EDITORIAL

Craniopharyngioma classification

Stephen T. Magill, MD, PhD, 1 John A. Jane Jr., MD, 2 and Daniel M. Prevedello, MD 1

1Department of Neurosurgery, The Ohio State University, Wexner Medical Center, Columbus, Ohio; and 2Department of Neurosurgery, University of Virginia, Charlottesville, Virginia

Craniopharyngiomas (CPs) are among the most surgically complex brain tumors due to their deep location and intimate involvement with critical neural and vascular structures. Furthermore, injury to the adjacent hypothalamus, infundibulum, pituitary gland, optic apparatus, or vasculature can have devastating consequences including hypothalamic obesity, autonomic dysregulation, panhypopituitarism, blindness, and major strokes. Their location, arising from the sella up through the third ventricle, can be accessed via multiple surgical approaches. Broadly, the approaches include variants of the transcallosal, transsylvian, subfrontal, and endonasal approach, all of which are viable options for CP resection. Determining the ideal approach has been a source of lively debate among neurosurgeons for many years, and as such, several classification systems based on surgeon experience have been proposed, including the classification by Fan et al. in the current issue.1

The ideal classification system is one that would predict functional outcomes, extent of resection, and recurrence rates, based on tumor characteristics, patient anatomy, and approach. This would allow the neurosurgeon to select the approach that would provide the best outcome for each patient’s unique tumor. The first classification was put forward in 1990 by Gazi Yaşargil based on his microsurgical experience with 144 CPs (Table 1).2 His classification system was based on the relationship of the tumor with the surrounding anatomical structures, foremost of which were the diaphragma sellae, the tuber cinereum/floor of the third ventricle, and the third ventricle/hypothalamus. The primary challenge during this era was in preoperative diagnostic imaging to understand relationships of the tumor with these structures, because MRI was a relatively new technology at the time. Nevertheless, this anatomical relationship was key to guiding the surgical approach. The pterional approach was used most frequently by Yasargil because it allowed early identification of the stalk, anterior circulation, and protection of the optic chiasm. When tumors extended superiorly in the third ventricle, he would combine the pterional with a transcallosal approach. He used the transcallosal approach for tumors primarily involving the third ventricle and reserved transsphenoidal approaches only for intrasellar infradiaphragmatic (type A) tumors.

Additionally, the relationship between the optic chiasm and sella is important for approach selection, whether the chiasm was prefixed (over the tuberculum), over the middle of the sellae (normal), or postfixed (over the dorsum sellae).3 CPs that are considered prechiasmatic (postfixed) push the optic chiasm posteriorly and can be resected via a subfrontal approach, whereas those that are retrochiasmatic push the chiasm anteriorly toward the tuberculum sellae (prefixed), making a subfrontal approach more challenging because most of the tumor is covered by the optic apparatus.

During the mid- to late 1990s and early 2000s, advances in endoscopy and improved instrumentation spurred the development of expanded endonasal approaches.4 The development of the vascularized nasal septal flap provided a much-needed improvement in reconstruction techniques that had been hampered by postoperative CSF leaks,5 and allowed the expanded endonasal approach to be considered for CPs that extended supradiaphragmatically and even up into the third ventricle.6 As the endonasal approach matured and became effective for managing lesions that extended beyond the sella, a new classification system was needed to account for the expanded surgical access.

As the expanded endonasal approach developed, it was appreciated that the amount of additional exposure needed to access a tumor was determined by the relationship between the tumor and the infundibulum, which led Kassam and colleagues to develop their classification scheme that may be used to tailor the endonasal approach for resection of CPs (Table 1).7 Because the axis of the endonasal approach parallels the infundibulum, working below the optic chiasm, the position of the chiasm relative to the sella became less important than when coming from a transcerebral approach. Tumors with a preinfundibular location (type 1) benefit from a transplanum approach. Type II CPs...
are those that are transsphenoidal and grow within and along the axis of the infundibulum. They often extend into the third ventricle. In addition to a tranplanum approach, they benefit from resection of the floor of the sella, allowing the pituitary to be moved caudally. Type III CPs are retroinfundibular and are the most challenging, requiring additional inferior exposure and, often, mobilization of the pituitary gland in order to create a working corridor under the gland. These tumors often extend into the interpeduncular cistern and must be meticulously dissected from the cranial nerves and basilar apex, which will often require a posterior clinoidectomy and removal of the dorsum sellae. Type IV tumors are purely third ventricular, and although it is possible to approach them endonasally, most neurosurgeons find that transchoroidal or transalinear techniques are necessary for removal and optimal protection of the hypothalamus and pituitary stalk. Finally, this scale was expanded to include a type 0, defined as a purely sub-diaphragmatic CP, which typically expands the sella and can be resected via a standard endonasal transsphenoidal approach. 

It is into this landscape that Fan et al. add their experience and proposed classification system. Their contribution to the literature is important, because it represents the largest surgical experience with craniopharyngiomas in the modern era. The series is composed of only patients undergoing primary treatment with surgery, excluding those treated for recurrent tumors or also treated with radiotherapy, making their series very comparable to the Yaşargil series. Further, they thoughtfully report their outcomes and how their practice has evolved as the endoscopic endonasal approach has emerged as the workhorse approach for CP surgery in recent years. In addition to reporting outcomes, they propose a new classification system based on presumed tumor origin (Table 1). They classify tumors as “QST” types: infrasellar/subdiaphragmatic (type Q-CP); subarachnoidal (type S-CP); and pars tuberalis/third ventricle (type T-CP). They then compare outcomes between tumors resected via a transcranial approach and those resected via an endonasal approach. Importantly, they show that regardless of tumor type, visual outcomes were significantly better in the endonasal group compared to the transcranial group. For tumors they classify as type T-CP, they found improved hypothalamic status in the transcranial group compared to the endonasal group. In type Q-CP tumors, hypopituitarism was much more common with the transcranial group. Their mortality incidence of 2%–3% in both transcranial and endonasal groups reflects a marked improvement from Yaşargil’s 16% mortality rate, but still reflects the gravity of the disease and complexity of management, because most of the mortality is related to severe hypothalamic/pituitary axis dysfunction or surgical complications. With their aggressive surgical strategy, regardless of tumor QST type or approach, they achieved a 90% rate of gross-total resection, but this success is tempered by a 27%–35% rate of severe hypothalamic dysfunction or surgical complications. With their aggressive surgical strategy, regardless of tumor QST type or approach, they achieved a 90% rate of gross-total resection, but this success is tempered by a 27%–35% rate of severe hypothalamic dysfunction (author’s grade 3/4), a 50% rate of permanent diabetes insipidus, a 40% rate of new hypopituitarism, and a 4%–7% rate of meningitis.

The study by Fan et al. provides a large, modern series of outcomes with an aggressive surgical strategy for CP in the absence of radiotherapy. These results are important to present to patients when discussing management, noting the morbidity that accompanies this surgery-only strategy. With regard to classification systems, the proposed QST classification is a simplification of the Yaşargil classification (Table 1). Although type 0 (Kassam), type A (Yaşargil), and type Q (Fan) all describe subdiaphragmatic tumors, that is where the parallels end. The Kassam classification is fundamentally different in that it does not consider the extent of the tumor along the hypothalamic stalk corridor, but rather focuses on the relationship with the stalk, which guides the endonasal exposure. Furthermore, it seems challenging to apply the QST classification in a generalized manner given the subjectivity of determining tumor origin, particularly for type S-CP and T-CP tumors. And finally, the QST classification does little to inform surgical approach or planning, or to predict functional outcomes by surgical approach. Their finding that type T-CP tumors (pars tuberalis/third ventricle) have better hypothalamic outcomes when resected via a transcallosal approach is consistent with Yaşargil’s and our practice of using the transcallosal transchoroidal approach for purely third ventricular tumors, which allows better visualization and dissection of the tumor from the hypothalamic walls bilaterally. Similarly, for subdiaphragmatic tumors (type 0/A/Q), they find that a transcranial approach results in more hypopituitarism, which makes sense given that it is much easier to access the sella from below. In conclusion, it is not clear whether the proposed QST classification system will find usefulness in guiding surgical approach or predicting outcomes, particularly because it does not distinguish purely third ventricle tumors from those with a third ventricle extension. This is a critical weakness in the classification scale because tumors isolated to the third ventricle benefit from a transcranial approach, as shown.

### TABLE 1. Classification systems for CP

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<th>Yaşargil et al.</th>
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<td>Type A: intrasellar, infradiaphragmatic</td>
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<td>Type 0: sub- (infra) diaphragmatic</td>
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<td>Type B: intra- &amp; suprasellar, infra- &amp; supradiaphragmatic</td>
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<td>Type I: preinfundibular; type III: retro-infundibular, extends into the 3rd ventricle &amp; interpeduncular cistern</td>
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Type II: transsphenoidal

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Type 0: sub- (infra) diaphragmatic
again by the Fan data. Nevertheless, the findings of Fan et al. are important, strengthening the evidence for using the endonasal approach for most CPs.

The bane of CP surgery, ever since Cushing’s time, has been preserving functional outcome, specifically hypothalamic and pituitary function. Dysregulation of these important homeostatic systems is a leading cause of death for patients with CP and shortens the patient’s lifespan, with children having a standardized mortality ratio 17 times greater, and adults 3.5 times greater, than that of the general population.9 Although endoscopic endonasal surgery has reduced surgical morbidity for CP resection, we still need better outcomes for our patients. Adjuvant radiotherapy can improve outcomes for subtotally resected tumors and provide equivalent long-term survival, but less morbidity compared to gross-total resection alone.10 Nevertheless, the specific circumstances in which subtotal resection should be pursued remain undefined. Edema in the hypothalamus is associated with greater hypothalamic dysfunction and may be a useful preoperative marker to guide surgical strategy, with extra caution being taken at the tumor–hypothalamus interface, and consideration for leaving adherent tumor to preserve function. 11 Molecular therapy with BRAF V600E inhibition for papillary CPs is promising,12 but no such option exists for the more common adamantinomatous group. Future studies should consider strategies for better identification of the stalk in surgery, which remains a challenge even in experienced hands. Perhaps targeted fluorescent molecules could be used in surgery, or targeted gadolinium tracers could be used for preoperative planning to identify the stalk position. Until improved medical options arrive, surgery will remain a mainstay of treatment and neurosurgeons must continue striving to perform the most complete, function-preservation resection possible.

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References


Disclosures

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Correspondence

Daniel M. Prevedello: daniel.prevedello@osumc.edu.

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Response

Jun Fan, MD, PhD, and Songtao Qi, MD, PhD
Department of Neurosurgery, Nanfang Hospital, Southern Medical University, Guangzhou, China

We would like to thank Dr. Magill and his colleagues for their interest and insightful comments regarding our study, and the editor for allowing us the opportunity to respond.

All CPs in our institution were identified as Q, S, or T types based on preoperative imaging, and the classification was validated by intraoperative morphological observation and histological investigation based on each individual case in our institution.1,3 It seems inevitable that some tumors exhibiting similar imaging appearances could be difficult to classify in any classification system. In our experience, most CPs can be distinguished between Q, S, and T types according to characteristic radiological features, such as the size of pituitary fossa, the relationship between tumor and stalk/gland, the morphology and tumor extension, and the displacement or involvement of surrounding neurovascular structures. Specifically, T-CPs extend mainly upward to the third ventricle and present with hypothalamic involvement. The lower segment of the pituitary stalk can often be identified on MRI. S-CPs tend to extend among multiple subarachnoid cisterns. The entire stalk can usually be recognized on MRI. Q-CPs arise from the subdiaphragmatic intrasellar space. Typically, MRI shows an enlarged pituitary fossa and the gland is scarcely recognizable. Also, preoperative clinical presentation and endocrine results provide additional evidence.
for the identification of tumor type due to different impacts of each tumor type on the hypothalamic–pituitary axis associated with a different tumor origin.¹

Nevertheless, it should be noted that our classification system was established based on more than 1000 consecutive surgical cases, which means that the precise classification by preoperative imaging requires considerable experience and a relatively long learning curve for the understanding of CPs. Future imaging innovations, including preoperative identification of the hypothalamic nucleus and fiber tracts on higher-resolution MRI, may facilitate the classification in a more generalized manner and reduce the confusion between tumor subtypes.

Unlike other classifications of CPs,⁴–⁹ our QST classification system lays emphasis on the tumor origin and its relationship with surrounding membranous (dura, diaphragma, arachnoid, and pia) and neurovascular structures.¹⁰–¹³ Specifically, Q-CPs arise inside the sellae, and severe adhesion often exists between the tumor and residual pituitary gland. Thus, preoperative early, severe hypopituitarism occurs commonly in patients with this type of tumor. The major challenge for tumor resection is how to totally remove the intrasellar tumor while preserving the residual gland as much as possible. The suprasellar portions of these tumors, however, are separated from the hypothalamus by several membranous layers (diaphragma, basal arachnoid membrane, and bundles of trabecular arachnoid), and are easy to dissect even for those tumors with significantly suprasellar extension. Accordingly, we can predict excellent postoperative hypothalamic status despite the worst endocrine outcomes in patients with Q-CPs among all 3 tumor types. Taking these findings together, we advocate endonasal surgery for most Q-CPs, except for those with extremely suprasellar extension beyond the scope of the endonasal approach.

S-CPs typically originate from the middle-lower segment of the pituitary stalk, and the hypothalamus and gland are usually not involved. Therefore, severe adhesion is commonly found between the tumor and stalk, and dissection with maximized stalk preservation will be challenging. By contrast, the hypothalamus is separated from the tumor by bundles of trabecular arachnoid; thus, the hypothalamus can be well preserved during dissection, even in tumors with significantly ventricular extension. Given these findings, we can predict the best endocrine outcomes and good postoperative hypothalamic status in patients with S-CPs. Theoretically, the endonasal approach is superior to the transcranial approach for this type of tumor, due to less brain retraction and better visual outcomes. However, a considerable number of S-CPs tend to occupy multiple cisterns beyond the scope of the endonasal approach because of their subarachnoidal origin, which is different from T-CPs or Q-CPs. Therefore, we suggest that endonasal surgery could be indicated for S-CPs not widely involving multiple cisterns.

T-CPs originate from the top of the pars tuberalis with mainly upward ventricular extension, and they present with varying degrees of hypothalamic involvement. In contrast, the lower segment of stalk and pituitary gland usually remain intact. This theory may possibly explain why preoperative hypothalamic dysfunction is more common, but preoperative panhypopituitarism occurs rarely in T-CPs. Similarly, we can predict the worst prognosis of postoperative hypothalamic status in T-CPs due to the involvement of the hypothalamus. In addition, we found better postoperative hypothalamic function when T-CPs were removed by craniotomy than by endonasal surgery, especially in those tumors extending significantly upward and occupying the entire space of the third ventricle, and this is probably attributable to less preservation of the hypothalamus associated with limited surgical freedom of endonasal surgery. Therefore, we advocate the endonasal approach for T-CPs of moderate size, whereas the transcranial approach should be used for large tumors with significantly ventricular extension. Nevertheless, future study with a larger sample size and a modified scale for hypothalamic status is still required to evaluate the impact of the surgical approach on postoperative hypothalamic function in T-CPs.

In summary, the QST classification system helps to improve our understanding of the morphological features and growth patterns of CPs, as well as their real relationships with the hypothalamic–pituitary axis. Based on an improved understanding of the tumor, we could gain useful information for approach selection, surgical planning, or the prediction of hypothalamic–pituitary outcomes on the basis of surgical approach.¹⁴–¹⁷ However, it should also be noted that the incidence of CP is relatively low compared with other intracranial tumors, which means the study samples are small in most neurosurgical institutions, and therefore thoughtful studies regarding the tumor remain sparse. Future studies including innovative molecular imaging techniques may improve our understanding of tumor origin and the relationship between the tumor and hypothalamic–pituitary axis, and thereby better inform preoperative surgical approach or planning by tumor classification.

References


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