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How long is the tail end of the learning curve? Results from 1000 consecutive endoscopic endonasal skull base cases following the initial 200 cases

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OBJECTIVE Endoscopic endonasal approaches (EEAs) to the skull base have evolved over the last 20 years to become an essential component of a comprehensive skull base practice. Many case series show a learning curve from the earliest cases, in which the authors were inexperienced or were not using advanced closure techniques. It is generally accepted that once this learning curve is achieved, a plateau is reached with little incremental improvement. Cases performed during the early steep learning curve were eliminated to examine whether the continued improvement exists over the "tail end" of the curve.

METHODS A prospectively acquired database of all EEA cases performed by the senior authors at Weill Cornell Medicine/NewYork-Presbyterian Hospital was reviewed. The first 200 cases were eliminated and the next 1000 consecutive cases were examined to avoid the bias created by the early learning curve.

RESULTS Of the 1000 cases, the most common pathologies included pituitary adenoma (51%), meningoencephalocele or CSF leak repair (8.6%), meningioma (8.4%), craniopharyngioma (7.3%), basilar invagination (3.1%), Rathke's cleft cyst (2.8%), and chordoma (2.4%). Use of lumbar drains decreased from the first half to the second half of our series ($p < 0.05$) as did the authors' use of fat alone ($p < 0.005$) or gasket alone ($p < 0.005$) for dural closure, while the use of a nasoseptal flap increased ($p < 0.005$). Although mean tumor diameter was constant (on average), gross-total resection (GTR) increased from 60% in the first half to 73% in the second half ($p < 0.005$). GTR increased for all pathologies but most significantly for chordoma (56% vs 100%, $p < 0.05$), craniopharyngioma (47% vs 0.71%, $p < 0.05$) and pituitary adenoma (67% vs 75%, $p < 0.05$). Hormonal cure for secreting adenomas also increased from 83% in the first half to 89% in the second half ($p < 0.05$). The rate of any complication was unchanged at 6.4% in the first half and 6.2% in the latter half of cases, and vascular injury occurred in only 0.6% of cases. Postoperative CSF leak occurred in 2% of cases and was unchanged between the first and second half of the series.

CONCLUSIONS This study demonstrates that contrary to popular belief, the surgical learning curve does not plateau but can continue for several years depending on the complexity of the endpoints considered. These findings may have implications for clinical trial design, surgical education, and patient safety measures.

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KEYWORDS endonasal; endoscopic; transsphenoidal; follow-up; outcomes; learning curve; tail end; complication; gross-total resection; pituitary surgery

Endoscopic skull base surgery (ESBS) has rapidly gained acceptance over the past 2 decades as a minimally invasive approach for a variety of pathologies of the skull base.[12,35] Recent technical advances in endoscopes, monitors, stereotaxy, the development of extended endonasal approaches, and reliable closure techniques have pushed the field into the forefront of modern skull base surgery.

In the early days of ESBS, several pioneers emphasized the steep learning curve, highlighting complications that

ABBREVIATIONS ACTH = adrenocorticotropic hormone; EEA = endoscopic endonasal approach; ESBS = endoscopic skull base surgery; GH = growth hormone; GTR = gross-total resection; RCC = Rathke's cleft cyst.
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can occur for the novice practitioner.[5,20,21] As the field evolved, the concept of a learning curve became less critical and the focus was shifted to the safety and efficacy of the approach as compared to microscopic and open transcranial approaches.[15–19] The classic surgical learning curve is S-shaped with a tail end that plateaus and supposedly becomes flat, indicating mastery.[13,32] However, in a complex field such as neurosurgery, it is possible that with continued effort and improvement, the learning curve will persist even after several hundred cases. In this paper, we examine outcomes and complications in a consecutive series of 1000 ESBS cases. With an understanding of which outcomes continue to improve, which decline, and which plateau, will come a greater understanding of which areas require persistent and potentially unending practice and which areas may benefit from novel strategies for improvement.

Methods

Patient Population and Surgical Approach

We analyzed a prospectively acquired database of a consecutive series of surgeries utilizing the endoscopic endonasal approach (EEA) from 2004 to 2018 at NewYork-Presbyterian Hospital, Weill Cornell Medicine. From these cases, the first 200 cases were eliminated and considered part of our learning curve. The study was approved by our IRB. All surgeries were performed by the senior author (T.H.S.). Technical aspects of surgery remained relatively consistent for all cases. Specifically, every case was assisted by an otolaryngologist and by either a resident or a fellow. There were no technical innovations or major instrument changes introduced during the course of this series. The use of the gasket seal, nasoseptal flap, and endonasal bipolar cauterization all occurred after the first 200 cases, which is why they were eliminated. A detailed description of our EEA technique for a variety of skull base lesions has been extensively reported.[34] We have also previously described an algorithm for reconstruction of the skull base and a case-specific protocol to reduce CSF leak after ESBS.[26,31,41] Our gasket-seal closure and nasoseptal flap reconstruction protocols have also been described in detail.[8,24,26,28]

Patient Demographics, Clinical Characteristics, and Complications

Our institution began utilizing a prospective password-protected database of all EEA cases in which the senior neurosurgeon (T.H.S.) entered the following data immediately after surgery and for the duration of the patients' hospital stay until the final pathology returned: name, medical record number, date of surgery, final pathology, approach (sinus opened), use of lumbar drainage, use of intrathecal fluorescein, presence of intraoperative CSF leak, closure technique/graft materials used, and occurrence of postoperative CSF leak. Additional data collected and analyzed retrospectively for each case included the patient's sex, age, follow-up period, procedure length, radiographic extent of resection based on review of postoperative MRI by a board certified neuroradiologist performed within a week after surgery, previous surgery, previous radiation, confirmation of final pathology, endocrine outcomes, and complications. Complete biochemical remission for prolactinomas was determined by normalization of serum prolactin levels <20 μg/L; for growth hormone (GH)–producing tumors, by normalization of serum GH <1 μg/L or nadir GH after oral glucose tolerance test ≤0.4 μg/L; and for adrenocorticotropic hormone (ACTH)–producing tumors, by morning serum cortisol levels <3 μg/dl 3–5 days after surgery. Complications were tracked in the immediate postoperative period and at long-term follow-up. Infections were reported as confirmed meningitis or other infection. In cases in which meningitis was suspected, CSF samples were collected and cultured. Neurological deficits were reported as specific cranial nerve palsy when applicable. Vascular injuries were reported based on the vessel involved. Postoperative CSF leak was defined as clear CSF rhinorrhea, confirmed by the senior author, where reoperation was required for repair.

Statistical Analysis

The SPSS statistical software package (version 24, IBM Corp.) was utilized for all analyses. Univariate analysis was performed using Pearson chi-square and Fisher's exact tests for categorical variables, and the independent-samples t-test for continuous variables. For all tests, statistical significance was determined with an alpha level <0.05.

Results

Patient Demographics and Clinical Characteristics

A consecutive series of 1000 cases that underwent EEA for more than 40 different skull base pathologies were included in the study. The cohort comprised 52% females and 48% males. There was no statistically significant difference in sex between the first 500 and latter 500 cases in the cohort (Table 1). The mean patient age was 50 ± 18 years and 23% were over the age of 65 years. The mean patient age was 50.5 ± 18 years for the first half versus 49.5 ± 18 years for the latter half of the cohort. Reoperations accounted for 15% of cases in the first half of the cohort compared to 16% of cases in the latter half. Gross-total resection (GTR) was achieved in 67% of 827 cases in which it could be assessed. GTR was accomplished in 60% of 400 applicable cases in the first half compared to 73% of 427 applicable cases in the latter half of the cohort ($p < 0.005$). The mean follow-up duration for the cohort was 707 ± 849 days. The mean procedure length was significantly longer for cases in the latter half (247 ± 108 mins) compared to the first half (224 ± 101 mins, $p < 0.05$) of the cohort. The mean procedure length based on pathology is summarized in Fig. 1A.

Pathology and Surgical Approaches

The most common pathology encountered was pituitary adenoma (51%, Table 2). Other pathologies encountered were meningoencephalocele/CSF leak repair (8.6%), meningioma (8.4%), craniopharyngioma (7.3%), basilar invagination (3.1%), Rathke's cleft cyst (RCC; 2.8%), chordoma (2.4%), other malignancies (2.2%), and metastasis (1.6%). Pathologies performed more frequently

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TABLE 1. Comparison between the first- and latter-half cases

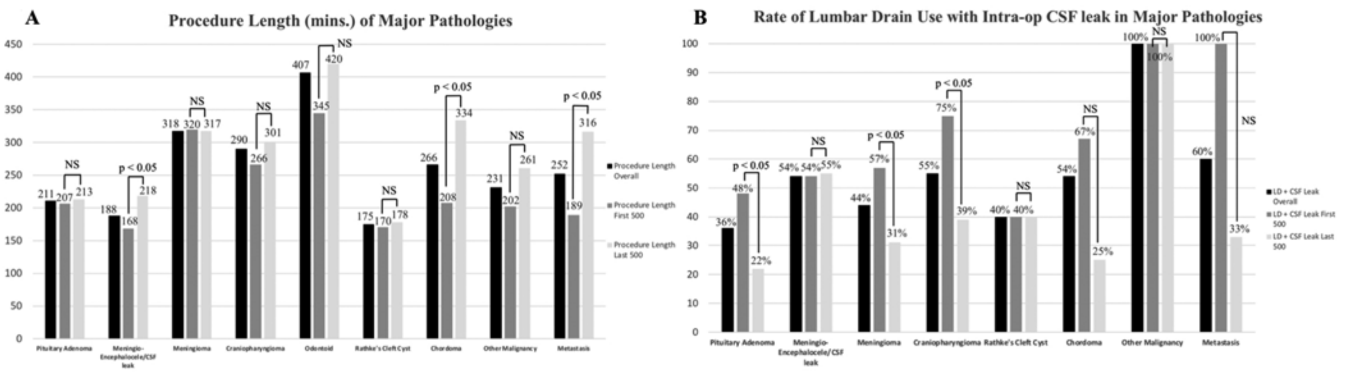
Variable	First 500 Cases (%)	Last 500 Cases (%)	p Value
Sex			
Females	263 (53)	253 (51)	NS
Males	237 (47)	247 (49)	NS
Mean age ± SD, yrs	50.5 ± 18	49.5 ± 18	NS
Reoperations	73 (15)	78 (16)	NS
GTR	238/400 (60)	312/427 (73)	**<0.005**
Mean procedure length ± SD, mins	224 ± 101	247 ± 108	**<0.05**
Intraop CSF leak	299 (60)	255 (51)	NS
Lumbar drain			
In all patients	162 (32)	79 (16)	**<0.005**
In patients w/ intraop CSF leak	162/299 (54)	79/255 (31)	**<0.005**
Any complication	32 (6.4)	31 (6.2)	NS
Postop CSF leak	10 (2)	10 (2)	NS
Neurological deficit	8 (1.6)	13 (2.6)	NS
Infection	8 (1.6)	8 (1.6)	NS
Hematoma	5 (1)	7 (1.4)	NS
Vascular injury	3 (0.6)	0	NS
DVT/PE	4 (0.8)	0	NS
Mortality	1 (0.2)	1 (0.2)	NS

DVT/PE = deep vein thrombosis/pulmonary embolism; NS = not significant. Boldface type indicates statistical significance.

in the second half of the series were basilar invagination (p <0.005) and RCC (p <0.05), while cases performed less frequently were meningoencephalocele/CSF leak repair (p <0.005) and chordoma (p <0.005; Table 2). The remaining pathologies all had a frequency <1%. The most common approach was transellar (46%), which was performed more commonly in the latter half compared to the first half of the cohort (54% vs 46%, p <0.05). Other approaches were transplanum (27%), transclival (7.5%), transcribriform (6.4%), transethmoidal (4.4%), transpterygoid (4.3%), transodontoid (3.4%), and transorbital (1.2%). The transclival and transcribriform approaches were both more commonly performed in the first half compared to the latter half of the cohort (p <0.005). The transodontoid approach was significantly more common in the latter half compared to the first half of the cohort (74% vs 26%, p <0.005).

Extent of Resection Based on Pathology

The overall rate of GTR for pituitary adenomas was 71% (67% first half vs 75% latter half, p <0.05; Fig. 2B). The overall rate of GTR for meningiomas was 63% (55% first half vs 70% latter half, p = 0.18). The overall rate of GTR for craniopharyngioma cases was 62% (47% first half vs 71% latter half, p <0.05). The overall rate of GTR for chordoma cases was 67% (56% vs 100% for the first half vs latter half of cases, respectively; p <0.05). GTR was not included for odontoid resection, in which the goal of surgery was decompression of the cord, or RCC, in which the goal of surgery was fenestration. When excluding reoperations and analyzing only first-time operations, the overall rate of GTR for pituitary adenomas was 73%



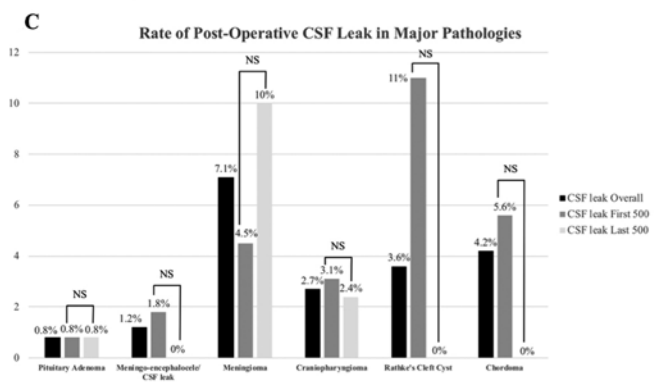


FIG. 1. Comparison of overall (*black bars*), first 500 (*dark gray bars*), and latter 500 cases (*light gray bars*). **A:** Procedure length was significantly longer for meningoencephalocele/CSF leak repair, chordoma, and metastasis in the latter half of the cohort compared to the first half (p <0.05). **B:** Rate of lumbar drain use in patients with intraoperative CSF leak was significantly lower for pituitary adenoma, meningioma, and craniopharyngioma in the latter half of the cohort compared to the first half (p <0.05). **C:** Rate of postoperative CSF leak showed no significant differences between the first half and latter half of the cohort for major pathologies. NS = not significant.

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TABLE 2. Summary of pathologies in 1000 EEA cases

Pathology	Overall (%)	First 500 (%)	Last 500 (%)	p Value
Pituitary adenoma	514 (51)	246 (48)	268 (52)	NS
Meningoencephalocele/CSF leak repair	86 (8.6)	57 (66)	29 (34)	**<0.005**
Meningioma	84 (8.4)	44 (52)	40 (48)	NS
Craniopharyngioma	73 (7.3)	32 (44)	41 (56)	NS
Basilar invagination	31 (3.1)	6 (19)	25 (81)	**<0.005**
RCC	28 (2.8)	9 (32)	19 (68)	**<0.05**
Chordoma	24 (2.4)	18 (75)	6 (25)	**<0.005**
Other malignancies	22 (2.2)	13 (59)	9 (41)	NS
Metastasis	16 (1.6)	7 (44)	9 (56)	NS
Epidermoid	9 (<1)	4 (44)	5 (56)	NS
Xanthogranuloma	9 (<1)	4 (44)	5 (56)	NS
Fibroma	8 (<1)	5 (62)	3 (38)	NS
Lymphoma	8 (<1)	6 (75)	2 (25)	NS
Chondrosarcoma	7 (<1)	4 (57)	3 (43)	NS
Angiofibroma	7 (<1)	6 (86)	1 (14)	**<0.05**
Squamous cell carcinoma	7 (<1)	2 (29)	5 (71)	NS
Hemangioma	6 (<1)	4 (67)	2 (33)	NS
Mucocele	5 (<1)	3 (60)	2 (40)	NS
Schwannoma	5 (<1)	4 (80)	1 (20)	NS
Esthesioneuroblastoma	4 (<1)	1 (25)	3 (75)	NS
Arachnoid cyst	3 (<1)	2 (67)	1 (33)	NS
Cholesteatoma	3 (<1)	2 (67)	1 (33)	NS
Clival mass unknown	3 (<1)	2 (67)	1 (33)	NS
Germinoma	3 (<1)	1 (33)	2 (67)	NS
Hemangiopericytoma	3 (<1)	2 (67)	1 (33)	NS
Plasmacytoma	3 (<1)	1 (33)	2 (67)	NS
Rhabdomyosarcoma	3 (<1)	1 (33)	2 (67)	NS
Neurosarcoidosis	3 (<1)	1 (33)	2 (67)	NS
Dermoid	2 (<1)	1 (50)	1 (50)	NS
Chondromyxoid fibroma	2 (<1)	0	2 (100)	NS
Ependymoma	2 (<1)	2 (100)	0	NS
Hypophysitis	2 (<1)	0	2 (100)	NS
Inverted papilloma	2 (<1)	2 (100)	0	NS
Osteomyelitis	2 (<1)	1 (50)	1 (50)	NS
Optic nerve pathology	2 (<1)	1 (50)	1 (50)	NS
Pituicytoma	2 (<1)	1 (50)	1 (50)	NS
Pituitary carcinoma	2 (<1)	2 (100)	0	NS
Aspergilloma	1 (<1)	1 (100)	0	NS
Epithelioid hemangioendothelioma	1 (<1)	0	1 (100)	NS
Fibrosarcoma	1 (<1)	1 (100)	0	NS
Enterogenous cyst	1 (<1)	1 (100)	0	NS
Phlegmon	1 (<1)	1 (100)	0	NS

Boldface type indicates statistical significance.

(68% first half vs 78% latter half, p <0.05), for meningiomas 81% (80% first half vs 83% latter half), for craniopharyngiomas 74% (59% first half vs 88% latter half, p <0.05), and for chordomas 70% (53% first half vs 100% [n = 6] latter half).

Intraoperative CSF Leak Based on Pathology and Closure Type

Intraoperative CSF leak occurred in 52% of cases. Rates of intraoperative CSF leaks based on pathology are summarized in Table 3. The rate of intraoperative CSF

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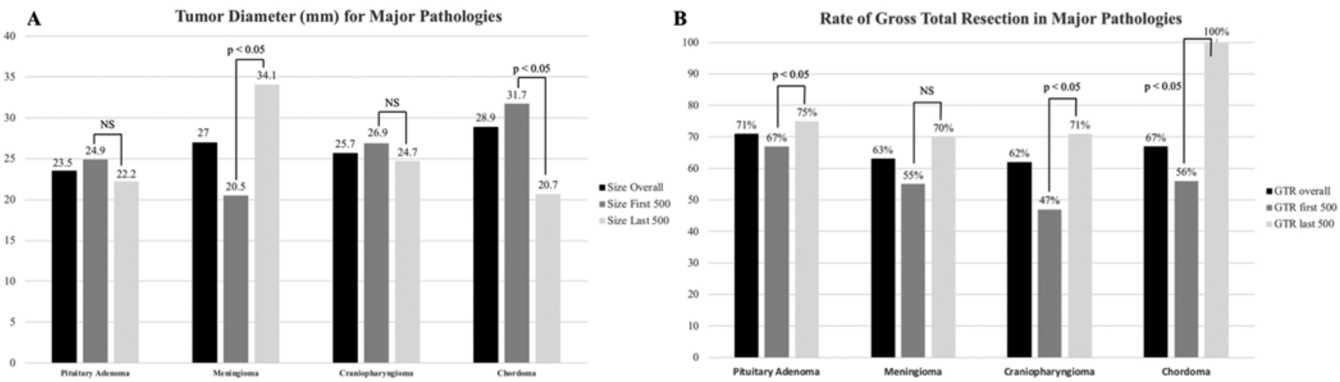

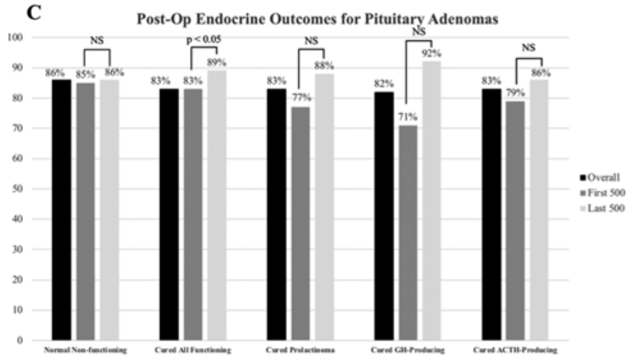

FIG. 2. Comparison of overall (*black bars*), first 500 (*dark gray bars*), and latter 500 cases (*light gray bars*). **A:** Tumor diameter was significantly larger for meningiomas in the latter-half cases compared to the first half (p <0.05). Tumor diameter was significantly larger for chordomas in the first-half cases compared to the latter half (p <0.05). **B:** The rate of GTR was significantly higher for pituitary adenoma, craniopharyngioma, and chordoma in the latter half of the cohort compared to the first half (p <0.05). **C:** For nonfunctioning adenomas, 86% had normal endocrine status at last follow-up with no change over time (85% first half vs 86% latter half). Cure rates for hormone-producing tumors increased significantly over time when grouped together (p <0.05).

leak significantly decreased only for pituitary adenomas in the latter half of the cohort compared to the first half (40% vs 52%, p <0.05). The most common type of closure was nasoseptal flap with fat (25%) and was associated with a 2% rate of postoperative CSF leak (Table 4). This closure was most commonly used for pituitary adenoma (61%) followed by meningoencephalocele (16%). Closure with fat only was performed in 19% and associated with a 2.1% rate of CSF leak. Closure using fat only was significantly more common in the first half of the cohort compared to the latter half (77% vs 23%, p <0.005). This closure was generally used for pituitary adenomas (64%) and meningoencephalocele/CSF leak repair (13%). Gasket seal closure with nasoseptal flap and fat was performed in 19% of cases and associated with a 3.6% rate of CSF leak. This closure was the most commonly used for craniopharyngiomas (29%), meningiomas (26%), and pituitary adenomas (26%). Closure with Gelfoam alone or nothing was performed in 19% of cases and associated with a 0.5% rate of CSF leak. Closure with Gelfoam alone or nothing was also significantly more common in the latter half of the cohort compared to the first half (63% vs 37%, p <0.005). This type of closure was generally used when there was no intraoperative CSF leak and depending on the amount of bleeding. Closure with a nasoseptal flap only was performed in 14% of cases, mostly in pituitary adenomas (63%), and was associated with no postoperative CSF leaks. Closure with a nasoseptal flap

TABLE 3. Major pathologies and rate of intraoperative CSF leak

	Intraop CSF Leak			
Pathology	Overall (%)	First 500 (%)	Last 500 (%)	p Value
Pituitary adenoma	234/514 (46)	127/246 (52)	107/268 (40)	**<0.05**
Meningoencephalocele/CSF leak repair	70/86 (81)	48/57 (84)	22/29 (76)	NS
Meningioma	70/84 (83)	35/44 (80)	35/40 (88)	NS
Craniopharyngioma	73/73 (100)	32/32 (100)	41/41 (100)	NS
Odontoid	4/31 (13)	0/6 (0)	4/25 (16)	NS
RCC	10/28 (36)	5/9 (56)	5/19 (26)	NS
Chordoma	13/24 (54)	9/18 (50)	4/6 (67)	NS
Other malignancies	7/22 (32)	4/13 (31)	3/9 (33)	NS
Metastasis	10/16 (63)	4/7 (57)	6/9 (66)	NS

Boldface type indicates statistical significance.

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TABLE 4. Summary of closure technique and rate of postoperative CSF leak

Closure	Overall (%)	First 500 (%)	Last 500 (%)	p Value	CSF Leak (%)
Nasoseptal flap ± fat or fascia lata	245 (25)	124 (51)	121 (49)	NS	5 (2)
Fat	193 (19)	149 (77)	44 (23)	**<0.005**	4 (2.1)
Gasket + nasoseptal flap + fat or fascia lata	192 (19)	88 (46)	104 (54)	NS	7 (3.6)
Gelfoam only, or nothing	186 (19)	68 (37)	118 (63)	**<0.005**	1 (0.5)
Nasoseptal flap	150 (15)	59 (39)	91 (61)	**<0.005**	0
Nothing	71 (7.1)	32 (45)	39 (55)	NS	1 (1.4)
Gasket ± fat or fascia lata (no nasoseptal flap)	23 (2.3)	23 (100)	0	**<0.005**	3 (13)
Fat + middle turbinate flap	11 (1.1)	5 (45)	6 (55)	NS	0

Boldface type indicates statistical significance.

increased significantly in the latter half of the cohort compared to the first half (61% vs 39%, $p < 0.005$). Gasket seal closure alone with fat was performed in 2.3% of cases, all of which were in the first half of the cohort ($p < 0.005$), and was associated with a 13% rate of postoperative CSF leak. In the latter half of our series we never used a gasket alone and always combined it with a flap. Closure with no graft other than dural sealant was performed in 7.1% of cases and associated with a 1.4% rate of CSF leak. Closure with a middle turbinate flap and fat was performed in 1.1% of cases and associated with no CSF leaks. This closure was often used with meningoencephalocele/CSF leak repair (64%).

Use of Lumbar Drains

We used a lumbar drain in 24% of our cases (32% first half vs 16% latter half, $p < 0.05$; Table 1). Based on pathology, lumbar drains were used in pituitary adenoma (17%), meningioma (37%), craniopharyngioma (55%), meningoencephalocele/CSF leak repair (44%), RCC (14%), chordoma (29%), other malignancies (32%), and metastasis (38%). The rate of lumbar drain use in pituitary adenomas significantly decreased between the first half and latter half of the cohort (25% vs 9%, $p < 0.05$). The rate of lumbar drain use in craniopharyngioma (75% vs 39%, $p < 0.05$) and metastasis (57% vs 13%, $p < 0.05$) also significantly decreased between the first half and latter half of the cohort, respectively. Usage of a lumbar drain also decreased in all other pathologies between the first half and latter half of the cases, although the difference was not statistically significant. Using the denominator of intraoperative CSF leak, lumbar drains were used in 42% of patients (54% first half vs 31% latter half, $p < 0.005$; Table 1). Based on pathology as well as presence of intraoperative CSF leak, lumbar drain use is summarized in Fig. 1B.

TABLE 5. Summary of complications

Complication	Value (%)
Any complication	63 (6.3)
Neurological deficit	21 (2.1)
Postop CSF leak	20 (2)
Any infection	16 (1.6)
Meningitis	6 (0.6)
Hematoma	12 (1.2)
DVT/PE	4 (0.4)
Vascular injury	3 (0.3)
Mortality	2 (0.2)

Some patients had more than one complication.

Complications Excluding CSF Leaks

Postoperative complications occurred in 6.3% of cases (Table 5). The rate of any complication was 6.4% in the first half and 6.2% in the latter half of cases. The most common complication was neurological deficit occurring in 2.1% cases. Neurological deficit was present in 1.6% of cases in the first half of the cohort compared to 2.6% of cases in the latter half of the cohort. The most commonly encountered neurological deficits were from visual loss (14 patients) or cranial nerve palsy (7 patients). Cranial verve VI palsy occurred in 4 cases and cranial nerve III palsy occurred in 3 patients. Infection, either intracranial or extracranial, occurred in 1.6% of cases. The rate of infection was 1.6% in both the first half and latter half of the cohort. Systemic infections including urinary tract infection, urosepsis, and bacteremia accounted for 1% of cases and meningitis accounted for 0.6% of cases. Postoperative hematoma requiring reoperation occurred in 1.2% of cases, with pituitary adenoma accounting for the majority (n = 9) of cases. Other cases requiring reoperation for hematoma were craniopharyngioma (1 patient), meningioma (1 patient), and RCC (1 patient). The rate of hematoma was 1% in the first half of the cohort compared to 1.4% in the latter half of the cohort. Vascular injury occurred in 0.6% of cases, involving the internal carotid artery in 2 cases and the ophthalmic artery in 1 case. Pulmonary embolism occurred in 0.8% of patients and mortality in 0.2% of cases caused by dilated cardiomyopathy (1 patient) and metastatic prostate cancer (1 patient). The rate of vascular injury, pulmonary embolism, and mortality was <1% for both the first half and latter half of the cohort.

Rate of Postoperative CSF Leak

Postoperative CSF leak requiring reoperation occurred in 20 cases (2%). Postoperative CSF leak was 2% in both the first half and latter half of cases. Revision of dural closure was performed in all cases. The overall rate of post-

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operative CSF leak based on pathology is summarized in Fig. 1C.

Tumor Size

The mean tumor diameter for the entire cohort of tumors was 24.6 ± 11.4 mm and did not change from the first half to the second half (25.5 ± 10.8 mm vs 24.2 ± 11.8 mm). The mean tumor diameter based on pathology is summarized in Fig. 2A.

Endocrine Outcomes

Nonfunctioning adenomas accounted for 73% of all pituitary adenomas. The remainder were prolactinomas (10.5%), GH (9.7%), and ACTH (6.8%) producing. For nonfunctioning adenomas, 86% had normal endocrine status at last follow-up with no change over time (85% first half vs 86% latter half). Cure rates for hormone-producing tumors increased significantly over time when grouped together ($p < 0.05$). Endocrine outcomes for functioning and nonfunctioning pituitary adenomas are summarized in Fig. 2C.

Discussion

The article reports the largest series of consecutive EEA cases reported in the literature and the only study that documents incremental changes in surgical outcome that can occur during the presumed "plateau" or "tail end" of the learning curve after a large number of cases. Although the steep initial learning curve in ESBS cases has been extensively reported in the literature by our group and others,[4,10,14,20,25,27,30,31,33,37,39] there are few data on the tail end of the learning curve in EEA surgeries, or any neurosurgical procedures for that matter. While most previously published studies examine the initial learning curve in ESBS, we eliminated our first 200 cases to focus uniquely on the tail end of the curve. The main finding in this study is that the tail end of the learning curve evolves differently depending on the outcome measure being examined. More specifically, complex outcomes such as GTR rates and hormonal cure continued to improve even after 700 cases, while other outcomes such as complications, CSF leak rates, and hormone preservation in non–hormone producing tumors remained stable. An increase in GTR and hormonal cure cannot merely be attributed to environment, because case complexity can be assumed to increase over time, caused by an increase in the daring of the surgeon to tackle more difficult cases as well as increased rate of complex case referrals from other nearby centers that may have less experience. Likewise, there were no new technical advances in equipment that could explain our improvements. The most likely explanation is that the technical ability and judgment required to master a complex skill such as achieving a GTR in an EEA case requires a significant amount of time and has a long, slow learning curve. Whether such a long, drawn-out learning curve exists for all complex surgical procedures or is unique to ESBS and its implications will be discussed.

Steep Early Learning Curve

The early learning curve in surgical training has been a focus of study in all fields of surgery. The classic learning curve, originally described in aircraft manufacturing, has an S-shape with three stages (Fig. 3).[43] The first stage involved slow acquisition of new skills, the second phase a rapid increase in proficiency, and the last stage a plateau indicating mastery.[1,6,11,13,22,32,36,38,44] One of the primary goals of studying the surgical learning curve is to establish a minimum number of cases after which a surgeon can be considered "proficient" in their specialty.[7,9] The slope of the early learning curve is dependent on the skill of the trainee, the complexity of the procedure, and the number of repetitions.[40] ESBS is no exception and several reports have described the early learning curve. The conclusion of these studies is that over the course of the first 50–200 cases, most centers noticed a decrease in postoperative CSF leaks and operative time as well as an increase in extent of resection, after which results tend to plateau.[4,5,10,20,21,33,37] Nix et al. examined the success of skull base closure and found that there was a learning curve only for complex skull base closure for high-flow leaks, indicating that complexity may be a factor in the learning curve.[27]

These studies on the early learning curve not only fail to examine the tail end of the curve but also reveal one of the major criticisms of learning-curve evaluation, namely the differential effect of skill acquisition on different outcome variables. Two main types of variables are generally studied, either the surgical process or patient outcomes.[13] The former includes length of the procedure, success of the procedure, and extent of resection, and the latter includes blood loss, length of stay, complications, and survival. The most common variable measured is also the easiest to measure, namely procedure length. However, procedure length is often not a good measure of outcome. In fact, several studies of procedure length have demonstrated that the classic S-shaped curve fails to adequately characterize operative duration because surgeons tend to take on more complex cases and spend more time teaching once they gain proficiency, so operative time may increase at the tail end of the curve (Fig. 3).[32] Our data confirm this finding. However, as we show in our data, some outcome measures demonstrate a plateau while others continue to improve even after hundreds of cases. More specifically, complications and CSF leak can be stabilized based on algorithms and standard critical pathways for managing postoperative patients. However, the skill set, experience, and anatomical knowledge required to perform delicate microdissection around critical neurovascular structures defies most systematized or regimented teaching curricula and cannot be reduced to an algorithm. Simulations and cadavers can provide some of the required practice venues but do not adequately mimic the complexity, feel, and stakes of actual surgery.

Tail End of the Learning Curve

There has been little study of the tail end of the learning curve in surgical practice, and in fact, there is no definition of exactly where the tail begins and even less information on surgical progress over the course of the tail. In most studies of the tail end, the definition is the moment in time after the steep learning curve has been surpassed. This is generally believed to be anywhere from 35 to 200 cases.[32]

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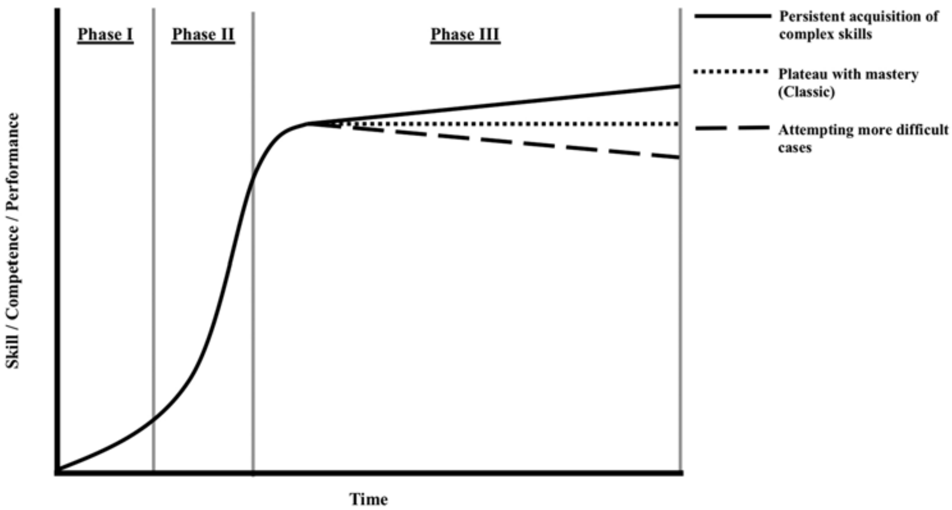

FIG. 3. Three phases of the surgical learning curve. Phase III has three options that vary according to what is being measured. In the classic view, the tail end plateaus as the surgeon masters the technique (*dotted line*). If procedure length is measured, there can be an increase in the length of procedures as more difficult cases are attempted and there is more time spent on teaching (*dashed line*). For complex tasks such as achieving a GTR, there is continued learning that may persist indefinitely (*solid line*).

The assumption is that once the early learning curve is overcome, there exists a flat plateau with little incremental improvement. For example, in studies professing to examine the tail end of the curve, Ooman et al. find the tail end of the learning curve after only 35 laparoscopic pyloromyotomies, and Voitk et al. define the tail of the learning curve after 200 laparoscopic cholecystectomies.[29,42] These studies do not examine whether incremental learning occurs in the later plateau phase of the learning curve and thus do not really address the length of the tail, but rather only the start of the tail. Moreover, the outcome measures used in these studies were uniquely complication rates, which as we have shown, can certainly plateau.

In oncology, another important endpoint not examined in these studies is extent of resection. The only prior study in ESBS with sufficient cases to address this question for the tail end of the learning curve was one published by Kassam et al. in which they retrospectively analyzed a series of their initial 800 cases of ESBS. This was the first large study to describe the perioperative safety and short-term outcomes of endoscopic endonasal surgery for skull base lesions.[12] However, this study was specifically concerned with complications and did not examine the learning curve, nor did they measure extent of resection. Complication rates were correlated with case complexity. Although their postoperative CSF leak decreased over time from 15.9% to 5.4%, this was associated with a specific technical advance, namely the adoption of the vascularized nasoseptal flap.

What are the causes of the long duration of the tail end of the learning curve for GTR in ESBS, why has this not been appreciated in the past, and what are the implications? One explanation of the extended duration of the learning curve for GTR could be the complexity of the task. Removing a meningioma, chordoma, or craniopharyngioma whose margins may be stuck to critical neurovascular structures through a long narrow corridor is certainly challenging, as are many other neurosurgical procedures. Support for this conclusion can be found in a study performed by Subramonian and Muir in which they gave a group of medical students intense surgical training for 12 weeks in open and laparoscopic surgery.[40] At the end of their training period, while their overall proficiency at both techniques was similar, on detailed analysis of the different components of surgery, the laparoscopic skills were deficient in finer dissection, identification of correct planes, and 2D perception when compared to open surgery, and required more operative time. Hence, depending on the endpoint measured, the learning curve could be considered overcome or still in existence and the complexity of the task dictated the length of the learning curve. Clearly the S-shape of the surgical learning curve is an idealized version of reality and for the most complex aspects of any surgical procedure, the tail end of the learning curve likely continues to slope upward for several years or even decades (Fig. 3). The most relevant publication in the neurosurgical literature assessed the ability of a surgeon to estimate the extent of resection during glioma surgery.[23] The senior author demonstrated that over a 17-year period, this ability increased almost linearly throughout the entire period of observation, indicating that surgical judgment for complex tasks is honed over periods of decades and not just months or years. The reason there has been little documentation of such a long slow trend in improving outcomes can be attributed to the fact that most studies examine endpoints such as complications and length of surgery rather than extent of resection, and the former reach an earlier plateau or have a decline rather than an increase. Moreover, in a mature surgical practice GTR rates are generally high and small increases would require very large numbers of patients to achieve statistical significance. Interestingly, we also found increases in the rate of GTR for our pituitary adenomas. These are considered easier to remove than meningiomas, craniopha-

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ryngiomas, or chordomas, and indicate that perhaps such high complexity is not required for a long incremental tail in improvement. Indeed, the rate of GTR for adenomas was already high in the first 500 cases, yet continued to increase even after several hundred cases. Given the high numbers of cases of adenomas in our study, we were able to find statistical significance. Likewise, hormonal cure in secreting adenomas increased over time, indicating that the ability to achieve an extracapsular plane and remove the tumors en bloc requires hundreds of cases to achieve proficiency. The same can be said about the reduction in intraoperative CSF leak in our adenoma cases. Even after 700 cases, this rate decreased as we became more and more skilled at finding the pseudocapsule and maintaining an intact diaphragma sella without compromising GTR. For lower-volume pathologies, finding a significant increase in GTR rates in the tail would take a very large numbers of cases. Such is the case with meningiomas, in which we saw the rate of GTR increase from 55% to 70% but were not able to show statistical significance due to the small number of cases performed.

Implications of the Long Tail End of the Learning Curve

The existence of a long, drawn-out tail of a surgical learning curve for specific endpoints such as GTR has profound implications for clinical trial design as well as health care delivery and reimbursement. Most clinical trials begin to enroll patients once surgeons are believed to have adequate training to achieve equipoise. While such a long learning curve may complicate such trials and potentially render them uninterpretable, it can be assumed that all complex surgical approaches likely have equally long tails that may balance out. More importantly, such trials may have to examine individual surgeon's learning curves throughout the entire length of their enrollment to assess the impact of their unique learning curve. Another important ramification of this study speaks to the increasing understanding of surgeon experience and outcome and the call for centers of excellence where certain pathologies should be centralized in the hands of high-volume surgeons.[2] It is well accepted that with increasing volume, individual surgeons and centers report improved outcomes.[2] However, centralization is controversial because the underlying assumption and perhaps myth of medical training is that once a surgeon has emerged from a residency program, they are adequately trained to perform all procedures regardless of complexity.[2] Government bureaucrats, insurance company executives, and hospital administrators often fail to account for surgical experience and expertise when directing patients to the most expedient and cheapest option to suit their prioritized financial endpoints. Our data indicate that not only is there a minimal threshold to become a center of excellence, but there are also incrementally higher degrees of excellence that likely evolve over the lifetime of the surgeon.

Evolution of Skull Base Closure

Numerous studies comparing EEA to transcranial surgery have demonstrated that in experienced hands, EEA can offer high rates of resection with low complications.[35] However, even after hundreds of cases, there are subtle changes in practice that indicate how the field is evolving. For example, our CSF leak rate was fairly constant and did not markedly improve over time, although our use of lumbar drains decreased. Our approach to lumbar drains is that they play an important role in preventing CSF leaks in high-risk cases. This conclusion is borne out by the randomized study performed by the Pittsburgh group as well as our own study in patients with high BMIs.[3,45] Over time, the cases that were believed to be high risk were mostly intradural cases such as meningiomas, craniopharyngiomas, some chordomas, and giant adenomas, as well as lower-risk cases in patients with very high BMIs such as meningoencephaloceles. We also moved away from fat graft placement in intradural cases relying on the gasket and the nasoseptal flap, and moved away from using the gasket by itself and always combined the gasket with the nasoseptal flap. These subtle shifts in practice did not dramatically alter our rates of CSF leak but rather made the closure algorithm simpler and easier to implement.

Limitations

The limitations of this study are its retrospective design involving a single institution, which is subject to imprecision of the medical record system and inherent bias. However, this is a consecutive series of cases and the database was created prospectively, so no cases are missing.

Another potential limitation of this study is the arbitrary decision to start the data collection at 200 cases to eliminate the initial phases of the learning curve. Although the exact length of phase I and phase II of the surgical learning curve (Fig. 3) cannot be determined, 200 cases is the upper limit of most studies of the surgical learning curve and we wanted to be conservative.[32] Moreover, the division into the first 500 and second 500 cases is also arbitrary but seemed like a reasonable cutoff. Analysis based on quartiles might yield different results but would be equally arbitrary and further reduce our numbers and any potentially statistically significant results.

Conclusions

ESBS is becoming increasingly safe and effective over time. With practice, experience, and an algorithm for closure based on pathology, location, and presence of a leak, rates of CSF leak and complications can be quite low. Nevertheless, even after several hundred cases, there are noticeable improvements in outcome, particularly extent of resection and hormonal cure for more complex tumors, indicating a long, albeit flatter tail end of the learning curve. Our study demonstrates that contrary to popular belief, the surgical learning curve does not plateau but can continue for several years when complex endpoints are considered. These findings may have dramatic implications for clinical trial design, surgical education, government policy, and patient safety measures.

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Disclosures

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

Author Contributions

Conception and design: Schwartz, Younus, Uribe-Cardenas, Morgenstern. Acquisition of data: all authors. Analysis and interpretation of data: Schwartz, Younus, Gerges, Uribe-Cardenas, Morgenstern, Eljalby. Drafting the article: Schwartz, Younus. Critically revising the article: Schwartz, Younus, Gerges. Reviewed submitted version of manuscript: all authors. Approved the final version of the manuscript on behalf of all authors: Schwartz. Statistical analysis: Schwartz, Younus. Administrative/technical/material support: Tabaee, Greenfield, Kacker, Anand. Study supervision: Schwartz, Younus.

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