Skull Base Dural Thickness and Relationship to Demographic Features: A Postmortem Study and Literature Review

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Abstract

Keywords

- dura
- dural thickness
- cerebrospinal fluid
- spontaneous CSF leak
- idiopathic intracranial hypertension
- pseudotumor cerebri
- skull base

Dural membrane is an important anatomic structure that surrounds and protects the entire central nervous system. Physical properties of the dura have many pathophysiological and therapeutic implications in cranial surgery, especially skull base disorders. The aim of this study is to investigate variation in skull base dural thickness and correlation with different demographic parameters. At the time of autopsy, the petrous apex dura with the underlying bone of 20 cadavers was harvested. Dural thickness was independently measured by two pathologists at the thinnest and thickest segments in the specimen. Correlational analyses were then performed to compare dural thickness with gender, age, neck circumference, height, weight, and body mass index (BMI). Mean, minimum, and maximum skull base dural thickness in our study was 0.36, 0.27, and 0.46 mm, respectively. Age demonstrated a negative correlation with dural thickness with significantly thinner dura in the older subjects, $p = 0.01$. There was a trend toward thinner dura in females that approached statistical significance, $p = 0.06$. No strong correlation could be found with body weight, height, neck circumference, or BMI. Our findings show a considerable intersubject and intrasubject variability in skull base dural thickness. Some demographic parameters also seem to impact dural thickness. Additional histological studies are needed for better understanding of the pathophysiological mechanisms pertaining to the tensile properties of the dural membrane.

Introduction

The dura is the outermost and strongest of the meningeal layers enclosing the central nervous system. In addition to its structural role, the membrane possesses many physiological functions pertaining to central nervous system homeostasis, which

is made possible by the rich innervation and vasculature.^{1,2} The physical properties of the dura have been implicated in the pathogenesis of many neurosurgical and skull base disorders. Despite its importance, very little is known about the structural characteristics of the dura and its variability that can help explain the pathophysiology of disorders like idiopathic

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intracranial hypertension (IIH), idiopathic, as well as post-operative cerebrospinal fluid (CSF) leak. The aim of this study is to investigate possible associations between skull base dural thickness and demographic features for better understanding of spontaneous and iatrogenic skull base and CSF pathology. We hypothesize that high body mass index (BMI) and female gender (features of IIH) are associated with decrease in skull base dural thickness.

Materials and Methods

Subjects

Approval for this study was obtained through the University of Iowa Decedent Care Center autopsy services request for research materials. Institutional Research Board approval was not required for research purposes on anonymous deceased patients. Deceased patients undergoing full post-mortem examination at the Department of Pathology, University of Iowa Hospitals and Clinics were screened to exclude those with history of any head and neck or neurological disorders or perimortem trauma. Twenty sequential decedents undergoing full postmortem examination were enrolled. For all included subjects, we collected age, gender, height, weight, BMI (calculated), and neck circumference from medical records. After data collection, all subjects' identifiers were anonymized and replaced by a study-generated case number for analysis.

Specimen Preparation

At the time of autopsy, the dura overlying the mid portion of the right petrous apex of all decedents enrolled in the study was marked with India ink (red square, ►Fig. 1). This area of the dura along with the underlying bone was harvested with a bone saw. Specimens were preserved in 10% buffered formalin (Leica Biosystems Formaldehyde Solution) for a minimum of 24 hours. Upon adequate fixation, the specimens were then transferred to a decalcification solution (Stat Laboratory Decal Decalcifier). Once decalcified, a portion of the dura and underlying bone was trimmed and then embedded in paraffin, sectioned at 5 μ m, and stained with hematoxylin and eosin (Leica Biosystems).

Microscopic Measurements

Each paraffin block specimen was sliced and three representative slides were selected, out of which the slide with

best structural integrity and orientation was used for measurement. Two pathologists (M.P. and R.R.) independently performed microscopic examination and recorded both the minimum and maximum dural thicknesses (as measured from the inked surface of the dura to the surface of the underlying periosteum; ►Fig. 2). Measurements were made utilizing an ocular micrometer at 20 $\times$. The measurements of minimum, maximum, and mean dural thickness used in the analysis represented the average made by two of the investigators. Microscopic examination and measurements utilized Olympus BX51 optical microscopes (Olympus, Japan).

Statistical Analysis

Pearson's correlation coefficient was calculated to measure inter-observer concordance between the two measurements for dural thickness. The relationship between dural thickness (min, max, and average) and each of the demographic variables was then analyzed. Linear regression was used to test direct correlation between age, height, BMI, and neck circumference as continuous variables against minimum and maximum dural thickness assuming Gaussian distribution. Unpaired Student's *t*-test was used to test difference in genders as well as median-split variables including age, height, BMI, and neck circumference. Minimum dural thickness was used in the comparative analyses as a surrogate of risk of dural dehiscence. Statistical analysis was performed using GraphPad Prism (v7.00, GraphPad Software, La Jolla, California, United States).

Results

Measurements of dural thickness by two clinicians were highly correlated, with an r^2 of 0.98 and 0.99 ($p < 0.0001$) for the minimum and maximum values, respectively. The analysis omitted case number 20, whose minimum and maximum dural thickness measurements were substantially higher than the next largest value. When scrutinized, it was found that a preparation mishap resulted in oblique sectioning of the specimen and hence the erroneously higher readings. Specimens from 19 subjects were therefore included in the final analysis with mean age of 63.4 years. Nine of the subjects were females and 10 were males. Demographic characteristics of the study group are summarized in ►Table 1.

Mean dural thickness overlying the petrous apex in our series was 0.36 mm (standard deviation [SD], 0.16, standard error of the mean [SEM], 0.04). Minimum and maximum thickness were 0.27 mm (SD, 0.13, SEM, 0.03) and 0.46 mm (SD, 0.20, SEM, 0.04), respectively. There was significant intraspecimen variability seen denoting heterogeneity of the skull base dural thickness. Difference between minimum and maximum thickness encountered ranged between 0.0025 and 0.45 mm.

Age demonstrated a negative correlation with both minimum and maximum dural thickness. Older patients in our series were found to have a significantly thinner dura (►Figs. 3A and 4A; $p = 0.015$). Likewise, our data suggest a gender difference, where females exhibited lower dural thickness that was just short of statistical significance (►Fig. 4C;

Fig. 1 The dura overlying the mid portion of the right petrous apex of all decedents enrolled in the study was marked with India ink. This area of the dura along with the underlying bone was harvested with a bone saw.

Fig. 2 A demonstration of a relatively thick (left) and thin (right) dural specimens. Measurements were made utilizing an ocular micrometer at 20× spanning from the inked surface of the dura to the underlying periosteum.

$p = 0.06$). No direct correlation was identified between dural thickness and body weight, height, BMI, or neck circumference (►Figs. 3 and 4).

Discussion

Histopathological theory in idiopathic CSF leak entails ectopic arachnoid granulations within the dural lining of the cranial

fossae and internal table of the calvaria. The theory is supported by histological studies demonstrating arachnoid granulations penetrating the basal dura and petrous temporal bone.^{3–5} Another hypothesis, the intracranial pressure (ICP) theory, is based on high prevalence of elevated ICP among patients with spontaneous CSF leak, reports of patients developing IIH symptoms for the first time after repair of spontaneous CSF leak, and finally the resemblances in demographic,

Table 1 Demographic features and dural thickness measurements of the study group

Case	Age	Gender	Weight (kg)	Height (m)	BMI (kg/m ²)	Neck circumference (cm)	Observer 1		Observer 2		Dural thickness (mm)		
							Min	Max	Min	Max	Min	Max	Mean
1	61	F	113.9	1.53	48.2	20.00	0.225	0.350	0.250	0.300	0.238	0.325	0.281
2	63	M	55.3	1.70	19.1	14.75	0.300	0.700	0.275	0.675	0.288	0.688	0.488
3	90	F	80.7	1.67	28.9	16.00	0.150	0.290	0.150	0.275	0.150	0.283	0.216
4	41	F	89.4	1.63	33.3	18.00	0.430	0.700	0.400	0.675	0.415	0.688	0.551
5	69	M	127.9	1.70	44.2	17.25	0.225	0.230	0.200	0.225	0.213	0.228	0.220
6	77	F	53.5	1.65	19.6	11.13	0.250	0.410	0.250	0.400	0.250	0.405	0.328
7	68	M	125.6	1.85	36.5	21.75	0.180	0.425	0.175	0.450	0.178	0.438	0.308
8	50	F	49.9	1.70	17.2	16.90	0.250	0.420	0.225	0.425	0.238	0.423	0.330
9	70	M	100.2	1.74	33.1	18.25	0.280	0.500	0.200	0.500	0.240	0.500	0.370
10	60	M	87.5	1.75	28.5	17.00	0.520	0.530	0.525	0.550	0.523	0.540	0.531
11	57	F	81.6	1.62	30.9	19.00	0.130	0.180	0.150	0.150	0.140	0.165	0.153
12	65	F	43.5	1.62	16.5	11.50	0.300	0.330	0.225	0.325	0.263	0.328	0.295
13	61	M	98.4	1.88	27.9	17.50	0.470	0.475	0.500	0.500	0.485	0.488	0.486
14	77	F	59.0	1.67	21.0	13.00	0.200	0.370	0.175	0.375	0.188	0.373	0.280
15	49	F	69.9	1.54	29.1	14.00	0.220	0.325	0.225	0.300	0.223	0.313	0.268
16	44	M	70.3	1.67	25.0	15.00	0.335	0.650	0.325	0.650	0.330	0.650	0.490
17	77	M	63.5	1.67	22.6	18.50	0.080	0.200	0.100	0.250	0.090	0.225	0.158
18	64	M	108.4	1.72	36.3	22.00	0.180	0.420	0.150	0.425	0.165	0.423	0.294
19	61	M	87.5	1.65	32.1	19.50	0.560	0.980	0.500	1.000	0.530	0.990	0.760
20	64	M	192.3	1.85	55.9	24	1.125	1.250	1.100	1.250	1.113	1.250	1.181

Abbreviations: BMI, body mass index; F, female; M, male.

Fig. 3 Dural thickness correlation with demographic variables. Minimum and maximum dural thickness were plotted and analyzed against age (A), height (B), neck circumference (C), weight (D), and body mass index (BMI) (E) as continuous variables in a linear regression model.

Fig. 4 Minimum thickness comparatively analyzed among median-split groups. Dural membrane was found to be significantly thinner in the older age group, $p = 0.01$ (A). There was also a trend toward thinner dura in females that approached statistical significance, $p = 0.06$ (C). Neither body height (B) nor body mass index (BMI) (D) demonstrated a direct impact on dural thickness.

clinical, and radiological features between the two disorders.⁶⁻¹² Of the earliest experimental work first establishing the negative linear correlation between ICP and dural thickness was Kuchiwaki et al. The group first described the pathophysiological relationship in canines and later utilized their findings in developing an ultrasonographic technique to compute ICP based on dural thickness and sonographic features measured via an ultrasound probe held against the temporal bone.¹³

The growing evidence in support of the ICP theory has led clinical investigators to hypothesize a common pathological pathway for the two disorders with obesity playing a role, either triggering or propagating the pathological process.^{8,9} Stucken et al found a significantly higher BMI among patients with spontaneous middle cranial fossa encephalocele and CSF otorrhea.¹² Similar findings were observed by Seth et al

in 105 patients undergoing CSF leak repair having a mean BMI of 38.5 kg/m².¹¹ While the exact mechanism is yet to be delineated, it is postulated that chronically raised intraabdominal pressure secondary to obesity leads to increased intrathoracic pressure which impedes venous return from the brain and consequently results in chronically elevated ICP. The increased pulsatile ICP ultimately leads to erosion of both the dura and the underlying skull base resulting in dehiscence and CSF leak.⁷⁻¹⁰

In our literature search, we encountered different modalities utilized in assessing dural thickness. While histological analysis remains the gold standard, some prior reports used magnetic resonance imaging (MRI) fluid attenuation inversion recovery (FLAIR) sequences and ultrasound in estimating dural thickness.^{13,14} Reina et al published landmark paper on the histoanatomical microstructure of the

dura reporting a mean thickness of 0.322 mm with thickness variations along the neural axis. In their work, the authors described the dural membrane ultrastructure to comprise a large number of sublaminae formed of elastic collagen fibers organized in parallel planes, a robust construct that is still liable to degeneration when subjected to mechanical irritation or aging.^{15–17} Vandenabeele et al, in addition, described the dense fibrous layer to be enclosed within an outer loosely arranged fibroelastic layer and an innermost cellular layer.¹⁸

Prior studies in the literature investigating the dural properties have validated the variability in dural thickness in relation to subject characteristics and intracranial location. Willatt et al reported skull base dura to range from 0.72 to 0.88 mm and found that the tegmen middle cranial fossa dura was significantly thinner than frontal sinus, cribriform plate, anterior cranial fossa dura, and posterior cranial fossa dura.¹⁹ Histological cadaveric studies in human spine also found variability in dural thickness not just between different segments and levels of the spine but also between ventral and dorsal dura. Kwon et al studied cervical spine dura and found a significant negative correlation with age but no difference among genders in a cohort of nine cadavers.²⁰ In contrast, Hong et al examined dura specimens harvested from thoracic and lumbar spine from 19 cadavers and found a strong positive correlation with age and a thinner lumbar dura in women.²¹ Both studies, however, validated intraindividual variability in dural thickness which challenges the concept that the dura is a uniform rigid protective structure but rather a dynamic tissue that responds to mechanical stress and degenerative changes in its local environment.²² In contrast to the spine, cranial dura is characterized by two distinct layers (endosteum and meningeal layers), obliterated epidural space and its relative motionless structure which might explain a different response to aging. Cranial dura is also known to acquire firmer attachment to the skull with aging as evidenced by the lower incidence of epidural hematomas in the elderly. A combination of these histoanatomical features and the general effects of advancing age might explain our findings of decreased dural thickness with aging.

Our study based on sampling from one location at the petrous apex confirmed variability in dural thickness between subjects and to a lesser degree within the same patient. The sampling location was chosen overlying the petrous apex to ensure consistency and reproducibility as an anatomical landmark in the middle cranial fossa. Additionally, the location allowed for minimal postsampling visible effects on the decedent's appearance. We hypothesized that the demographic variables in question pose a systemic effect on dural thickness throughout the cranium; however, additional study of samples from a variety of skull base locations is necessary to test this hypothesis. In addition, the petrous apex is not a common location for spontaneous CSF leak unlike the tegmen tympani and cribriform plate. It is likely that additional local anatomical factors such as bone thickness and proximity to skull base cavities impact dural thickness; this study is not able to address these questions. Sampling from one location limited our ability

to study the anatomical in-subject variation in dural thickness across the cranium and skull base.

Correlational analysis of patient characteristics showed significant decrease in dural thickness with aging and a trend toward thinner dural membrane in females. Findings are in keeping with the well-known demographic features of IIH which also represent the demographic risk factors for post-operative CSF leak after skull base surgery.^{23,24} However, our study failed to identify any correlation between dural thickness and body habitus as demonstrated by weight, height, neck circumference, or BMI. Our study was limited by the small number of subjects which might have undermined a truly significant gender difference or correlation to body habitus. Our analysis was also underpowered to correct for confounder such as age and gender to elucidate if other demographic variables might influence dural thickness. Lastly, our study did not investigate additional demographic and patient-related variables such as ethnicity, nutritional status, medical comorbidities, organ failure, or prolonged illness which can influence tissue structures and protein turnover throughout the body. Identifying the correlation between these demographic parameters and bone thickness in the skull base is also needed for better understanding of disorders like spontaneous CSF leak. All limitations considered, our findings illustrate decreased thickness with aging and perhaps thinner dura in females at the skull base. Additional studies are needed to validate our findings in larger cohorts.

Conclusion

Factors affecting the structural integrity of the dural membrane and its variability remain poorly understood, but knowledge of these factors is important to the surgeon to avoid CSF leak complications after skull base surgery and gain better understanding of the pathophysiology of idiopathic dural dehiscence. Our study found a significant decrease in dural thickness with advanced age and suggests that female gender may be associated with thinner dura. Additional histological studies are needed for better understanding of the histopathology of the dural membrane.

Conflict of Interest

None.

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