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ORIGINAL ARTICLE - PITUITARIES

The slope of the learning curve in 600 consecutive endoscopic transsphenoidal pituitary surgeries

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Abstract

Background Endonasal endoscopic transsphenoidal surgery (EETS) for pituitary adenoma has become a mainstay of treatment over the last two decades and it is generally accepted that once this learning curve is achieved, a plateau is reached with little incremental improvement.

Objective The objective of this study was to assess the slope of the learning curve over a long period of time for a variety of outcomes measures.

Methods We examined outcomes and complications in a consecutive series of 600 EETS for pituitary adenoma grouped into quartiles based on date of surgery.

Results GTR significantly increased across quartiles from 55 to 79% in the last quartile ($p < 0.005$). The rate of intraoperative CSF leak significantly decreased from 60% in the first quartile to 33% in the last quartile and the rate of lumbar drain placement from 28% in the first quartile to 6% in the last quartile ($p < 0.005$). Hormonal remission for secreting adenomas increased from 68% in the first quartile to 90% in the last quartile ($p < 0.05$). The rate of post-operative CSF leak trended lower (3% in first quartile to 0.7% in last two quartiles). The greatest improvement in outcome occurred between the first and second quartiles (19.9%), but persistent improvement occurred between the second and third (6.7%) and third and fourth quartiles (8.0%).

Conclusion Although the slope of the learning curve is steeper earlier in a surgeon's experience, the slope does not plateau and continues to increase even over more than a decade.

Keywords Endonasal · Endoscopic · Transsphenoidal · Follow-up · Outcomes · Learning curve · Tail end · Complication · Surgery · Gross total resection

Introduction

Endonasal endoscopic transsphenoidal surgery (EETS) for pituitary adenoma has evolved over the last 20 years to become a mainstay of treatment. The transsphenoidal approach was first successfully carried out by Hermann Schloffer in 1907. It was further refined by Harvey Cushing who performed the sublabial procedure, Oskar Hirsch who introduced the endonasal procedure, and Jules Hardy who introduced fluoroscopy and the microscope in transsphenoidal surgery [19]. With the introduction of perioperative antibiotics, mortality from the endonasal transsphenoidal procedure fell to around 1.5% [11, 14, 26]. Recent technical advances in endoscopes, monitors, stereotaxis, and the development of extended endonasal approaches and reliable closure techniques have pushed the field into the forefront of modern skull base surgery [5, 13, 28].

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A handful of studies have reported a learning curve from the earliest cases, where the authors were inexperienced or were not using advanced closure techniques [3, 6, 16, 18, 20, 22, 27, 31]. However, few studies have looked at the slope of the "tail end" of the learning curve to analyze which outcomes, if any, continue to improve over time and at what rate of change. In another paper in which we examined a variety of pathologies, our group showed that after the initial learning curve is overcome, improvements can occur even after several hundred cases for the most complex outcome measures [36]. In that paper, the earliest cases were excluded to avoid the presumed initial steep slope of the learning curve. In this paper, we examined our entire series of pituitary tumors to see if the rate of improvement changes from the earliest cases to those performed later in a surgeon's career and to measure the slope of the learning curve over time.

Methods

Patient population and surgical approach

The authors analyzed a prospectively acquired database of a consecutive series of EETS from 2004 to 2018 at a large tertiary academic medical center and selected only those cases with final histologic diagnosis of pituitary adenoma. Some of these cases were reported in a prior publication; however, additional cases were added to this series to increase the numbers substantially and provide a more comprehensive overview of our adenoma experience [36]. These cases were divided evenly into quartiles for analysis. The study was approved by our institutional review board and individual patient consent was not required. No funding was received for this study. All surgeries were performed by the senior author. 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.

Patient demographics, clinical characteristics, and complications

A password-protected database was used to prospectively collect data for every EETS case including name, medical record number, date of surgery, final pathology, use of lumbar drainage, presence of intraoperative CSF leak, closure technique/graft materials used, and occurrence of post-operative CSF leak. Additional data collected and analyzed retrospectively for each case included patient's sex, age, follow-up period, procedure length, radiographic extent of resection based on review of post-operative MRI by a board-certified neuroradiologist performed within a week after surgery, previous surgery, previous radiation, confirmation of final pathology, endocrine outcomes, and complications. Pre- and post-op MRIs were reviewed by the authors and max tumor diameter in any plane was reported for tumor size. Post-op MRI was done 2 days after surgery, which has been shown to be the most accurate measure of extent of resection [1, 24]. Biochemical remission for prolactinomas was determined by normalization of serum prolactin levels < 20 μg/L, for GH-producing tumors by normalization of serum growth hormone (GH) < 1 μg/L or nadir GH after oral glucose tolerance test (OGTT) ≤ 0.4 μg/L, and for ACTH-producing tumors by morning serum cortisol < 3 μg/dL 3–5 days after surgery. Complications were tracked in the immediate post-operative period and at long-term follow-up. Post-operative CSF leak was defined as clear CSF rhinorrhea, confirmed by the senior author, where re-reoperation was required for repair.

Statistical analysis

The SPSS v.24 (IBM Inc., Armonk, New York) statistical software package 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 < 0.05.

Results

Patient demographics and clinical characteristics

A consecutive series of 600 EETS for pituitary adenoma were included in the study and grouped into quartiles based on date of surgery. The cohort comprised 295 (49%) females and 305 (51%) males (Table 1). The mean age for the cohort was 52.0 ± 15 years. There were no differences in age or sex between quartiles. Re-operations accounted for 75 (13%) cases in the cohort and functioning adenomas accounted for 159 (27%) cases. The number of months in each quartile decreased from 72 months in the first quartile, 38 months in the second quartile, 36 months in the third quartile, and 30 months in the last quartile. These numbers indicate an increase in the volume at our center of 91% between the first and second quartiles, 27%

Table 1 Demographics and clinical characteristics of cohort

Variable	*N* (%)
Sex	295 F (49%)
	305 M (51%)
Age	52.0 ± 15 yrs.
Re-operations	75 (13%)
Functioning	159 (27%)

between the second and third quartiles, and 29% between the third and fourth quartiles.

Tumor characteristics

Tumor size was not significantly different between quartiles (Table 2). Mean tumor size was 23.3 ± 9.1 in the first quartile, 24.5 ± 9.4 in the second, 22.5 ± 10.5 in the third, and 23.3 ± 9.2 in the last quartile. Cavernous sinus invasion was present in 19%, 25%, 29%, and 27% of cases in the first through last quartiles respectively (NS). For the whole group, the rate of GTR significantly increased across quartiles from 55 and 68% in the first and second quartiles to 70% and 79% in the latter quartiles ($p < 0.005$) (Fig. 1). We examined the rate of GTR in first time operations only and found the rate significantly increased from 60 to 65 to 73 to 80% from first to last quartile respectively ($p < 0.005$). Since most hormone-producing adenomas represent smaller tumors, we separately examined the rate of GTR exclusively for the non-functioning adenomas. The rate of GTR for non-functioning tumors significantly increased across quartiles from 56 to 75 to 65 and finally to 89% in the latter quartiles ($p < 0.005$). The rate of intraoperative CSF leak significantly decreased, as did the rate of lumbar drain placement between quartiles ($p < 0.005$) (Fig. 2). The rate of lumbar drain placement for cases that had an intraoperative CSF leak also significantly decreased from 47% in the first and second quartile to 32% and 18% in the third and last quartile respectively ($p < 0.005$).

Rate of complications and post-op CSF leak

The rate of any complication did not significantly change between quartiles (Table 2). The rate of any complication was 4.7% in the first quartile, 3% in the second quartile, 2.7% in the third quartile, and 3% in the last quartile. The rate of post-operative CSF leak also did not significantly change between quartiles, although it did show a declining trend from 3% in the first quartile, 1.3% in the second quartile to 0.7% in the third and last quartiles. There was 1 case of vascular injury to the ICA and 1 death from pulmonary embolism, both of which occurred the first quartile.

Closure type

Closure with fat only was significantly more common in the first quartile (59%) and decreased to 8% and 7% in the third and fourth quartiles respectively ($p < 0.05$; Table 3). There was a significant increase in closure with nasoseptal flap + fat in the latter quartiles (37% second quartile, 46% third quartile, 53% fourth quartile) compared to the first quartile (17%; $p < 0.05$). Closure with nasoseptal flap also significantly increased from the first quartile (9%) to 21% in both third and fourth quartiles ($p < 0.05$). Closure with gelfoam only, or gasket + nasoseptal flap + fat, was not significantly different between quartiles.

Endocrine outcomes

Non-functioning adenomas accounted for 73% of the cohort (Table 4). The remainder were prolactinomas (11%) and GH (9%)- and ACTH (6%)-producing adenomas. For non-functioning adenomas, the rate of normal endocrine outcome increased for each quartile from 81 to 84 to 87 to 90%, a non-statistically significant trend (Fig. 3). Remission rates for hormone-producing tumors increased significantly over time when grouped together. The remission rate was 68% in the first quartile, 78% in the second, 88% in the third, and 90% in the last quartile ($p < 0.05$). The remission rates increased for each subtype of hormone-producing adenoma but there were insufficient numbers to reach statistical significance (Fig. 4).

Table 2 Comparison of tumor characteristics between quartiles

Variable	first quartile	Second quartile	Third quartile	Last quartile	*p* value
Tumor size (mm)	23.3 ± 9.1	24.5 ± 9.4	22.5 ± 10.5	23.3 ± 9.2	NS
Cavernous sinus invasion	28 (19%)	37 (25%)	44 (29%)	41 (27%)	NS
GTR overall	83 (55%)	102 (68%)	105 (70%)	118 (79%)	*< 0.005*
GTR excl. re-op	73/122 (60%)	90/138 (65%)	94/129 (73%)	109/136 (80%)	*< 0.005*
GTR non-functioning	61/109 (56%)	85/113 (75%)	72/110 (65%)	97/109 (89%)	*< 0.005*
Intra-op CSF leak	90 (60%)	68 (45%)	62 (41%)	50 (33%)	*< 0.005*
Lumbar drain placement	42 (28%)	32 (21%)	20 (13%)	9 (6%)	*< 0.005*
Lumbar drain with intra-op CSF leak	42 / 90 (47%)	32 / 68 (47%)	20 / 62 (32%)	9 / 50 (18%)	*< 0.005*
Any complication	7 (4.7%)	5 (3%)	4 (2.7%)	5 (3%)	NS
Post-op CSF leak	5 (3%)	2 (1.3%)	1 (0.7%)	1 (0.7%)	NS

Italics represents statistical significance

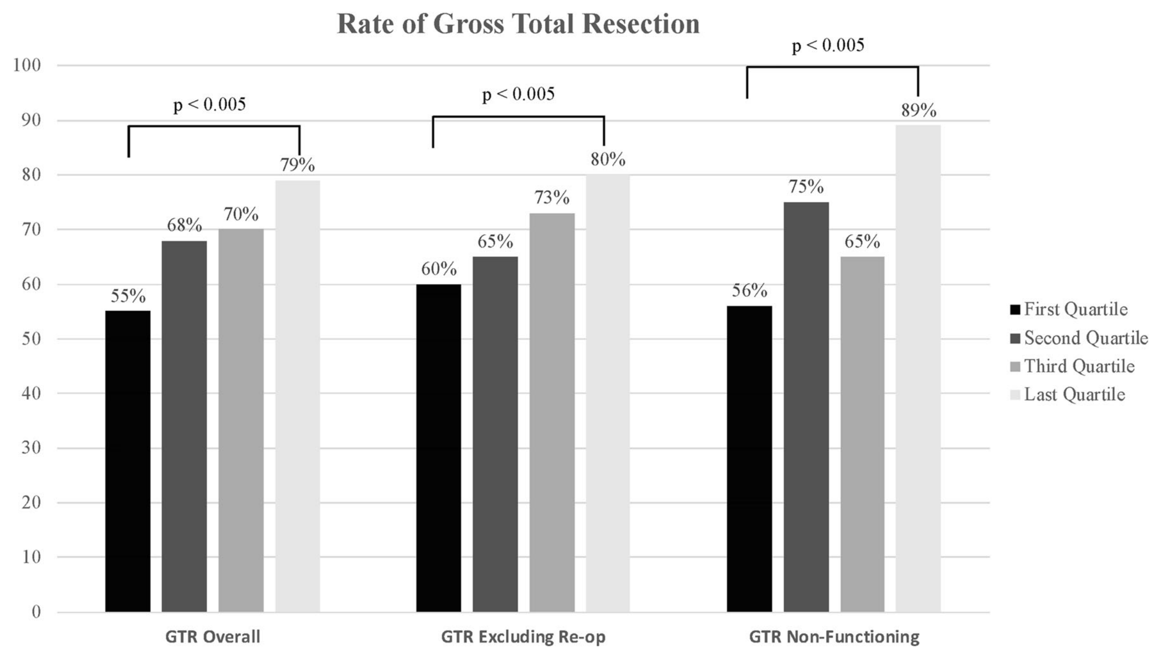

Fig. 1 The rate GTR by quartile for all patients as well as only first time operations or only non-functional tumors. Comparison of first quartile (black bars), second quartile (dark gray), third quartile (light gray), and last quartile (silver)

Vision and cranial neuropathy outcomes

There were no statistically significant differences in pre- and post-operative vision across quartiles (Table 5). Pre-operative vision was normal in 47–55% across quartiles and a deficit was present in 45–53%. Post-operatively, 93% had normal vision in the first quartile, 88% in the second quartile, 83% in the third quartile, and 89% in the last quartile (NS). None had worse post-operative vision in the first quartile, 1% had worse vision in the second quartile, 3% in the third quartile, and none in the last quartile (NS). Pre-operative cranial neuropathy was present 3% in the first quartile, 3% in the second quartile, 1% in the third quartile, and 1% in the last quartile (NS). Post-operatively, 1% continued to have a deficit in the first and second quartiles and 0.5% in the third and last quartiles.

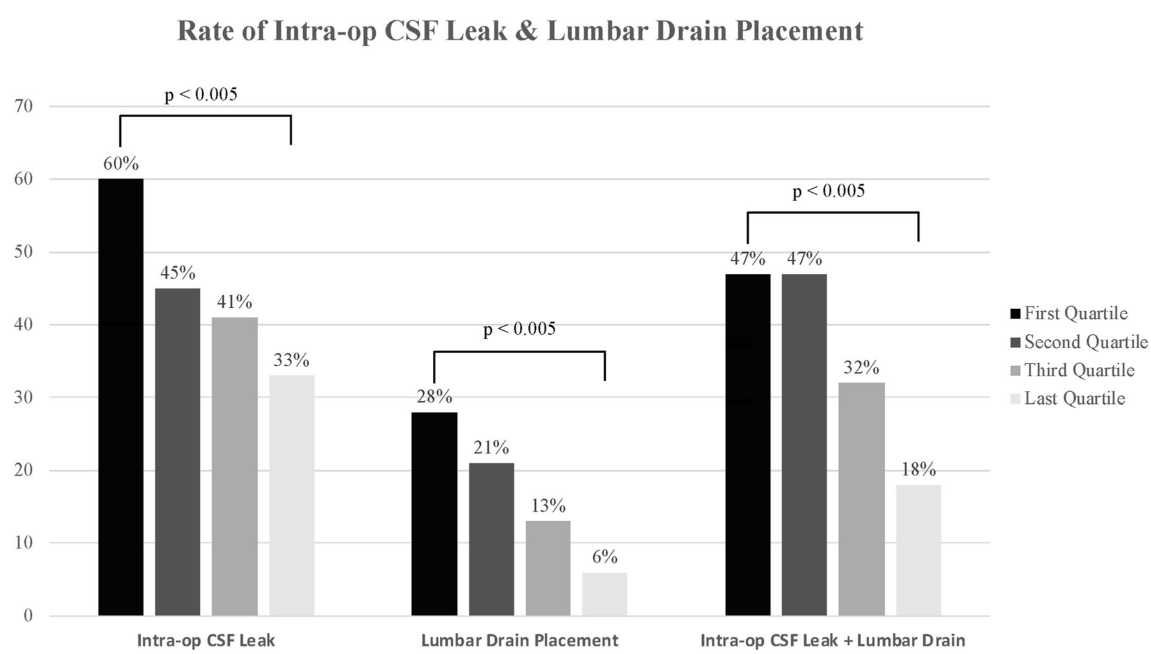

Fig. 2 The rate of intraoperative CSF leak and lumbar drainage for all patients and only patients with intraoperative CFS leak. Comparison of first quartile (black bars), second quartile (dark gray), third quartile (light gray), and last quartile (silver)

Table 3 Summary of closure technique by quartile

Closure	First quartile	Second quartile	Third quartile	Fourth quartile	*p* value
Nasoseptal flap ± fat	25 (17%)	55 (37%)	69 (46%)	80 (53%)	*< 0.05*
Fat	88 (59%)	32 (21%)	12 (8%)	10 (7%)	*< 0.05*
Nasoseptal flap	13 (9%)	23 (15%)	31 (21%)	31 (21%)	*< 0.05*
Gelfoam only or nothing	22 (14%)	38 (25%)	35 (23%)	25 (17%)	NS
Gasket + nasoseptal flap + fat	2 (1%)	2 (1%)	3 (2%)	4 (3%)	NS

Italics represents statistical significance

Slope of the learning curve

Although improvement occurred between every quartile, indicating persistent skill development, we examined those measures in which significant improvements occurred to determine between which quartiles we found the biggest improvements. The largest change occurred in our ability to avoid intraoperative CSF leak, an improvement of 37.5% between the first and second quartiles (Table 6). The second largest improvement occurred in the rate of GTR, an improvement in 23.6%, between the first and second quartiles. The next largest improvement was the endocrine remission rate, which improved by 14.7%, again between the first and second quartiles. The largest improvement between the second and third quartiles was again the endocrine remission rate which improved by an additional 12.8%. Finally, the greatest late improvement occurred in both avoidance of intraoperative CSF leak of 13.6% and GTR rates, of 12.9% between the third and fourth quartiles. If we combine all the results in which significant improvements occurred (GTR rates, endocrine remission rates, achieving normal hormone outcome, and avoiding intraoperative CSF leak), the increase between the first and second quartiles was 19.9%, between the second and third quartile was 6.7%, and between the third and fourth quartile was 8.0%.

Discussion

This article reports the results of a large consecutive series of EETS for pituitary adenoma and documents the significant changes in outcome that can occur even after several hundred cases. Many studies have reported the steep initial learning curve in EETS for pituitary adenoma [3, 6, 16, 18, 20, 22, 27, 31] but the assumption is that once a certain number of cases have been performed, there is a plateau in proficiency. Our data shows that even for a surgery considered relatively straightforward, such as resection of a pituitary adenoma, there are improvements in technique that continue for several years over hundreds of cases. These results mirror those we recently reported for a larger series of EETS with mixed pathology [36]. In that paper, the initial 200 cases were eliminated to remove the early learning curve. In this series, we included our earliest cases to compare the early with the late components of the learning curve. Our results indicate that once a surgeon has finished residency training, the classic S-shaped learning curve may not be an accurate depiction of surgical skill acquisition and will vary depending on the outcome being measured. Although the slope of the learning curve is steeper for the first few years after practice, the late plateau is not flat but shows a persistent positive slope indicating continued improvement.

The slope of the learning curve

The 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 [34]. 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 [2, 7, 12, 15, 17,

Table 4 Comparison of endocrine outcomes between quartiles

Tumor subtype (%)	Endocrine outcome	First quartile	Second quartile	Third quartile	Last quartile	*p* value
Non-functioning	Normal	88 (81%)	95 (84%)	96 (87%)	99 (90%)	NS
	Panhypopituitarism	11 (10%)	8 (7%)	5 (5%)	4 (4%)	
	Mixed or single axis	10 (9%)	10 (9%)	9 (8%)	6 (6%)	
All functional	Hormonal remission	28 (68%)	28 (78%)	35 (88%)	38 (90%)	*< 0.05*
	Not cured	13 (32%)	8 (22%)	5 (12%)	4 (10%)	
Prolactinoma	Hormonal remission	14 (74%)	12 (80%)	14 (93%)	16 (89%)	NS
	Not cured	5 (26%)	3 (20%)	1 (7%)	2 (11%)	
GH-producing	Hormonal remission	10 (67%)	8 (73%)	13 (87%)	11 (92%)	NS
	Not cured	5 (33%)	3 (27%)	2 (13%)	1 (8%)	
ACTH-producing	Hormonal remission	4 (57%)	8 (80%)	8 (80%)	10 (91%)	NS
	Not cured	3 (43%)	2 (20%)	2 (20%)	1 (9%)	

Italics represents statistical significance

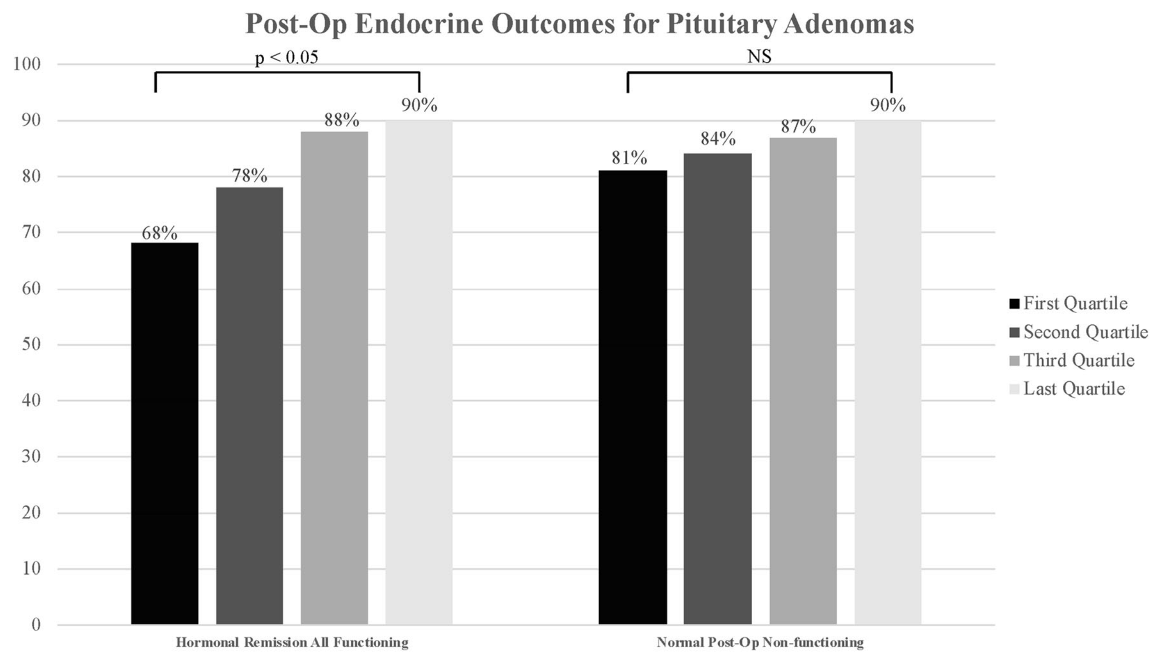

Fig. 3 Post-operative hormonal remission rate for functional adenomas and normal function for non-hormone-producing tumors. Comparison of first quartile (black bars), second quartile (dark gray), third quartile (light gray), and last quartile (silver)

25, 29, 30, 35]. 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 [8, 9]. This is generally felt to be anywhere from 35 to 200 cases. The slope of the early learning curve is dependent on the skill of the trainee, the complexity of the procedure, and number of repetitions [32]. EETS is no exception and several reports have described the early learning curve associated with endonasal endoscopic approaches to pituitary tumors. For example, Jakimovsky et al. showed that for adenomas, CSF leak rates decreased dramatically after the first 50 cases (0.7% vs. 10%; $p < 0.005$) [10]. Qureshi et al. investigated the learning curve for the endoscopic approach to pituitary adenomas in 78 patients divided into an early and late group [27]. They found a significant reduction in operating time and intraoperative CSF leaks between the early and late

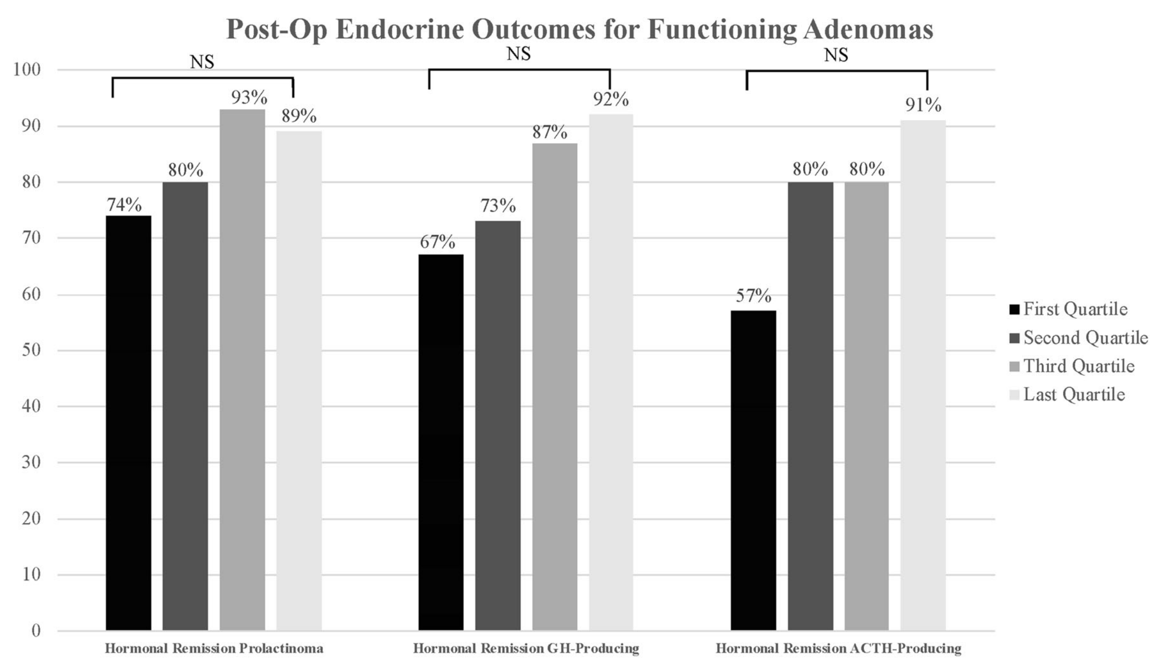

Fig. 4 Post-operative remission rates of subgroups of hormone-producing tumors show non-significant increases for all subtypes. Comparison of first quartile (black bars), second quartile (dark gray), third quartile (light gray), and last quartile (silver)

Table 5 Comparison of vision outcomes and cranial neuropathy between quartiles

Variable	First quartile	Second quartile	Third quartile	Last quartile	*p* value
Pre-op vision					NS
Normal	82 (55%)	71 (47%)	78 (52%)	70 (47%)	
Deficit	68 (45%)	79 (53%)	72 (48%)	80 (53%)	
Post-op vision					NS
Normal	139 (93%)	132 (88%)	125 (83%)	133 (89%)	
Stable	11 (7%)	16 (11%)	20 (13%)	17 (11%)	
Worse	0	2 (1%)	5 (3%)	0	
Pre-op cranial neuropathy					NS
Normal	145 (97%)	146 (97%)	148 (99%)	148 (99%)	
Deficit	5 (3%)	4 (3%)	2 (1%)	2 (1%)	
Post-op cranial neuropathy					NS
Normal	145 (97%)	146 (98%)	148 (99%)	148 (99%)	
Improved	3 (2%)	2 (1%)	1 (0.5%)	1 (0.5%)	
Deficit	2 (1%)	2 (1%)	1 (0.5%)	1 (0.5%)	

groups but found no difference in hospital length of stay or visual field improvement. The same is true in other fields of surgery. Ooman et al. find the plateau of the learning curve after only 35 laparoscopic pyloromotomies, and Voitk et al. define the plateau of the learning curve after 200 laparoscopic cholecystectomies [23, 33]. Our data indicates that the shape of the classic learning curve, with an initially very steep slope and a later plateau, is likely not accurate and may vary depending on the outcome measure.

The classic curve starts out at point 0, which is a moment of complete ignorance. Once a resident has finished training, there is already significant competence and, in fact, the surgeon is considered able to perform most surgical procedures independently with acceptable outcomes. Thus, the post-training surgical curve starts out well above 0 and as such, rapid progress with such a steep slope does not occur. Nevertheless, our data shows that there is a linear increase in results and that the initial slope (first to second quartile) is clearly steeper than the later slope. Second, the plateau is clearly not reached after only 100–200 cases if ever reached. Indeed, the slope between the third and fourth quartiles was slightly steeper than that between the second and third quartiles. These results demonstrate that linear increases in skill and outcome occur even after 450 cases of the same surgical procedure. Apparently, a surgeon's training, skill acquisition, and outcome improvement can be measured in decades rather than years.

The learning curve depends on the outcome measure

As we showed in our earlier paper involving a variety of different pathologies, the most complex tasks have the longest learning curve. For example, although gross total removal of craniopharyngiomas, meningiomas, and chordomas increased even after 700 cases, complications and CSF leak rates remained stable [36]. One explanation may be that CSF leak can be stabilized based on algorithms and standard critical pathways for managing post-operative patients. However, the skillset, experience, and anatomical knowledge required to perform delicate microdissection around critical neurovascular structures defy most systematized or regimented teaching curriculum 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. Support for this conclusion can be found in a study done by Subramonian et al. in which they gave a group of medical students intense surgical training for 12 weeks in open and laparoscopic surgery [32]. At the end of their training period, while their overall

Table 6 Change in slope between quartiles

Variable	1st to 2nd quartile (%)	2nd to 3rd quartile (%)	3rd to 4th quartile (%)
GTR overall	23.6	2.9	12.9
Normal post-op hormones	3.7	3.6	3.4
Hormonal remission	14.7	12.8	2.3
No Intra-op CSF leak	37.5	7.3	13.6
Average	19.9	6.7	8.0

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 two-dimensional perception when compared to open surgery and required more operative time. We did not include procedure length because studies have demonstrated that the classic S-shaped curve fails to adequately characterize operative time since surgeons tend to take on more complex cases and spend more time teaching once they gain proficiency and so operative time may increase in the tail end of the curve [25, 36]. 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 upwards for several years or even decades.

The learning curve in adenoma surgery

In surgery for pituitary adenomas, the goals of surgery differ based on the histological subtype. For non-functioning adenomas, which tend to be larger in size and present with optic chiasmal compression, the goal is to remove as much tumor as possible while preserving pituitary function and minimizing post-operative CSF leak. Minimizing intraoperative CSF leak is a secondary goal. For non-hormone-producing tumors, GTR rates of 56% as found in the first quartile or even 75% as found in the second quartile would seem to be fairly good for a benign tumor that can take years to grow back and which can also be managed with radiosurgery. However, in our last quartile, our GTR rates were 89%, which clearly would result in fewer recurrences and reduced need for radiation therapy to residual tumor. Similarly, intraoperative CSF leaks do not necessarily reveal themselves as important unless they result in post-operative CSF leaks. However, an intraoperative CSF leak requires a second incision for a fat graft, and possibly a lumbar drain and longer hospital stay which increases cost. These costs are not necessarily appreciated, since they are generally not tracked. However, our ability to reduce intraoperative CSF leak from 60 to 33% and reduce our need for lumbar drains from 28 to 6% certainly decreased overall costs to the hospital. The metric that is usually tracked is post-operative CSF leak. However, the decline over time from 3 to 0.7% was not significant given the small numbers and may not cross the radar as an important reduction in morbidity. Hence, the metric that is tracked is not necessarily the most important metric and may not accurately reflect the learning curve of the surgeon.

For hormone-producing tumors, which tend to be smaller in size, the goal is to remove the entire tumor to achieve an endocrinologic remission. As we have shown in our first quartile results, even early in a surgeon's career, the results can be fairly good and unless one is carefully tracking their results, it will be difficult to compare with other centers with more experience. To be more specific, the remission rates in the second quartile of 78% appear to be in line with national averages. Nevertheless, in our fourth quartile, remission rates as high as 90% were achieved. The ability to reliably identify the pituitary tumor pseudocapsule and perform an *en bloc* resection of a functional microadenoma is difficult and requires several years to master [21]. Likewise, the intraoperative decision-making required to identify the likely location of an MRI-negative ACTH-producing tumor similarly requires years of experience. Ciric et al. analyzed data from over 950 respondents and found that complications in transsphenoidal surgery are significantly higher in the hands of less experienced surgeons. However, the authors' rightfully point out that caution should be exercised in interpreting these data because they are based on respondents' self-reported estimates. Nonetheless, the results of our study echo what has been shown in prior articles, namely that the expertise of the surgeon has a significant impact on the outcome, which is the crux of the argument for the development of pituitary tumor centers of excellence [4, 6].

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 limitation is our inability to perfectly characterize the case mix index complexity. We used tumor size, cavernous sinus invasion, and ratio of function to non-functional tumors as our surrogate, which provided a general measure of complexity. We provide endocrine outcomes for all cases based on most recent follow-up. However, long-term follow-up of hormone outcome is not known. We do not have the power to perform a multivariate analysis since our sample size was diluted into four smaller groups to analyze based on quartile.

Conclusion

This article reports the results of a large consecutive series of EETS for pituitary adenoma and documents the slope of the learning curve over time. We show that although the initial slope is 2–3 times the later slope, there is never a plateau, particular for the more complex aspects of the surgery. Finally, this study further emphasizes that pituitary surgery requires years and hundreds of cases to reach a high level of proficiency and that results at high volume centers will be better than at lower volume centers. Unless complex outcome measures are tracked, these results will not be appreciated by hospitals, patients, and insurance companies.

Compliance with Ethical Standards

For this type of study formal consent is not required.

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee (name of institute/committee) and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

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