Indicators of a Reduced Intercarotid Artery Distance in Patients Undergoing Endoscopic Transsphenoidal Surgery

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Abstract

Objective To identify clinicopathologic factors associated with a reduced intercarotid distance (ICD) and subgroups at risk for internal carotid artery injury during transsphenoidal surgery.

Design A retrospective case-control study.

Setting This study was conducted at the McGill University Health Centre, a university-affiliated tertiary care center.

Participants Patients with a sellar or parasellar tumor and nontumor controls were included in the study.

Main Outcome Measures The smallest distance between the internal carotid arteries at the clival, cavernous, and paraclinoid segments on coronal magnetic resonance imaging was measured. Demographic profiles, cephalometric measurements, tumor dimensions, and sphenoid configuration were assessed as potential determinants of the ICD.

Results A total of 212 cases and 34 controls were analyzed. Widening of the ICD at the three segments of the internal carotid arteries was found in patients with pituitary macroadenomas ($p < 0.01$). Patients with a growth hormone-secreting adenoma had a markedly reduced ICD at the clivus compared with controls (1.59 cm versus 1.77 cm; $p = 0.02$; 95% confidence interval [CI], 0.03–0.32). The paraclinoid ICD was reduced in patients with an anterior fossa meningioma (1.24 cm versus 1.33 cm; $p = 0.04$; 95% CI, 0.01–0.45).

Conclusion Identifying clinicopathologic factors affecting the ICD can help surgeons recognize constraints to endoscopic access of the skull base and avoid inadvertent arterial injury.

Keywords

- skull base surgery
- intercarotid distance
- pituitary adenoma
- meningioma

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Introduction

The endoscopic transsphenoidal approach to the central skull base combines minimally invasive access with decreased postoperative complications and improved patient comfort.¹ A substantial degree of anatomical variation is known to exist at the level of the sphenoid sinus and sella turcica.^{2,3} The internal carotid arteries (ICAs), optic nerves, cavernous sinuses, and surrounding cranial nerves are all vulnerable during this approach. Preoperative imaging of the central skull base is imperative to recognize these anatomical variations. The most essential during midline approaches is the intercarnitid distance (ICD).¹ This distance represents the varying span between the ICAs, particularly as they transition from petrous, lacerum, and cavernous to the clinoid segments. The course of the ICA delineates the entire lateral limits of the operative window into the central skull base. In consequence, a reduced ICD can significantly affect the extent of tumor resection possible, specifically lesions with clival, suprasellar, or lateral extensions.^{1,4}

Several studies on the anatomical variation in the sphenoid sinus, sella, and surrounding neurovascular structures have emphasized the importance of identifying midline landmarks during endoscopic transsphenoidal surgery.^{1,5} This strategy is used intraoperatively as a guide for skull base surgeons to decrease the risk of inadvertent neurovascular injury.⁶ In addition to common anatomical variations, neoplastic growth can cause morphological changes within the sella; expansion and erosion can distort surrounding structures.⁵ Ebner et al demonstrated a statistically significant reduction in the ICD at the superior portion of the carotid canals in patients with acromegaly and in patients with systemic hypertension,⁶ whereas an increased ICD is not infrequently observed in patients with pituitary macroadenomas.^{1,5,7,8} There may also be differences in the ICD based on ethnicity.^{7,9} In effect, both common anatomical variants and pathologic processes contribute to the variation within the central skull base. The proper localization of the ICA pre- and intraoperatively is critical to decrease neurovascular injury during surgery.^{6,10} An understanding of such factors can allow skull base surgeons to better evaluate the variability in the course of the ICA as well as the surgical window into the central skull base.

Few studies have integrated the effect of both developmental and pathologic factors on variations in the ICD.¹¹ In this study, we measured the ICD in both a normal cohort and a variety of common central skull base pathologies, based on preoperative computed tomography (CT) and magnetic resonance imaging (MRI). Furthermore, we studied demographic profiles, common anatomical variations, and pathologic features as potential indicators of a reduced ICD.

Methods

Study Design

A retrospective case-control study of consecutive patients from the McGill University Health Centre (MUHC) and Jewish General Hospital (JGH) undergoing endoscopic endonasal

resection of sellar or parasellar mass from January 2006 to December 2013 was performed. A concomitant cohort of patients undergoing CT and MRI during the same time period who were found to have a normal study was also included. The objectives of the study were to measure the ICD in these populations at the clival, cavernous, and paraclinoid segments and to identify clinicopathologic factors associated with a reduced ICD. We used CT and MRI to assess the ICD at each segment, tumor size, obtain cephalometric dimensions, and determine sphenoid configuration. The ICD was also measured by CT angiography (CTA) in the control group to allow for optimal radiologic assessment of the ICD.¹² In doing so, a comparison of the ICD could be made between CTA and MRI, validating measures taken by the latter modality. The interpretation of CT, CTA, and MRI was performed independently by two of the authors (M.M. and R.F., a fellowship trained neuroradiologist). The research protocol was approved by the university institutional review board.

Patient Population

Patients undergoing endoscopic transsphenoidal resection of a pituitary adenoma, Rathke cleft cyst, craniopharyngioma, meningioma, or chordoma were included in the study. Those with a previous history of skull base or sinus surgery were excluded due to possible altered anatomy, as were patients with unavailable preoperative MRI or CT imaging. The control group consisted of adult patients seen at the MUHC or JGH during the same time period who underwent imaging for suspicion of carotid artery dissection but were found to have a normal CT and MRI. In addition, these patients were also required to have a normal head CTA.

Clinicopathologic Factors and Intercarnitid Distance Measurements

The ICD was measured as the smallest distance between the medial part of the ICA flow void on T2-weighted coronal MRI at the clival, cavernous, and paraclinoid segments. T2-weighted coronal MRI views with a 2-mm thickness per slice and interslice gap were used. For CT imaging, the views consisted of 1-mm-thick slices in the axial plane. For CTA, the slice thickness was 0.625 mm. The clival ICD was measured along the segment of the ICA after exiting the carotid canal inferiorly and before entering the cavernous sinus superiorly (►Fig. 1A). This corresponded to the smallest distance between the medial walls of the ICAs at the C3 or proximal (ascending) portion of the C4 segment of the ICA. The cavernous ICD was measured where the ICA courses through the cavernous sinus (►Fig. 1B). For the paraclinoid ICD, its measurement was taken along the supracavernous segment of the ICA after exiting the cavernous sinus and before branching into cerebral arteries (►Fig. 1B). This level corresponded to the C5 and C6 segments of the ICA. Medical charts were reviewed for demographic profiles including age, gender, body mass index (BMI), and comorbidities as well as the histologic diagnosis of the resected tumor.

T2-weighted MRI was used to measure the maximal tumor size in the transverse, cranio-caudal, and anteroposterior planes for cephalometric dimensions; the anteroposterior

Fig. 1 The intercarotid distance (ICD) as illustrated on T2-weighted coronal magnetic resonance imaging in a patient with a pituitary macroadenoma. (A) Clival ICD. (B) 1, paraclinoid ICD; 2, cavernous ICD.

diameter was measured as the maximal midline distance from the frontal to the occipital bones on axial CT.^{13,14} The bifrontal diameter was defined as the transverse distance, from the outer limits of skull, at the highest slice of the spur that the sphenoid wing was still observed on axial CT.^{13,14} The biparietal distance was the maximal distance between the outer limits of parietal bones at the level of the third ventricle where the cochlea was seen on coronal CT.^{13,14} We characterized the sphenoid sinus using CT imaging based on three categories: degree of pneumatization, presence of Onodi cells, and septal configuration. The degree of pneumatization was based on the level at which pneumatization occurred in the sphenoid body past the vertical plane created by the tuberculum sellae and the floor of the sella on midsagittal CT. The sellar type was pneumatized past the previously mentioned plane, extending into the body of the sphenoid while the presellar type did not. The conchal type had no pneumatization of the sphenoid body whatsoever.^{1,15} Onodi cells were present if pneumatization of the posterior

ethmoid cells into the sphenoid sinus was seen on axial or coronal CT. We also classified sphenoid septal configuration as described by Schwartz et al into two categories: simple or complex.¹ A simple septal configuration was defined as “no septation, one vertical septation, or two symmetrical vertical septations creating a tripartite sinus.” A complex septation was “two asymmetric vertical septations, three or more septations of any type, or any horizontal septations.”^{1,9}

Statistical Analysis

Clinicopathologic factors were analyzed among cases and controls using the unpaired Student *t* test and linear regression analysis. A value of $p < 0.05$ was considered statistically significant. Comparison of the ICD measured by MRI and CTA in the control group was evaluated by the Bland and Altman method. The interobserver variability for radiologic data collected in a subset of patients was compared among the two reviewers using the intraclass coefficient. A value > 0.8 was considered to indicate agreement.¹⁶ All data were

computed using the statistical calculator MedCalc, v.12.3 (MedCalc Software, Ostend, Belgium).

Results

A total of 257 patients who underwent transsphenoidal surgery and 34 controls were reviewed. Overall, 25 cases were excluded due to unavailable CT or MRI of the sella; another 20 patients were excluded because of past transsphenoidal surgery or functional endoscopic sinus surgery (→Fig. 2). Of the remaining 212 cases, 76% of patients (161) underwent surgery for a pituitary adenoma, 107 of which were nonfunctional adenomas. Those with a functional pituitary adenoma were further divided into: adrenocorticotrophic hormone (12), gonadotropin (3), growth hormone (25), prolactin (13), and thyroid-stimulating hormone (1). Other pathologies reviewed were of patients undergoing surgery for a craniopharyngioma (9), Rathke cleft cyst (17), anterior fossa meningioma (22), or clival chordoma (3).

→Table 1 shows the demographic profiles of the case and control groups. There was no statistical difference in age, gender, or BMI between the two groups. Both case and control patients had a similar prevalence of arterial hypertension and type 2 diabetes mellitus. The average clival, cavernous, and paraclinal ICD for control patients was 1.77 cm, 1.73 cm, and 1.33 cm, respectively. For the entire tumor cohort, the mean ICD at the corresponding segments was 1.89 cm, 1.89 cm, and 1.49 cm, respectively. The clival and paraclinal ICD were significantly wider in the case group than in controls (1.89 cm

Fig. 2 Selection of case patients. Breakdown of pathologies analyzed. CT, computed tomography; MRI, magnetic resonance imaging; TSSx, past transsphenoidal surgery or functional endoscopic sinus surgery.

Table 1 Patient characteristics

Patient characteristics	Cases	Controls	p value
Study size	212	34	
Demographic profile			
Age, yr	52.9 (± 14.3)	51.6 (± 17.1)	0.63
Gender (%)	115 (54)	18 (53)	0.9
Body mass index	29.9 (± 8.7)	26.7 (± 6.8)	0.26
Comorbidity (%)			
Arterial hypertension	74 (35)	8 (24)	0.28
Diabetes mellitus type II	25 (12)	3 (9)	0.84
Cephalometric dimensions			
Anteroposterior diameter	18.1 (± 0.9)	17.9 (± 0.8)	0.18
Bifrontal diameter	11.2 (± 0.6)	11.1 (± 0.6)	0.14
Biparietal diameter	13.9 (± 0.6)	13.7 (± 0.7)	0.29
Sphenoid configuration (%)			
Onodi cells	36 (17)	6 (18)	0.9
Septation, complex	40 (19)	9 (26)	0.42
Degree of pneumatization			
Conchal	2 (1)	0 (0)	
Presellar	23 (11)	3 (9)	0.86
Sellar	187 (88)	31 (91)	

Note: ± denotes a standard deviation.

versus 1.77 cm; $p = 0.04$; 1.49 cm versus 1.33 cm; $p = 0.01$, respectively).

► **Table 2** lists the association between sellar pathology and ICD among the cases. Patients with a pituitary macroadenoma were found to have a widened ICD at the three segments compared with controls (clival, cavernous, and paraclinoid ICD measured 1.97 cm, 2.02 cm, and 1.57 cm, respectively; $p < 0.01$). Patients diagnosed with a growth hormone (GH)-secreting adenoma had a reduced ICD at the clival segment compared with controls (1.59 cm and 1.77 cm, respectively; $p = 0.02$). The average tumoral dimensions for patients with a GH-secreting adenoma in the craniocaudal, transverse, and anteroposterior planes was 1.99 cm, 2.01 cm, and 1.86 cm compared with 2.67 cm, 2.48 cm, and 2.42 cm, respectively, for patients with a non-GH-secreting pituitary adenoma ($p < 0.01$). A potential trend for a reduced cavernous ICD was seen in patients with a pituitary microadenoma, although statistical significance was not reached ($p = 0.08$). Furthermore, patients with an anterior fossa meningioma had a reduced paraclinoid ICD compared with controls (1.24 cm versus 1.33 cm, respectively; $p = 0.04$).

A linear correlation between the transverse diameter of a pituitary macroadenoma and the ICD at all three segments was found, particularly at the cavernous segment ($r = 0.58$; $p < 0.001$; ► **Fig. 3**). There was no difference in the ICD among patients with arterial hypertension. As for cephalometric dimensions, a trend for a reduced ICD in patients with a smaller bifrontal diameter was noted, although statistical significance was not reached ($p = 0.07$; ► **Fig. 4**). The sphenoid sinus configurations between the two groups were not related to the ICD.

In the control group, the ICD measured by MRI was compared with measurements taken by CTA using the Bland and Altman method. The vast majority of data points on the Bland and Altman plot were within the 95% confidence interval. A slight bias for smaller measurements of the ICD using MRI was noted. The mean bias between the ICD measured by CTA and MRI was +0.01 cm at the clival, -0.05 cm at the cavernous, and -0.04 cm at the paraclinoid segments. The interobserver variability as assessed by the intraclass coefficient for ICD, cephalometric dimensions, tumor size, and sphenoid configuration were all > 0.9 .

Discussion

In this study, we sought to identify clinicopathologic factors associated with a reduced ICD. This is the first study that has measured and correlated the ICD in both normal subjects and those with central skull base tumors, comprehensively assessing both normal anatomical variations and features related to the underlying pathology. The identification of factors associated with a reduced ICD can help stratify risk during endoscopic transsphenoidal surgery.^{6,17} A narrow ICD diminishes the operative window to the sellar region, consequently limiting the extent of tumor resection or waiving the endoscopic endonasal approach altogether. The radiologic measurements we obtained by CT and MRI of the ICD, as well as the cephalometric dimensions and sphenoid configuration, are in

Table 2 The intercarotid distance in controls and cases as classified by pathology

ICD	Prolactin		Growth hormone		ACTH
Clival	1.94 (1.80-2.08)	$p = 0.03$	1.59 (1.51-1.67)	$p = 0.02$	1.86 (1.66-2.06)
Cavernous	1.99 (1.73-2.25)	$p = 0.10$	1.59 (1.44-1.74)	$p = 0.17$	1.71 (1.58-1.84)
Paraclinoid	1.34 (1.18-1.50)	$p = 0.88$	1.50 (1.42-1.58)	$p = 0.01$	1.19 (1.09-1.29)
ICD	Craniopharyngioma		Meningioma		Rathke cleft cyst
Clival	1.84 (1.58-2.00)	$p = 0.46$	1.74 (1.61-1.87)	$p = 0.94$	1.93 (1.64-2.20)
Cavernous	1.67 (1.40-1.94)	$p = 0.69$	1.76 (1.52-2.00)	$p = 0.09$	1.85 (1.55-2.15)
Paraclinoid	1.32 (1.11-1.53)	$p = 0.95$	1.24 (1.21-1.27)	$p = 0.04$	1.52 (1.28-1.76)
ICD	Controls		Pituitary adenoma		Macroadenoma
Clival	1.76 (1.68-1.84)	1.89 (1.83-1.95)	$p = 0.04$	1.97 (1.91-2.03)	$p = 0.01$
Cavernous	1.73 (1.61-1.85)	1.92 (1.84-2.00)	$p = 0.03$	2.01 (1.92-2.10)	$p = 0.01$
Paraclinoid	1.33 (1.27-1.39)	1.51 (1.44-1.56)	$p = 0.01$	1.57 (1.51-1.63)	$p = 0.01$

Abbreviations: ACTH, adrenocorticotropic hormone; ICD, intercarotid distance.

Fig. 3 Transverse tumor size and cavernous intercarotid distance (ICD) in pituitary adenoma patients. A linear correlation between transverse tumor size and cavernous ICD was found in patients with a pituitary adenoma.

keeping with the literature.^{2,5,7,18} Most of the patients with a sellar or parasellar tumor were found to have an increased ICD at the three segments compared with controls, likely secondary to disease-related mass effect. However, patients with a GH-secreting pituitary adenoma or an anterior cranial fossa meningioma had a reduced clival and paraclinoid ICD, respectively.

Our finding of a reduced clival ICD in patients with a GH-secreting pituitary adenoma was previously reported.⁶ In contrast to previous studies, we found that the smallest distance between the ICAs in this region extends beyond the carotid canals into the clival segment of the ICA, causing a restraint on access to the clivus during transsphenoidal surgery. The mechanism behind a reduced clival ICD in these patients can possibly be explained by structural changes in the arterial walls due to the systemic effects of chronic acromegaly.¹⁹ Specifically, thickening of the tunica media in

the walls of the ICA has been associated with long-standing acromegaly, independent of insulinlike growth factor 1 expression.¹⁹ The effect of an increased ICA wall thickness could be one contributing factor to the narrowing of the distance between the ICAs. It nevertheless remains unclear why only the clival ICD was found to be reduced. Furthermore, morphological differences in both the sphenoid bone and sinus due to acromegaly may also influence the ICD.²⁰

The ICD in patients with anterior cranial fossa meningiomas was not previously reported in the literature. Based on our series, most of the meningiomas originated from a paramedial position along the planum sphenoidale. It is possible that growth of the tumor medially causes compression of the surrounding clinoid ICA, reducing the ICD at this segment (**Fig. 5**). Local disease-related changes in bone erosion may also contribute to this effect.²¹ Nonetheless, only a small absolute difference was found between the paraclinoid ICD in these patients compared with controls. Further investigation in a larger cohort of meningiomas is required to further elucidate the mechanisms by which ICD is affected.

A linear correlation between the transverse tumor size of pituitary macroadenomas and the cavernous ICD was found in our study. This is likely secondary to the mass effect splaying the ICAs in patients with large sellar tumors. As would be expected, patients with a microadenoma did not have a widening of the ICD compared with normal subjects. It is probable that patients with a pituitary adenoma likely have a comparable ICD compared with normal subjects.

The interobserver variability in the interpretation of CT, MRI, and CTA by intraclass coefficient was > 0.9 , indicating substantial agreement. Moreover, the comparison of the ICD by CTA and T2-weighted MRI in control patients showed a significant similarity using the Bland and Altman method. In fact, measurements by MRI were within 3% of those obtained by CTA. Given that CTA provides optimal resolution of the ICA

Fig. 4 Bifrontal diameter and clival intercarotid distance (ICD) in pituitary adenoma patients. Linear trend between the bifrontal diameter and clival ICD in patients with a pituitary adenoma.

Fig. 5 Anterior cranial fossa meningioma. Paramedial origin of an anterior cranial fossa meningioma causing compression of the paraclinoid internal carotid artery.

and that a high level of correlation between the two modalities was established, the measurements of the ICD on T2-weighted MRI of the sella can provide an accurate estimate of the ICD at the central skull base based on our results.

An inherent limitation to the study lies in its retrospective nature. Cases were selected based on patients undergoing endoscopic transsphenoidal surgery; those undergoing an alternative approach to the sella or managed medically were not included. In addition, the numbers in some subgroups are small. Also, given that measurements of the ICD taken by T2-weighted MRI produced results smaller than CTA, it is possible that the ICD could have been underestimated, causing a falsely reduced ICD. However, because MRI was used in both cases and the controls and with a maximal mean bias of 0.05 cm, it is unlikely that a significant underestimation of the ICD occurred.

Conclusion

Patients with a GH-secreting pituitary adenoma were found to have a reduced ICD at the clival segment. Identifying these patients can help surgeons recognize constraints imposed by a reduced ICD to endoscopic access of the skull base and avoid inadvertent ICA injury. A prospective study is needed to better characterize the association between a reduced ICD and increased perioperative complications during transsphenoidal surgery.

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