3 (28 to 80)	55.0 (31 to 73)	0.27
BMI (SD)	23.3 (3.2)	33.9 (6.2)	35.1 (5.5)	<0.01
Sex (F/M)	17/4	17/1	21/5	0.57
Race				0.33
<i>Caucasian</i>	16	11	14	
<i>African American</i>	4	7	11	
<i>Other</i>	1	0	1	
Smoking Status				0.43
<i>Smoker</i>	4	2	4	
<i>Former Smoker</i>	5	9	7	

Table 2.

CT density measurements across groups. Measurements in HU (SD)

	Control Group Mean (SD)	CSF Leak Group	Obese Group	ANOVA p value	Intraclass Correlation Coefficient (<i>k</i>) (95% confidence interval)
Combined Skull Base (HU)	499.4 (178.8)	472.9 (154.9)	559.5 (207.2)	0.35	0.928 (0.724 to 0.992)
Combined Squamosa (HU)	1254.1 (183.0)	1157.40 (160.6)	1207.5 (170.7)	0.07	0.915 (0.718 to 0.981)
Combined Otic Capsule (HU)	1768.6 (69.8)	1821.2 (111.4)	1744 (6.8)	0.01	0.926 (0.689 to 0.974)
Combined Area of the Skull Base (cm ²)	0.21 (0.06)	0.19 (0.04)	0.20 (0.09)	0.18	0.921 (0.785 to 0.989)
Left skull base area (cm ²)	0.21 (0.06)	0.19 (0.05)	0.20 (0.09)	0.48	0.870 (0.681 to 0.955)
Right skull base area (cm ²)	0.22 (0.10)	0.19 (0.04)	0.19 (0.11)	0.19	0.937 (0.839 to 0.979)