OBJECTIVE: To evaluate the anatomic aspects of the diaphragma sellae and its potential role in directing the growth of a pituitary adenoma.

METHODS: Twenty cadaveric heads were dissected and measurements were taken at the level of the diaphragma sellae.

RESULTS: The diaphragma sellae is composed of two layers of dura mater. There is a remarkable variation in the morphology of the diaphragm opening. The average antero-posterior distance of the opening was 7.26 mm (range, 3.4–10.7 mm) and the average lateral-to-lateral distance was 7.33 mm (range, 2.8–14.1 mm).

CONCLUSION: The variability in the diameter of the opening of the diaphragma sellae could explain the growth of pituitary tumors toward the cavernous sinus or toward the suprasellar region.

KEY WORDS: Adenoma, Anatomy, Diaphragma sellae, Pituitary gland

The pituitary gland is located near the center of the head, supported by the sella turcica, at the cerebral surface of the body of the sphenoid bone. The diaphragma sellae forms the roof of the sella turcica (27). A combined wall of dura mater and bone protects the anterior, inferior, and posterior surfaces of the pituitary gland, whereas the lateral and superior portions are protected by dura mater only. The dural layer facing the lateral portion of the gland is single, but a double-layered dura covers all other surfaces. The diaphragm is the dural sheath that partially covers the superior surface of the gland, having a medial opening to transmit the pituitary stalk. There are several anatomic studies focusing on the dural walls of the cavernous sinus and sellae (3, 8, 9, 11, 24–28, 31, 33–35), but very little has been written about the diaphragma sellae (10, 12, 18). Furthermore, many articles have been written about identifying markers of pituitary tumor invasiveness (13, 14, 32) and many others have been written about magnetic resonance imaging diagnosis of pituitary tumor invasion (6, 7, 16, 17, 21), but no explanation exists regarding the reason why some tumors grow laterally toward the cavernous sinus and others grow superiorly toward the chiasmatic cistern. The aim of this study was to analyze the anatomic aspects of the diaphragma sellae that may have a potential role in directing the growth of sellar tumors.

MATERIALS AND METHODS

Twenty formalin-fixed, silicon-injected adult cadaveric heads were analyzed in this study. The brain and its skull covering were removed, exposing the skull base. The limits of the diaphragm were established as 1) anteriorly, the dural insertion at tuberculum sellae; 2) posteriorly, the dural insertion at the dorsum sellae; and 3) laterally, the point where the medial wall of the cavernous sinus meets its superior wall (Fig. 1). The measurements were taken with a caliper (accuracy 0.02 mm; Draper, Tokyo, Japan) (Fig. 2).

RESULTS

The diaphragma sellae is composed of two layers. Anteriorly, these layers form the dura mater that covers the sphenoid planum and the anterior cranial fossa. Posteriorly, they are continuous with the dura mater covering dorsum sellae and clivus. The superficial or meningeal layer is continuous laterally with the superficial...
layer of the roof and lateral wall of the cavernous sinus, the upper dural ring, and the optic sheath. The deeper or periosteal layer is continuous with the inner layer of the lateral wall of the cavernous sinus, the lower dural ring, and the periorbita (Fig. 3, A–D). The diaphragma sellae extends from the tuberculum sellae anteriorly to the dorsum sellae posteriorly. Laterally, its limits correspond to the area where the medial and superior walls of the cavernous sinus meet. In the center, the diaphragm has an opening through which the infundibulum courses, linking the pituitary gland to the floor of the third ventricle. The morphology of this opening is quite variable among individuals (Fig. 2; Table 1). On average, the anteroposterior distance of the diaphragm opening was $7.26 \pm 1.99$ mm, ranging from 3.4 to 10.7 mm. The lateral distance of the diaphragm opening was $7.33 \pm 2.79$ mm, ranging from 2.8 to 14.1 mm. The distance of the dural portion of the diaphragm anterior to its opening (between the opening and the insertion in the tuberculum sellae) was $1.89 \pm 1.49$ mm, ranging from 0 to 5.1 mm. The distance of the dural portion of the diaphragm posterior to its opening (between the opening and the insertion in the dorsum sellae) was $1.35 \pm 1.03$ mm, ranging from 0 to 2.8 mm. The distance of the dural portion of the diaphragm on the right side of its opening was $4.55 \pm 2.08$ mm, ranging from 1.3 to 8.8 mm. The distance of the dural portion of the diaphragm on the left side of its opening was $4.65 \pm 2.42$ mm, ranging from 0 to 8.2 mm. It is remarkable that the larger the diaphragm opening, the greater the amount of pituitary tissue in direct contact with the arachnoid of the chiasmatic cistern.

**Classification**

According to the results, the authors propose a classification of the diaphragma sellae according to the diameter of its opening:

- Group A: when the diameter of the opening is less than 4 mm (20% of the heads studied) (Fig. 3, A–D);
- Group B: when the diameter of the opening is between 4 and 8 mm (40% of the heads studied) (Figs. 1B and 2); and
- Group C: when the diameter of the opening is larger than 8 mm (40% of the heads studied) (Fig. 4).

**DISCUSSION**

The pituitary gland is located in the sella involved by dura mater. Its anterior, inferior, and posterior surfaces are surrounded by a double-layered dura mater and sellar bone, which represent a strong barrier to the expansion of a sellar tumor. In contrast, the lateral and superior surfaces of the
gland are covered only by dura mater, and both the lateral and superior walls have special features that can turn them into a less resistant path of growth to pituitary tumors. Different from all other dural coverings in the sellae, the dura covering its lateral walls, which comprise the sellar portion of the medial walls of the cavernous sinus, is formed by a single layer of dura (Fig. 5) (35).

The questions of why some pituitary adenomas present an aggressive course, and especially why some may grow toward the cavernous sinus, have generated many different hypotheses. Nevertheless, the factors involved in growth and invasiveness are not yet well understood (2). Much has been written about the value of cellular proliferation markers for the identification of subgroups of adenomas prone to invasiveness, including Ki-67, MIB-1, matrix metalloproteinase-9, and cathepsin B, with conflicting results (13, 14, 20, 32, 36–38). Some suggest that cavernous sinus invasion is more frequent in specific groups of adenomas, such as growth hormone-secreting tumors, but the results are inconclusive (13, 19). Yokoyama et al. (36) suggest a defective medial wall as the most probable reason for cavernous sinus extension. However, according to their work, these authors consider the cavernous sinus medial wall and the pituitary capsule to be the same structure. According to previous studies by our group, the pituitary capsule is a well-defined structure that involves the pituitary gland and is different from the medial wall (35). Other authors agree with this idea (5). Oldfield (23) proposed that the medial wall is pierced by veins that link the pituitary gland to the cavernous sinus, suggesting that these are susceptible points along these walls. Some reports support the notion that the medial wall is entirely

<table>
<thead>
<tr>
<th>Measurements</th>
<th>Average (mm)</th>
<th>Standard deviation (mm)</th>
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</thead>
<tbody>
<tr>
<td>Anteroposterior distance of the diaphragm opening (A–B)*</td>
<td>7.26</td>
<td>1.99</td>
<td>3.4–10.7</td>
</tr>
<tr>
<td>Lateral distance of the diaphragm opening (C–D)*</td>
<td>7.33</td>
<td>2.79</td>
<td>2.8–14.1</td>
</tr>
<tr>
<td>Distance of the dural portion of the diaphragm anterior to its opening (A–E)*</td>
<td>1.89</td>
<td>1.49</td>
<td>0–5.1</td>
</tr>
<tr>
<td>Distance of the dural portion of the diaphragm posterior to its opening (B–F)*</td>
<td>1.35</td>
<td>1.03</td>
<td>0–2.8</td>
</tr>
<tr>
<td>Distance of the dural portion of the diaphragm on the right side of its opening (C–G)*</td>
<td>4.55</td>
<td>2.08</td>
<td>1.3–8.8</td>
</tr>
<tr>
<td>Distance of the dural portion of the diaphragm on the left side of its opening (D–H)*</td>
<td>4.65</td>
<td>2.42</td>
<td>0–8.2</td>
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* See Figure 2.
absent (9, 15). In a dedicated anatomic study of the medial wall, including 44 cavernous sinuses, it has been observed that this wall is present and continuous in 100% of cases (Fig. 5) (35).

The variable size of the opening at the diaphragm sellae has been observed previously. Schaeffer (30) was one of the first authors to study the variations of the diaphragm opening. Busch (4), studying the anatomic aspects of 788 sellar regions, presented a comprehensive classification of the diaphragm sellae. In anatomic studies, Renn and Rhoton (25) and Bergland et al. (3) reported a diaphragm opening greater than 5 mm in diameter in 56% and 39% of all cases, respectively. A magnetic resonance imaging–based study demonstrated the ability to detail the diaphragm opening in 42.3% of the cases (22). This study showed that 20% of the cases have a diaphragm opening smaller than 4 mm, 40% have a diaphragm opening between 4 and 8 mm, and 40% have a diaphragm opening larger than 8 mm.

The role of the diaphragm opening in directing the power vectors along this area has been addressed previously (10, 12, 29). A similar rationale has been proposed to explain empty sellae syndrome (1, 4, 10, 27). In these cases, the presence of a competent diaphragm represents a barrier against the pulsatile action of the cerebrospinal fluid on the sellar contents. In Figure 4, it is possible to observe one specimen with a large opening of the diaphragm, an empty sellae, and lateral extension of the gland toward both cavernous sinuses.

Although there are many studies describing the anatomy around the sellae, none addresses the influence of the dural layers on the direction of growth of a pituitary adenoma. This article demonstrates, from an anatomic point of view, that the only one among the six sellar walls surrounding the pituitary gland that consistently varies with respect to structure is the superior wall, and that this variation depends directly on the size of the diaphragm sellae. Thus, although the diaphragm sellae is composed of two dural layers and theoretically is more resistant than the single-layered dura of the lateral surface of the gland, it presents the infundibular opening at its center, which can, at times—depending on its dimensions—be truly incompetent. The resistance of this sector is therefore dependent on the anatomic variant of the diaphragm opening presented in a given patient. Individuals with small diaphragm openings, which block the tumor enlargement superiorly,
would have this growth directed along the least resistant path, the sellar border with the cavernous sinus. Others, harboring large, incompetent diaphragm openings, would have superiorly directed tumor growth (Fig. 6).

CONCLUSION

The anatomic variability of the diaphragm opening, added to the special dural composition of the medial wall of the cavernous sinus, may explain the pattern of growth of pituitary tumors.

REFERENCES

This anatomical report focuses attention on the anatomy of the diaphragma sellae, whose variations in shape and dimensions could affect the direction of growth of a pituitary adenoma (a large opening of the diaphragma results in easier tumor growth toward the suprasellar area, whereas a small opening could lead to easier growth toward the cavernous sinus). Hence, the authors clearly support their hypothesis by providing two illustrative clinical cases.

As the authors state, although different factors could condition the growth pattern of pituitary adenomas, the size of the opening of the diaphragma sellae should be carefully evaluated preoperatively. Indeed, a small opening of the diaphragma sellae with a large suprasellar component of the tumor could lead the surgeon to consider the possibility of performing a different approach, such as a transcranial or an “extended” transsphenoidal route, has been recently proposed in selected patients, as an alternative to the transcranial route. With such an approach, by removing the tuberculum sellae and the posterior portion of the planum sphenoidale, coagulating the superior intercavernous sinus, and sectioning the diaphragma sellae, wide access to the suprasellar portion of the lesion can be gained. The diaphragma sellae is one of the structures directly involved in such approach and, therefore, knowledge of its anatomy and possibly related variations may play a role.

Luigi M. Cavallo
Paolo Cappabianca
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The authors carefully studied the anatomy of the diaphragma sella in 20 normal cadavers and demonstrated considerable variation in the dimensions of the diaphragm opening. Their hypothesis that the competency of the diaphragm and the size of its opening may determine the direction of pituitary tumor growth is intriguing but totally speculative. I did not appreciate the significance of the classification scheme, as it does not relate to any clinical or predictive data.

Marc R. Mayberg
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This article comes from a very distinguished dissection laboratory. The anatomic pictures are excellent as usual. However, there have been many previous articles describing the dural layers surrounding the sella and pituitary gland. The single and double layers are well known. In this article, the authors are trying to present a correlation with the direction that a pituitary adenoma may take in its growth pattern. It is reasonable to consider the possibility that there will be suprasellar growth if there is a large opening in the diaphragma sella. It is also logical to presume growth laterally into the cavernous sinus through areas of a single dural layer or along a vein, but there is no definitive evidence for this. The authors have not dissected specimens with adenomas to demonstrate that growth at all. It would be interesting to dissect adenomas that have expanded laterally in only one direction to correlate the anatomical defect. Why does the sella expand inferiorly into the sphenoid sinus if there is both a double layer of dura and bone? There is some speculation in this article as to how adenomas truly expand.

Kalmon D. Post
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This anatomic study, based on cadaveric dissections, joins a number of prior descriptions of the anatomy of the sella turcica, the dura of the sella, and the diaphragma sellae, specifically. These studies are necessary static in nature, and therefore the authors are unable to consider the dynamic nature of the sella, its contents, and the diaphragm, as these are modified by both physiological and pathological processes.

It has been well established by similar cadaveric studies that the diaphragm and the remainder of the sellar dura has 2 layers throughout most of its extent, although these layers may fuse, particularly along the lateral walls of the sella. It has also been established that the lateral dura may exhibit perforations, some of which may be related to vascular channels.

It is not surprising that this and other studies have demonstrated remarkable variation in the size of the diaphragmatic aperture. Although these variations may in some cases simply be normal anatomic anomalies, in many cases the variations are reflections of normal physiologic changes. For example, it is well known that the pituitary gland enlarges during pregnancy, occasionally doubling in size. The empty sella syndrome, with its large diaphragmatic aperture, is associated with multiparity. The pituitary gland regularly enlarges during puberty and in response to other physiological stresses.

Pathological conditions that can cause pituitary enlargement such as thyroid-stimulating hormone hyperplasia resulting from primary hypothyroidism are also capable of causing enlargement of the diaphragmatic aperture. Another mechanism for this phenomenon is chronic increased intracranial pressure, wherein the cerebral arachnoid herniates through the diaphragmatic aperture and enlarges within the sella, a finding that may be seen with suprasellar craniohypophysiomias that obstruct the foramina of Monro.

Other important changes in the diaphragm and the sellar dura occur in the setting of pituitary adenomas. Because of the anatomy of the sella, it is logical to assume that the path of least resistance for an expanding lesion within the sella would be upward, where the diaphragm is unsupported by bone. It is true, as the authors have noted, that the actual nature of the diaphragmatic capsule of pituitary adenomas that extend in the suprasellar region remains a matter of debate. Lateral extension of pituitary adenomas, or inferior extension into the sphenoid sinus, as is often seen in growth hormone-secreting macroadenomas, is most often a result of tumor invasion of dura and bone rather than being related directly to the sellar dura.

Our experience with endoscopic visualization of the sellar dura after removal of pituitary adenomas has demonstrated lateral tumor extensions through what appear to be pits of varying size in the dura. Additionally, we have regularly observed in patients with invasion of...
the cavernous sinus that the path of least resistance in early invasion appears to be a thin area of dura posterior to the carotid siphon in the posterolateral corner of the sella.

It is hoped that with a better understanding of both the static and dynamic aspects of the sella and its contents and further insights from endoscopic evaluation in patients, our knowledge and its clinical application will steadily increase.

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Edward R. Laws, Jr.
Stanford, California

The direction of growth of a pituitary adenoma is not well understood, but it is safe to assume that the determining factors are multiple and complex. In this study of 20 cadaveric specimens, Campero et al. have evaluated anatomic aspects of the sellar diaphragm and considered their potential influence on the vector of pituitary tumor growth, i.e., superiorly into the suprasellar cistern versus laterally into the cavernous sinus. Although several previous studies have described the anatomy of the sella, none have addressed the influence of the dural layers on the growth vector of a pituitary tumor. The authors’ conclusion that relative incompetency of the diaphragma sellae opening would be one of multiple determining factors is a reasonable speculation, perhaps even self-evident. However, there are numerous other potential factors to consider, such as histological type; with some tumors, such as growth hormone adenomas, showing a greater propensity for dural sinus invasion; site of origin within the pituitary gland, superior versus inferior versus lateral, and so on; variabilities in thickness of the dura itself, and in the case of tumors growing inferiorly, sellar floor and sphenoid sinus anatomy; and fibrous capsular formation around tumors. It is probably reasonable to speculate that all of these have some role. What remains for better illumination in future studies is determining the relative contributions of these multiple potential factors.

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In this detailed and well-illustrated anatomical study of the diaphragma sellae, the authors propose that variability in the size of the opening of the diaphragma sellae may explain the variable growth patterns of pituitary adenomas. As the authors acknowledge, this factor, however, may be only one of several dictating adenoma growth patterns, and their findings raise an interesting issue that remains unanswered. Specifically, after removing the suprasellar extension of a pituitary macroadenoma, the diaphragma sellae can typically be seen herniating into the sella. If 40% of individuals have a large dural diaphragmatic opening of more than 8 mm, then how is it possible to remove most large adenomas that have presumably grown through the diaphragma sellae without creating a large cerebrospinal fluid leak? Perhaps the growing adenoma causes a stretched and incompetent diaphragma sellae to fuse with the tumor pseudocapsule or the suprasellar arachnoid forming a relatively resilient barrier.

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