



# The impact of surgeon's academic leave on surgical outcomes for endoscopic transsphenoidal resection of pituitary tumors

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**Background:** Endoscopic surgery has become the mainstay of pituitary surgery, but requires comprehensive surgical training. We evaluate the impact of a surgeon's academic leave during endoscopic training on surgical outcomes of patients with pituitary tumors.

**Methods:** This retrospective study reviewed the surgical outcomes of endoscopic transsphenoidal surgery for pituitary tumors performed by a single surgeon. The last 56 surgical cases were performed between July 2010 and August 2014 before academic leave (Phase 1 surgery group), while another 56 consecutive cases were performed between November 2017 and March 2020 immediately after the surgeon's academic leave (Phase 2 surgery group). Demographic and clinical characteristics were collected and compared between the two surgery groups.

**Results:** Overall, most surgical outcomes of endoscopic transsphenoidal surgery were not affected adversely by the period of academic leave. The operative time and length of hospital stay was lower in the Phase 2 surgery group compared to the Phase 1 surgery group ( $P < 0.05$ ). Postoperative tumor residual, intraoperative cerebrospinal fluid (CSF) leaks and reoperation also decreased significantly in the Phase 2 group compared to the Phase 1 group ( $P < 0.05$ ). Similar results were observed in patients operated using a one-hand/mono-nostril and two-hand/one-and-half nostril technique.

**Conclusions:** Academic leave had no negative impact on most surgical outcomes for endoscopic transsphenoidal resection of pituitary tumors. Moreover, a trend toward shorter operative times and length of hospital stays was noted for patients receiving surgery immediately after surgeon's return from leave.

**Keywords:** Academic leave; endoscopic transsphenoidal surgery; pituitary tumor

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## Introduction

Pituitary tumors are the second most common primary brain tumors, with an adult prevalence of approximately 1 in 1,000 (1). The development of the endoscopic approach to pituitary tumours in the 1990's has yielded superior rates of gross total resection and hormone control when compared to the traditional microscopic approach (2,3). In addition, endoscopic resection is associated with lower rate

of diabetes insipidus and shorter hospital stay (2). However, endoscopic endonasal transsphenoidal pituitary surgery can be challenging, and surgical outcome depends on surgeon's experience using the technique (4-6).

Individual surgeon outcome improves with accumulation of surgical experience (7). A survey questionnaire found a significant drop in all morbidity and mortality after 200 cases experience (4), with another study reporting

a continued improvement in the rate of postoperative cerebrospinal fluid (CSF) leaks up to 100 cases experience, and operative time up to 120 cases (8). These suggest that a sustainable surgical volume is required in learning endoscopic resection of pituitary tumors.

However, breaks from surgical practice may be necessary for maternity, paternity, family, extended travel, or study leave. There are some concerns over potential loss of surgical competency in countries where surgeons take long maternity or parental leave (9,10). The maximum ‘safe’ time away from surgical practice is unknown, but the best evidence suggests a degradation of surgical skill becomes measurable after 6–18 months (11). This “skills fade” implies a potential loss of surgical skill and consequent effect on patient outcome and safety following such breaks in training.

MD-PhD programs are becoming increasingly popular (12), but this potential “skills fade” may need considering by neurosurgeons in training contemplating a higher academic degree: measuring it would support neurosurgeons, their employers, and their regulatory bodies identify means of addressing any training or support needs to mitigate “skills fade” and minimize risk to patients. However, to date, no studies have correlated surgeons’ academic leave with patient surgical outcome, particularly

among neurosurgeons. In this study, we evaluate the effect of a break from surgical practice (academic leave) on surgical outcome following endoscopic transsphenoidal surgery for pituitary tumor. We present this article in accordance with the STROBE reporting checklist (available at <https://gs.amegroups.com/article/view/10.21037/gS-23-347/rc>).

## Methods

### *Patient and public involvement*

This retrospective study reviewed the surgical outcomes of endoscopic transsphenoidal surgery for pituitary tumors performed by a single surgeon. The last 56 surgical cases were performed between July 2010 and August 2014 before academic leave (Phase 1 surgery group), while another 56 consecutive cases were performed between November 2017 and March 2020 immediately after the surgeon’s academic leave (Phase 2 surgery group). These patients were not asked to assess the burden of the intervention and time required to participate in the research.

### *Study design and patient population*

We retrospectively reviewed surgical outcome after endoscopic transsphenoidal resection of pituitary tumors performed between July 2010 and March 2020 by a single surgeon (J.L.Y.). Phase 1 was defined as the 56 consecutive cases performed preceding academic leave for full-time PhD study (July 2010 to August 2014). Phase 2 was defined as the 56 consecutive cases performed after returning to full time practice (November 2017 to March 2020). The neurosurgeon attended the clinical neuroscience PhD academic training program in the UK as a full-time student and did not perform any clinical work during the study leave. The topic of his PhD thesis was “Characterising Peritumoural Progression of Glioblastoma using Multimodal magnetic resonance imaging (MRI)”. Surgery for pituitary carcinoma, double tumor of the sellar region, and patients without postoperative MRI scan follow-up at 6 months were excluded.

### *Ethics approval*

The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the Institutional Review Board of Chang Gung

## Highlight box

### Key findings

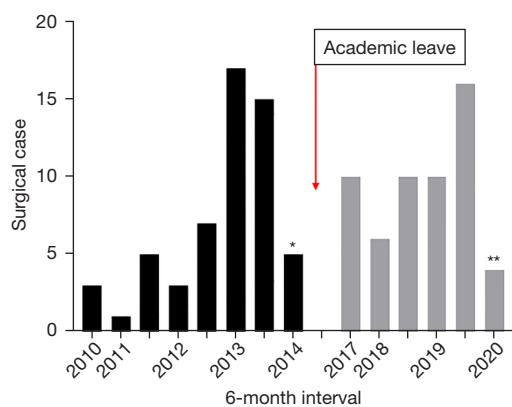
- Surgical skills are not significantly eroded after a period of not being exercised. Most endoscopic transsphenoidal surgical outcomes of pituitary tumors were not affected adversely by academic leave.

### What is known and what is new?

- The maximum ‘safe’ time away from surgical practice is unknown, but the best evidence suggests a degradation of surgical skill becomes measurable after 6–18 months. This is the first study to evaluate the impact of a break from clinical work. We looked at the impact of neurosurgeon academic leave (3 years) on the surgical outcome of endoscopic transsphenoidal surgery in patients with pituitary tumor using a single-surgeon with one-hand/mono-nostril or a two-hand/one-and-half nostril approach.

### What is the implication, and what should change now?

- Our results support the hypothesis that surgical skills are not significantly eroded by a period of academic leave, which provides the evidence for many neurosurgeons who want an academic leave in order to pursue research-oriented careers and to meet the growing complexities in clinical care.



**Figure 1** Surgical cases presented in 6-month intervals. Fifty-six cases were performed in Phase 1 (July 2010 to August 2014; before academic leave), and 56 in Phase 2 (November 2017 to March 2020; after academic leave). The author attended a full-time clinical neuroscience PhD academic program in the UK, during which no clinical work was performed. \*, until August 2014. \*\*, until March 2020.

Memorial Hospital (No. 201901259B0C602) and waived the need for patient informed consent because the study classified as retrospective study with expedited review.

### Data collection and analysis

Demographic, description of tumor and clinical characteristics were collected and compared between the two surgery groups. The tumor volume was calculated based on the preoperative MRI. Tumor invasion was assessed using the parasellar extension as assessed by Knop's classification and Hardy suprasellar extension grading. Extent of tumor resection and intra-operative CSF were evaluated by the surgeon during the operation, and postoperative MRI scan was obtained for evaluation of residual tumor at 3–6 months follow-up. After follow-up, the operative time, duration of hospital stays, visual field change, residual tumor, diabetes insipidus, hypopituitarism, postoperative radiotherapy and CSF leaks, nasal and surgical complications, endocrine function, and reoperations for CSF leak and nasal complications were analyzed and compared between these two groups.

### Surgical procedure

Endoscopic endonasal transsphenoidal surgery was carried out using either a one-hand/mono-nostril or a two-hand/

one-and-half nostril approach [as described in our previous study (13)], with the assistance of an endoscope holder (Martin Arm, Karl Storz, Germany). Surgical approach and equipment was unchanged between Phase 1 and Phase 2.

The surgical procedure with one-hand/mono-nostril or two-hand/one-and-half nostril approach was performed as described in our previous study (13).

### Statistical analysis

Continuous variables were represented as median or mean with the corresponding standard deviation (SD), and comparison between groups was performed with the independent-sample *U*-test. Categorical variables were expressed as number (percentage), and comparison between categorical variables were analyzed using the chi-square test or Fisher's exact test. A univariate regression model was used to determine the effects of academic leave on operation-related cumulative volume of postoperative residual tumor, intra-operative CSF leak, and need for repeat surgery. A *P* value of <0.05 was considered statistical significant. SPSS statistical software package Version 22.0 for Windows (SPSS, IBM Corp., Armonk, NY, USA) was used for all statistical analyses.

## Results

### Patient characteristics

Our retrospectively collected series of endoscopic transsphenoidal pituitary resection performed by a single surgeon between July 2010 and March 2020 consisted of 112 operations (*Figure 1*). Fifty-six patients were in Phase 1 (20 males, 36 females) with a mean age of  $45.8 \pm 14.7$  years; 36/56 (64.3%) were clinically non-functioning tumors. Fifty-six patients were in Phase 2 (27 males, 29 females) with a mean age of  $51.7 \pm 15.2$  years; and 39/56 (69.6%) were clinically non-functioning tumors (*Table 1*). No significant differences were found between groups in gender, tumor type, preoperative tumor volume, previous surgery, history of apoplexy or surgical approach ( $P > 0.05$ ; *Table 1*). The mean age in Phase 1 was lower than Phase 2 ( $P = 0.037$ ).

### Surgical outcomes

The distribution of operative time and hospital stay by case number are shown in *Figure 2A, 2B* for Phase 1 and Phase 2. Significantly lower operative times and hospital

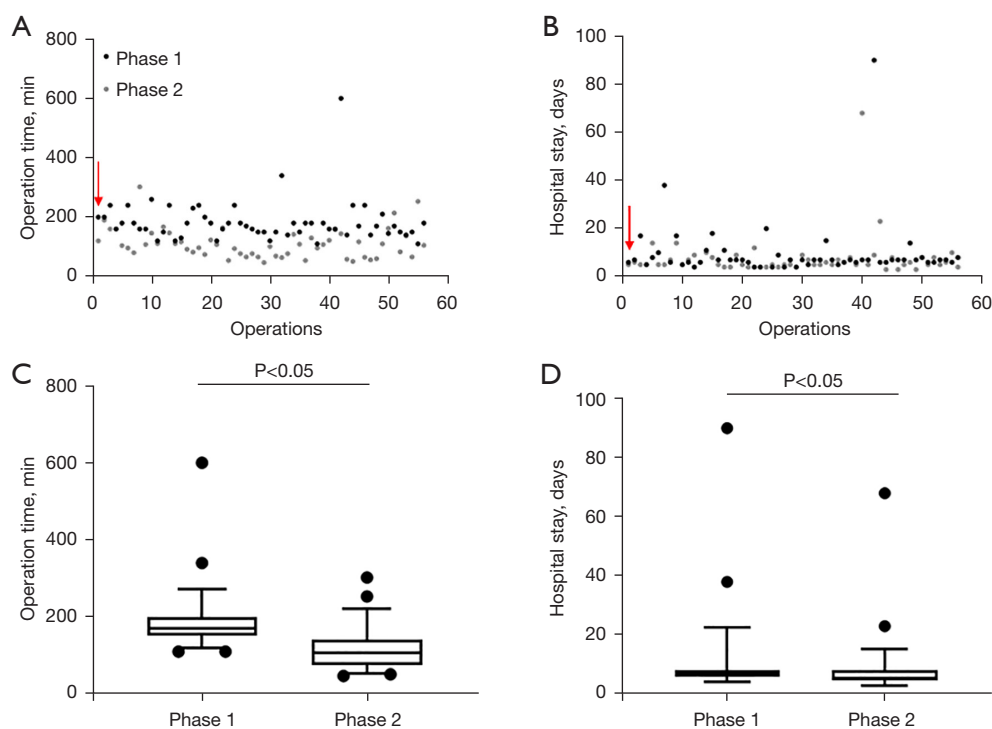
**Table 1** Patient demographics and clinical characteristics

| Variable                                     | Phase 1 (n=56) | Phase 2 (n=56) | P value |
|----------------------------------------------|----------------|----------------|---------|
| Age (years)                                  | 45.8±14.7      | 51.7±15.2      | 0.037*  |
| Gender, male                                 | 20 (35.7)      | 27 (48.2)      | 0.251   |
| Tumor type                                   |                |                | 0.688   |
| Non-functional                               | 36 (64.3)      | 39 (69.6)      |         |
| Functional                                   | 20 (35.7)      | 17 (30.4)      |         |
| Prolactin                                    | 6 (10.7)       | 9 (16.1)       |         |
| Growth hormone                               | 13 (23.2)      | 3 (5.4)        |         |
| Thyroid stimulating hormone                  | 0 (0.0)        | 2 (3.6)        |         |
| ACTH                                         | 1 (1.8)        | 3 (5.4)        |         |
| Previous operation                           | 7 (12.5)       | 10 (17.9)      | 0.599   |
| Apoplexy                                     | 20 (35.7)      | 14 (25.0)      | 0.304   |
| Preoperative tumor volume (cm <sup>3</sup> ) | 6.4±10.0       | 6.1±8.4        | 0.534   |
| Size of tumor                                |                |                |         |
| Microadenoma                                 | 8              | 13             |         |
| 10–30 mm                                     | 29             | 24             |         |
| >30 mm                                       | 19             | 19             |         |
| Knop's grade                                 |                |                | 0.645   |
| 0                                            | 5 (8.9)        | 7 (12.5)       |         |
| 1                                            | 11 (19.6)      | 14 (25.0)      |         |
| 2                                            | 13 (23.2)      | 10 (17.9)      |         |
| 3                                            | 14 (25.0)      | 17 (30.4)      |         |
| 4                                            | 13 (23.2)      | 8 (14.3)       |         |
| Hardy suprasellar extension                  |                |                | 0.325   |
| A                                            | 17 (30.4)      | 19 (33.9)      |         |
| B                                            | 22 (39.3)      | 15 (26.8)      |         |
| C                                            | 12 (21.4)      | 19 (33.9)      |         |
| D                                            | 5 (8.9)        | 3 (5.4)        |         |
| Surgical approach                            |                |                | 0.088   |
| One-hand                                     | 35 (62.5)      | 25 (44.6)      |         |
| Two-hand                                     | 21 (37.5)      | 31 (55.4)      |         |

Data are presented as number, n (%) or mean ± SD. \*, P<0.05. ACTH, adrenocorticotropic hormone; SD, standard deviation.

stay were found in Phase 2 (P<0.05; *Figure 2C,2D, Table 2*). After 3 months follow-up, no significant differences (extent of resection on postoperative MRI, correction of endocrine dysfunction, improvement in visual fields, or need for postoperative radiotherapy) were found between

the two groups (P>0.05; *Table 2*). Similarly, there was no difference in complication rate, including diabetes insipidus, hypopituitarism, postoperative CSF, nasal morbidity, nor repeat surgery for CSF leak or nasal morbidity (P>0.05; *Table 2*). Subsequent analysis using a univariate regression



**Figure 2** Surgical outcomes for endoscopic transsphenoidal resection of pituitary tumors. Phase 1 (July 2010 to August 2014; before academic leave), Phase 2 (November 2017 to March 2020; after academic leave). (A,B) The distribution of operative times and hospital stays by case number for a single surgeon during Phase 1 and Phase 2. There was a significant shorter operative time and hospital stay in Phase 2 (closed arrow). (C,D) Comparison of operative times and hospital stays between two groups.  $P < 0.05$ , univariate regression model.

model found a significantly lower tumor residual on postoperative MRI, rate of intra-operative CSF leak, and need for reoperation for CSF leak in Phase 2 compared to Phase 1 ( $P < 0.05$ ; *Figure 3*).

Surgical outcomes were also compared subdivided by one-hand/mono-nostril and two-hand/one-and-half nostril surgical approach. As shown in *Table S1*, patients' characteristics were equivalent between these two groups ( $P > 0.05$ ). However, for patients operated using a one-hand approach, the Phase 2 surgery group had a lower preoperative tumor volume than the Phase 1 surgery group ( $P < 0.05$ ). For patients operated using the two-hand approach, patients in the Phase 2 group were older than those in the Phase 1 group ( $P < 0.05$ ). Surgical outcomes (*Table S2*) were similar to those presented in *Table 2*, except operative time which was significantly shorter in the Phase 2 group; in patients operated with both the one-hand and two-hand approaches ( $P < 0.05$ ). Hospital stay was lower in patients who received the one-hand approach during the Phase 2 period ( $P < 0.05$ ), but this result did not reach statistical significance in patients operated using the two-

hand approach ( $P > 0.05$ ).

## Discussion

These results support the hypothesis that surgical skills are not significantly eroded after a period of not being exercised. Surgical outcomes (operative time, hospital stay, cumulative residual tumor, intra-operative CSF leak and need for further surgery) for endoscopic transsphenoidal resection of pituitary tumors by a single surgeon were even better after the three-year period of academic leave. Most endoscopic transsphenoidal surgical outcomes were not affected adversely by academic leave. This appears to be the first study to address the association between a single neurosurgeon's academic leave and surgical outcome for endoscopic transsphenoidal surgery for resection of pituitary tumors. Moreover, this study includes cases using both one-hand/mono-nostril and two-hand/one-and-half nostril approaches.

Increasing focus is placed on wider professional issues that may impact surgical outcomes, evinced in the previous

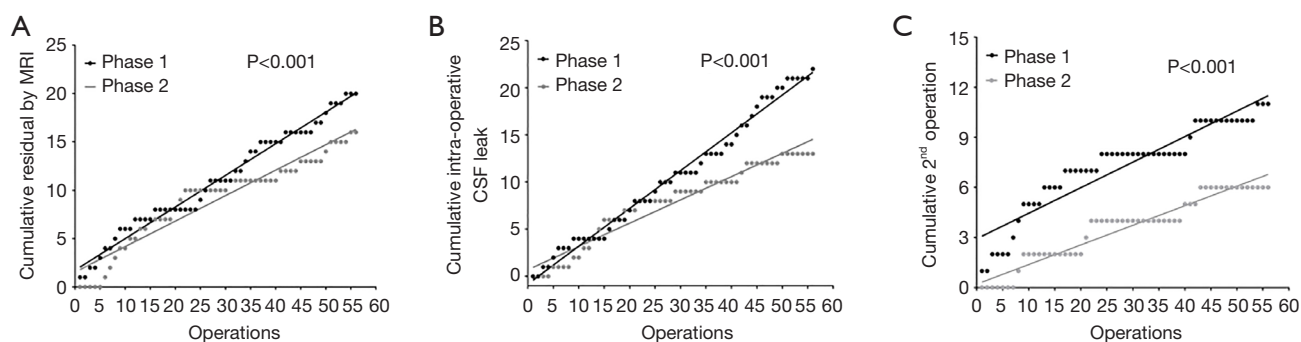
**Table 2** Postoperative outcome and complications after endoscopic transsphenoidal resection of pituitary tumors

| Variable                                                                 | Phase 1 (n=56)  | Phase 2 (n=56) | P value |
|--------------------------------------------------------------------------|-----------------|----------------|---------|
| Operation time (mins)                                                    | 170.0 [110–600] | 106.5 [47–302] | <0.001* |
| Hospital stay (days)                                                     | 7 [4–90]        | 5 [3–68]       | 0.010*  |
| Intraoperative extent of resection                                       |                 |                |         |
| Total or near total (>90%)                                               | 38 (67.9)       | 44 (78.6)      |         |
| Subtotal (≤90%)                                                          | 18 (32.1)       | 12 (21.4)      |         |
| Postoperative MRI extent of resection                                    |                 |                | 0.544   |
| Total (100%)                                                             | 36 (64.3)       | 40 (71.4)      |         |
| Subtotal (<100%)                                                         | 20 (35.7)       | 16 (28.6)      |         |
| Visual field change/improve<br>(improve/preoperative visual disturbance) | 13/16 (81.3)    | 19/24 (79.2)   | 1.000   |
| Diabetes insipidus                                                       | 7 (12.5)        | 10 (17.9)      | 0.599   |
| Hypopituitarism                                                          | 7 (12.5)        | 4 (7.1)        | 0.527   |
| Postoperative RT                                                         | 11 (19.6)       | 6 (10.7)       | 0.292   |
| Intraoperative CSF leak                                                  | 22 (39.3)       | 13 (23.2)      | 0.102   |
| Postoperative CSF leak                                                   | 7 (12.5)        | 3 (5.4)        | 0.321   |
| Nasal complications                                                      | 9 (16.1)        | 16 (28.6)      |         |
| Sinusitis                                                                | 6 (10.7)        | 9 (16.1)       |         |
| Epistaxis                                                                | 3 (5.4)         | 6 (10.7)       |         |
| Hyposmia                                                                 | 0 (0.0)         | 1 (1.8)        |         |
| Surgical complications                                                   | 4 (7.1)         | 3 (5.4)        | 1.000   |
| Intracerebral hemorrhage                                                 | 2 (3.6)         | 1 (1.8)        |         |
| Meningitis                                                               | 1 (1.8)         | 1 (1.8)        |         |
| Cranial nerve palsy                                                      | 1 (1.8)         | 1 (1.8)        |         |
| Postoperative endocrine dysfunction                                      |                 |                | 0.369   |
| Complete remission                                                       | 19/20 (95.0)    | 11/14 (78.6)   |         |
| Partial remission                                                        | 1/20 (5.0)      | 2/14 (14.3)    |         |
| Stable disease                                                           | 0 (0.0)         | 1/14 (7.1)     |         |
| Re-operation for CSF leak                                                | 6 (10.7)        | 3 (5.4)        | 0.489   |
| Re-operation for nasal complication                                      | 9/13 (69.2)     | 10/26 (38.5)   | 0.096   |

Data are presented as n (%), n/N (%) or median [range]. \*, P<0.05. MRI, magnetic resonance imaging; RT, radiation therapy; CSF, cerebrospinal fluid.

study (14). Neurosurgeons are increasingly taking breaks of academic leave to pursue more research-oriented careers and to meet the increasing complexities of clinical care. Most studies of breaks in surgical practice focus on maternity, paternity or parental leave. In some countries,

surgeons take substantial pregnancy leave followed by maternity or parental leave, with concerns over potential loss of surgical skills (9-11,15). The American Board of Surgery suggests that surgeons should retrain after two years or more away from surgical practice, a policy also followed



**Figure 3** The effect of academic leave on cumulative residual tumor, intra-operative CSF leak, and reoperation. A univariate linear regression scatterplot demonstrating the relationship between (A) academic leave and cumulative tumor residual on postoperative MRI, (B) academic leave and cumulative intra-operative CSF leak, and (C) academic leave and cumulative reoperation. MRI, magnetic resonance imaging; CSF, cerebrospinal fluid.

in other countries, including Australia and Latvia (15). For surgeons, there is a concern that a break from practice may have a detrimental effect on surgical skills, but this was not found in our study. Interestingly, we found that the cumulative postoperative residual tumor, intra-operative CSF leak, and need for further surgery was better after a break in surgical practice (Phase 2 compared to Phase 1). This was mainly due to more complications occurring in the very beginning of Phase 1, which was also the phase of skill building. On the other hand, our findings showed that there was only small skill pick-up time after the academic leave. Two of the three postoperative CSF leakage happened in the first ten cases in Phase 2.

Most of papers dealing with learning curve in endoscopic pituitary surgery report the experienced surgeons moving from microscopy to endoscopy and may explain the important range of cases required to acquire skills (7,8). As in other surgical specialties, a clear relationship between surgeon experience and outcome has been demonstrated in endoscopic transsphenoidal surgery for resection of pituitary tumors (16). Patients treated by more experienced surgeons have fewer complications, a lower mortality rate and lower hospital costs (4,17,18). Nowadays, most of surgeons are only trained in endoscopic surgery, which may shorten the learning curve. In the present study, the surgeon only received a training of endoscopic surgery before the Phase 1 period. Hence, the present study showed that academic leave had no negative impact on most surgical outcomes for endoscopic transsphenoidal resection of pituitary tumors. Furthermore, the evidence examined patient outcomes from surgeons with different experience levels who used two different surgical techniques

but practiced using a common clinical pathway (19). Those surgeons demonstrated that a less experienced surgeon performing endoscopic transsphenoidal surgery was able to achieve similar outcomes to those of very experienced surgeons using a microscopic transsphenoidal surgery technique in a cohort of patients with nonfunctioning tumors under 60 cm<sup>3</sup> in size (19). That study raises the notion that certain advantages afforded by an endoscopic transsphenoidal technique may influence the learning curve for nonfunctioning pituitary adenoma surgery (19). Compared to these findings, the present study showed that most surgical outcomes were not affected by a single surgeon carrying out endoscopic transsphenoidal surgery after academic leave. A similar result was also observed in patients who received either one-hand/mono-nostril or two-hand/one-and-half nostril approaches. This supports the above speculation regarding the impact of academic leave on operation-related cumulation of residual tumor, intraoperative CSF leak and reoperation, suggesting that the post-academic leave surgeries performed using the one-hand/mono-nostril and two-hand/one-and-half nostril approaches may increase the surgeon's experience, resulting in improving most surgical outcomes.

Prolonged inpatient stays after transsphenoidal surgery are predominantly due to postoperative endocrine abnormalities, frequently caused by over-manipulation of the intra-operative gland (20,21). A study analyzing surgical experience and length of inpatient stay found no difference between experienced and less-experienced surgeons (22). In our present study, we found that length of hospital stay and operative time was significantly shorter after academic leave (Phase 2 group). This suggests that surgical skill may not

necessarily decline during a period of academic leave, and has the potential to even continue to improve.

This study has several limitations, including that it is a retrospective study that suffers from biases common to non-randomized studies. The study cohort was modest in size, and the study was conducted in a single medical center in Taiwan that specializes in surgery for pituitary tumors, so generalizations cannot be made for all populations. In addition, there is a variation in the number of cases per year between the Phase 1 and 2. In the Phase 1, surgeon practiced less than 10 cases per year in 2010–2011 period, which may lengthen the learning curve of pituitary surgery. Prospective, large, cohort studies are needed to reliably compare the impact of academic leave on surgical outcomes for endoscopic transsphenoidal resection of pituitary tumors and other neurosurgical procedures.

## Conclusions

This is the first study to address the impact of academic leave on surgical outcomes for endoscopic transsphenoidal resection of pituitary tumors with one-hand/mono-nostril or two hand/one-and-half nostril approaches. This study showed that three-year academic leave did not have a negative impact on surgical outcomes. Instead, a trend toward shorter operative times and hospital stays were noted for patients operated on immediately after a surgeon's return from leave.

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## Footnote

*Reporting Checklist:* The authors have completed the STROBE reporting checklist. Available at <https://gs.amegroups.com/article/view/10.21037/gS-23-347/rc>

*Data Sharing Statement:* Available at <https://gs.amegroups.com/article/view/10.21037/gS-23-347/dss>

*Peer Review File:* Available at <https://gs.amegroups.com/article/view/10.21037/gS-23-347/prf>

*Conflicts of Interest:* All authors have completed the ICMJE uniform disclosure form (available at <https://gs.amegroups.com/article/view/10.21037/gS-23-347/coif>). The authors have no conflicts of interest to declare.

*Ethical Statement:* The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the Institutional Review Board of Chang Gung Memorial Hospital (No. 201901259B0C602) and waived the need for patient informed consent because the study classified as retrospective study with expedited review.

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## Supplementary

**Table S1** Demographic and clinical characteristics of patients undergoing endoscopic transsphenoidal surgery for pituitary tumors who received the one- or two-hand approaches

| Variable                                     | One-hand approach |                |         | Two hand approach |                |         |
|----------------------------------------------|-------------------|----------------|---------|-------------------|----------------|---------|
|                                              | Phase 1 (n=35)    | Phase 2 (n=25) | P value | Phase 1 (n=21)    | Phase 2 (n=31) | P value |
| Age (years)                                  | 47.9±14.6         | 44.6±14.2      | 0.280   | 42.1±14.6         | 57.7±13.7      | 0.001*  |
| Gender, male                                 | 12 (34.3)         | 9 (36.0)       | 1.000   | 8 (38.1)          | 18 (58.1)      | 0.258   |
| Tumor type                                   |                   |                | 0.412   |                   |                | 0.076   |
| Non-functional                               | 25 (71.4)         | 15 (60.0)      |         | 11 (52.4)         | 24 (77.4)      |         |
| Functional                                   | 10 (28.6)         | 10 (40.0)      |         | 10 (47.6)         | 7 (22.6)       |         |
| Prolactinoma                                 | 2 (5.7)           | 6 (24.0)       |         | 4 (19.0)          | 3 (9.7)        |         |
| Growth hormone                               | 7 (20.0)          | 1 (4.0)        |         | 6 (28.6)          | 2 (6.5)        |         |
| Thyroid stimulating hormone                  | 0 (0.0)           | 2 (8.0)        |         | 0 (0.0)           | 0 (0.0)        |         |
| Cushing                                      | 1 (2.9)           | 1 (4.0)        |         | 0 (0.0)           | 2 (6.5)        |         |
| Previous operation                           | 5 (14.3)          | 3 (12.0)       | 1.000   | 2 (9.5)           | 7 (22.6)       | 0.283   |
| Apoplexy                                     | 12 (34.3)         | 5 (20.0)       | 0.260   | 8 (38.1)          | 9 (29.0)       | 0.556   |
| Preoperative tumor volume (cm <sup>3</sup> ) | 6.9±11.5          | 2.28±3.6       | 0.003*  | 5.7±6.9           | 9.2±9.9        | 0.192   |
| Knop's grade                                 |                   |                | 0.150   |                   |                | 0.638   |
| 0                                            | 5 (14.3)          | 7 (28.0)       |         | 0 (0.0)           | 0 (0.0)        |         |
| 1                                            | 6 (17.1)          | 9 (36.0)       |         | 5 (23.8)          | 5 (16.1)       |         |
| 2                                            | 7 (20.0)          | 4 (16.0)       |         | 6 (28.6)          | 6 (19.4)       |         |
| 3                                            | 8 (22.9)          | 3 (12.0)       |         | 6 (28.6)          | 14 (45.2)      |         |
| 4                                            | 9 (25.7)          | 2 (8.0)        |         | 4 (19.0)          | 6 (19.4)       |         |
| Hardy suprasellar extension                  |                   |                | 0.088   |                   |                | 0.228   |
| A                                            | 11 (31.4)         | 16 (64.0)      |         | 6 (28.6)          | 3 (9.7)        |         |
| B                                            | 15 (42.9)         | 5 (20.0)       |         | 7 (33.3)          | 10 (32.3)      |         |
| C                                            | 6 (17.1)          | 3 (12.0)       |         | 6 (28.6)          | 16 (51.6)      |         |
| D                                            | 3 (8.6)           | 1 (4.0)        |         | 2 (9.5)           | 2 (6.5)        |         |

Data are presented as n (%) or mean ± SD. \*, P<0.05. SD, standard deviation.

**Table S2** Postoperative outcomes and complications in patients with pituitary tumor receiving one- or two-hand approaches

| Variable                                                              | One-hand approach |                |         | Two-hand approach |                |         |
|-----------------------------------------------------------------------|-------------------|----------------|---------|-------------------|----------------|---------|
|                                                                       | Phase 1 (n=35)    | Phase 2 (n=25) | P value | Phase 1 (n=21)    | Phase 2 (n=31) | P value |
| Operation time (minutes)                                              | 180 [120–600]     | 77 [47–142]    | <0.001* | 160 [110–240]     | 120 [65–302]   | 0.020*  |
| Hospital stay (days)                                                  | 7 [4–90]          | 5 [3–23]       | 0.003*  | 7 [4–14]          | 6 [3–68]       | 0.299   |
| Intraoperative extent of resection                                    |                   |                |         |                   |                | 0.003*  |
| Total or near total (>90%)                                            | 23 (65.7)         | 22 (88.0)      | 0.071   | 15 (71.4)         | 31 (100.0)     |         |
| Subtotal (≤90%)                                                       | 12 (34.3)         | 3 (12.0)       |         | 6 (28.6)          | 0 (0.0)        |         |
| Postoperative MRI extent of resection                                 |                   |                | 0.052   |                   |                | 0.558   |
| Total (100%)                                                          | 21 (60.0)         | 21 (84.0)      |         | 15 (71.4)         | 19 (61.3)      |         |
| Subtotal (<100%)                                                      | 14 (40.0)         | 4 (16.0)       |         | 6 (28.6)          | 12 (38.7)      |         |
| Visual field change/improve (improve/preoperative visual disturbance) | 7/9 (77.8)        | 5/5 (100.0)    | 0.505   | 6/7 (85.7)        | 14/19 (73.7)   | 1.000   |
| Diabetes insipidus                                                    | 4 (11.4)          | 5 (20.0)       | 0.470   | 3 (14.3)          | 5 (16.1)       | 1.000   |
| Hypopituitarism                                                       | 7 (20.0)          | 3 (12.0)       | 0.499   | 0 (0.0)           | 1 (3.2)        | 1.000   |
| Postoperative RT                                                      | 9 (25.7)          | 1 (4.0)        | 0.035*  | 2 (9.5)           | 5 (16.1)       | 0.687   |
| Intraoperative CSF leak                                               | 15 (42.9)         | 4 (16.0)       | 0.047*  | 7 (33.3)          | 9 (29.0)       | 0.768   |
| Postoperative CSF leak                                                | 7 (20.0)          | 0 (0.0)        | 0.035*  | 0 (0.0)           | 3 (9.7)        | 0.264   |
| Nasal complications                                                   | 4 (11.4)          | 8 (32.0)       |         | 5 (23.8)          | 8 (25.8)       |         |
| Sinusitis                                                             | 3 (8.6)           | 5 (20.0)       |         | 3 (14.3)          | 4 (12.9)       |         |
| Epistaxis                                                             | 1 (2.9)           | 2 (8.0)        |         | 2 (9.5)           | 4 (12.9)       |         |
| Hyposmia                                                              | 0 (0.0)           | 1 (4.0)        |         | 0 (0.0)           | 0 (0.0)        |         |
| Surgical complications                                                | 4 (11.4)          | 1 (4.0)        | 0.390   | 0 (0.0)           | 2 (6.5)        | 0.509   |
| ICH                                                                   | 2 (5.7)           | 0 (0.0)        |         | 0 (0.0)           | 1 (3.2)        |         |
| Meningitis                                                            | 1 (2.9)           | 1 (4.0)        |         | 0 (0.0)           | 0 (0.0)        |         |
| CN palsy                                                              | 1 (2.9)           | 0 (0.0)        |         | 0 (0.0)           | 1 (3.2)        |         |
| Postoperative endocrine function                                      |                   |                | 0.721   |                   |                | 0.333   |
| Complete remission                                                    | 9/10 (90.0)       | 7/9 (77.8)     |         | 10/10 (90.0)      | 4/5 (80.0)     |         |
| Partial remission                                                     | 1/10 (10.0)       | 1/9 (11.1)     |         | 0 (0.0)           | 1/5 (20.0)     |         |
| Stable disease                                                        | 0 (0.0)           | 1/9 (11.1)     |         | 0 (0.0)           | 0 (0.0)        |         |
| Re-operation for CSF leak                                             | 6 (17.1)          | 2 (8.0)        | 0.222   | 0 (0.0)           | 1 (3.2)        | 1.000   |
| Re-operation for nasal complication                                   | 4/7 (57.1)        | 6/11 (54.5)    | 1.000   | 5/6 (83.3)        | 4/15 (12.9)    | 0.045*  |

Data are presented as n (%), n/N (%) or median [range]. \*, P<0.05. MRI, magnetic resonance imaging; RT, radiation therapy; CSF, cerebrospinal fluid; ICH, intracerebral hemorrhage; CN, cranial nerve.