Novel Radiographic Assessment of the Cribriform Plate

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Abstract

Background: The cribriform plate (CP) is a common site of spontaneous cerebrospinal fluid (SCSF) leaks. Radiographic assessment of the anterior and lateral skull base has shown thinner bone in patients with SCSFs; however, prior assessment of the CP has required postmortem cadaver dissection.

Objective: To develop novel radiographic techniques to assess the anatomy of the CP.

Methods: Computed tomography (CT) scans were performed on cadaveric specimens. Bone density and anatomy of a predefined volume of interest of the posterior CP were assessed by two independent reviewers. CT assessment of olfactory foramina was also performed and validated using anatomic dissection of cadaver specimens.

Results: Interclass correlation coefficients (ICCs) for measuring the same volume of each CP was 0.96, confirming reproducible anatomic localization. Cadaver CPs had a mean Hounsfield units of 263, indicating a mix of bone and soft tissue, and ICC was 0.98, confirming reproducible radiographic measurements. Optimal CT estimates of bone composition of CPs averaged 85% (range 76% to 96%) compared to actual anatomic dissection which averaged 84% bone (range 74% to 91%, $r = .690$, $P = .026$).

Conclusion: Our novel, noninvasive CT method for assessing CP anatomy is reproducible and correlates with anatomic dissection assessing bone composition. The clinical implications of anatomic changes in the CP are an area for further study.

Keywords

cribriform plate, ethmoid bone, skull base, cerebrospinal fluid leak, computed tomography, bone density, craniofacial, encephalocele, olfactory foramina, anatomy

Introduction

Radiographic assessments of the anterior and lateral skull base have found the bone to be thinner at various sites in patients with spontaneous cerebrospinal fluid (SCSF) leaks, likely due to prolonged hydrostatic pressure from elevated intracranial pressure (ICP).^{1–3} Additionally, it appears that elevated ICP results in encephaloceles and leaks at sites of anatomic weakness, resulting in radiographic findings such as empty sella, optic nerve sheath dilation, and meningoceles at natural skull base foramina.^{3,4} The cribriform plate (CP)—one of the thinnest regions of the skull base—is a site that is vulnerable to spontaneous leaks both due to its inherent thinness and through preexisting olfactory foramina

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Figure 1. Coronal CT of patient with spontaneous CSF leak through the right cribriform plate. Absence of bone noted in bilateral CPs. CP, cribriform plate; CSF, cerebrospinal fluid leak; CT, computed tomography.

(Figure 1).^{2,3,5} Unfortunately, assessment of the CP has historically required cadaveric dissection. The purpose of this study was to validate novel radiographic metrics to assess anatomic variations in the CP.

Methods

Cadaver Dissection

Human cadaver specimens underwent noncontrast axial head computed tomography (CT) scans with 0.6 mm cuts from vertex of the scalp to the inferior border of the mandible. Following this, endoscopic resection and en bloc removal of the entire anterior skull base were then performed by two attending rhinologists. Enzymatic proteolysis of the cribriform specimen was then performed by immersion in Pronase® (Sigma-Aldrich, St. Louis, MO) on a rocker for 24 h at 37°C. Further proteolysis was inhibited by the addition of fetal bovine serum, then residual soft tissue was removed from the specimen. Olfactory foramina were identified under an operating microscope and patency confirmed using otologic probes. Digital photographs were taken of the CP specimens with a ruler to ensure accurate scaling of length measurements, then uploaded into ImageJ (National Institutes of Health, Bethesda, MD).⁶⁻⁸ All cadaver measurements were reconciled with the lengths and widths of each side of the CP measured in OsiriX (Pixmeo, Geneva, Switzerland) as described below. Foramina that had been confirmed with dissection were outlined in ImageJ, and the cross-sectional area of the olfactory foramina as a percentage of the total CP area was calculated (Figure 2). The remainder of the cross-sectional area of the CP that was not identified as a patent olfactory foramina was considered bone, and this measure was used to define the percentage of bone composition.

Figure 2. Olfactory foramina in cadaveric specimen were examined under an operating microscope to confirm patency of foramina. An area matching dimensions outlined on CT was then analyzed using ImageJ to determine the percentage of actual bone present. CT, computed tomography.

Localization of CP Volume of Interest

Cadaver CT scans were windowed for optimal differentiation between CP bone and air. Digital Imaging and Communications in Medicine images were uploaded into OsiriX Lite imaging software version 9 (Pixmeo, Bernex, Switzerland).⁹ Two trained research personnel reviewed all scans and interclass correlation coefficients (ICCs) were confirmed as described below. Throughout the study, we analyzed a predefined segment of the posterior CP between the anterior and posterior ethmoid arteries (AEA and PEA, respectively). This provided a means to exclude the AEA and PEA foramina, which can be quite large and would impede our ability to detect changes in bone density and CP bone composition.⁵ Additionally, the posterior half of the CP has been reported to show changes in olfactory foramina, and the anterior portion of the CP is not as well defined with cadaveric dissection being hampered by the crista galli.¹⁰ The AEA and PEA were identified on coronal view and marked in the sagittal plane. Anterior measurements were recorded beginning 1 slice posterior to the AEA and extended to the posterior boundary 1 slice anterior to the PEA. As the length between the AEA and PEA is known to be approximately 12 mm, this length was approximated in order to identify the PEA in scans where it was difficult to identify.¹¹ Four sagittal slices were then integrated to create a volume of interest (VOI) of the right and left CPs as shown in Figure 3. All sagittal measurements were drawn to a height of 0.6 mm. Using the plugin software pyOsiriX 1.0.1, the raw voxel data from each VOI were exported and recorded in Microsoft Excel.¹²

Figure 3. Sample screenshots from Osirix software program demonstrating multiplanar imaging of CT and confirmation of anatomic localization of boundaries of CP sample. (a) The anterior–lateral boundary of the right CP segment with the outlined area demonstrating mean HU value, range, and length, and cross-sectional area. (b) The anterior–medial boundary of the right CP segment with similar information. The software then integrates intervening slices to create the volume of interest. HU, Hounsfield units; CP, cribriform plate; CT, computed tomography.

Radiographic Definitions of Tissue Types

In order to validate CT measurements of olfactory foramina, it was necessary to develop radiographic definitions for the 3 expected items found on CT—bone, neural/soft tissue, and air—and correlate Hounsfield units (HU) measurements with cadaveric assessments of bony composition. In CT scans, cortical bone typically has high values (up to 1000 HU or higher), air has low values (down to –1000 HU), while soft tissue is neutral (around 0 HU). We defined mean and standard deviation (*SD*) of neural/soft tissue based on measurements of a random sample of the frontal lobe of the brain on each CT. This sample served as a reasonable surrogate measure for other neural structures including olfactory nerve filaments. Bone voxels were then designated as voxels with HU values >2 *SD* above soft tissue. Air voxels were designated as voxels with HU values <2 *SD* below soft tissue (Figure 4).

Calculating Bone Density and Bone Composition of Olfactory Foramina

We calculated mean HU of VOIs as a surrogate measure of bone density. We calculated the percentage of bone composition using 2 methods. The first was using the number of voxels defined as bone divided by the total number of voxels in the VOI. Inevitably, this included some voxels defined as air. While air is often present in the foramina of cadavers, it should not be present in the CPs of live patients. In order to examine another method that may potentially translate to use in live patients, we used a second method to calculate the percentage of bone. We calculated the number of voxels defined as bone divided by the total number of voxels defined as bone or soft tissue, that is, removing all air voxels from the VOI. The results from both CT methods were correlated to the percentage of bone determined through cadaver dissection.

Figure 4. Sample graph of HU values for 333 individual voxels in a VOI. Soft tissue was defined as mean of frontal lobe of brain ± 2 SD. Bone voxels have HU values above soft tissue, while air voxels were those with HU values below soft tissue. HU, Hounsfield units; SD, standard deviation; VOI, volume of interest.

Statistical Analysis

Statistical analysis was performed using commercially available software applications (SPSS v24; IBM Corporation, Armonk, NY). Descriptive statistics are reported using mean and SD where appropriate. Raw voxel data were used to obtain HU for CT measurements. The mean of the independent measurements of the two raters was recorded. Pearson and Spearman correlation coefficients were calculated for parametric and nonparametric data, respectively. The ICCs and their 95% confidence intervals were calculated as a mean of $k=2$ raters, absolute agreement, two-way random effects model for volume, and mean HU.¹³

Results

The mean volume of the sampled segment of posterior CP was 7.2 mm³. Similar volumes were sampled by the independent reviewers, as we found an ICC of 0.96 (95% confidence interval: 0.080–0.99). After confirming reproducible anatomic selection, we then examined radiographic parameters. In sampling the frontal lobe of the brain to define neural/soft tissue, our mean HU was -22 ± 11 , and thus, “soft tissue voxels” were defined

as those with values between -44 HU and 0 HU. The mean HU of the CP when including all voxels in the VOI was 263.3 HU. This mean increased to 314.5 HU when cropping out “air voxels” defined as those less than 2 SD of soft tissue (< -44 HU). Similar radiographic data were obtained by both reviewers for mean HU of the VOIs with an ICC = 0.98 (Table 1).

While the mean HU of the CPs was between 0 and 1000 HU, indicating a mix of bone and soft tissue, it is difficult to understand the utility of these values as clinically meaningful measures of bone composition and olfactory foramina patency. We thus calculated the percentage of radiographic bone composition by categorizing voxels with a HU value > 2 SD of soft tissue as “bone voxels.” When examining the percentage of bone voxels out of the entire number of voxels in the VOI, the bone composition averaged 85.7% (range 76% to 96%). This estimate was within 7% of the actual measured bone composition for each CP. Anatomic and CT measures using this method correlated ($r = .691$, $P = .026$, Table 1). Using our second method in which we cropped or deleted all air voxels (< 2 SD soft tissue) led to a similar correlation with anatomic dissection ($r = .743$, $P < 0.05$). The percentage of bone estimated by CT

Table 1. Radiographic Measurements of the Cribriform Plate.

Cadaver dissection		All voxels in VOI			Air voxels cropped from VOI		
Specimen	Percentage of bone	Mean HU	Percentage of bone voxels	Difference from cadaver (%)	Mean HU	Percentage of bone voxels	Difference from cadaver (%)
1	74.1	198.1	76	−2	279.4	92	−18.1
2	85.3	362.0	89	−4	415.0	98	−12.4
3	88.3	155.1	85	3	188.4	94	−5.4
4	77.8	86.9	84	−6	117.9	92	−14.0
5	91.7	335.9	96	−5	341.3	98	−5.9
6	85.2	300.0	93	−7	307.5	94	−9.3
7	82.6	372.5	77	5	505.2	97	14.2
8	91.3	296.0	85	6	361.7	98	6.7
Average	84.5	263.3	85.7	−1.2	314.5	95.3	−10.7
Correlation to the percentage of cadaver bone		0.459	0.691*		0.266	0.743**	

Abbreviations: HU, Hounsfield units; VOI, volume of interest.

Interclass correlation coefficient means HU and 95% confidence interval: 0.98 (0.88–0.99).

* $P = .026$.

** $P < .05$.

varied from actual cadaver measurements by an average of nearly 11%, making direct clinical correlations challenging (Table 1).

Conclusions

Radiographic techniques offer unique, noninvasive methods to assess anatomy, particularly in areas such as the skull base. The importance of these methods has been demonstrated both in the anterior and lateral skull base in patients with SCSF leaks.^{1,2} Anatomic changes may predispose to development of spontaneous encephaloceles or even traumatic cerebrospinal fluid (CSF) leaks in certain locations and impact surgical repair. While measurement of the thickness of the ethmoid roof, planum, frontal sinus, and tegmen is relatively straightforward, the CP has natural olfactory foramina, necessitating the development of novel radiographic techniques to assess this area.

CT assessment provides 2 important pieces of information—first is that it reflects bone density and second is the potential absence of bone if an actual skull base defect or foramina is present. It can be imagined that both of these may factor into development of SCSF leaks in the CP, for example, through either existing olfactory foramina or bone that is relatively thin and with lower density. While we do not know the actual bone density of our cadaver specimens, and HU does not directly measure bone mineral content, previous studies have demonstrated that CT attenuation correlates with dual X-ray absorptiometry and that HU can serve as a surrogate measure for bone density.^{14–20}

In addition to measuring bone density, we developed novel radiographic methods to measure olfactory

foramina versus bone composition of CP. Prior studies have reported changes in olfactory foramina stenosis, but these studies required postmortem cadaver dissection.¹⁰ Olfactory foramina may not always be visible on standard CT scans of living patients due to slice thickness, resolution of reconstructed images, and small microforamina. Theoretically, calculations using integrated CT attenuation of VOIs would automate this process and overcome many of these limitations.

When comparing our results on bone composition of the CP and olfactory foramina with prior studies, there are several differences. Previous cadaver studies examining stenosis of olfactory foramina describe bony stenosis ranging from 22% to 48% of CP depending upon the age of the cadaver.¹⁰ This would correlate with 52% to 78% of CP consisting of olfactory foramina. In contrast, during our cadaver dissections, we found that 74%–91% of CPs were composed of bone, that is, 9%–26% of the CP consists of olfactory foramina. This seems to be consistent with clinical experience in that the majority of the CP is bone with a small portion consisting of neural foramina. Explanations for these contrasting findings may include variations in defining the anatomic region of the CP being studied. It is possible that prior studies included arterial foramina in their measurements and based upon our cadaver studies, these can be quite large and would lower estimates of bone composition.⁵ It is for this reason that we sampled a segment of the CP between the AEA and PEA. Additionally, prior cadaver studies may have included the anterior segment of the CP, and there may be variations in the foramina in that location.

Limitations of our study include lack of demographic and medical information on cadavers. The impact of sex,

race, age, medications, and other conditions is uncertain. Additionally, cadaver tissue undergoes tissue changes, including atrophy of soft tissue structures that affect both anatomic dissection findings, as well as radiographic characteristics that may limit the direct translational value to live patients. Finally, the clinical impact of anatomic changes in the CP remains an area for further investigation. The bone density of the CP and related risk factors such as vitamin D deficiency, race, female sex, older age, smoking history, medication use, and obesity could be assessed in future studies of spontaneous CSF leaks.

Declaration of Conflicting Interests

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