

## Peer Review File

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### **Reviewer A**

*The authors studied the impact of a 3-year academic leave (PhD) on operative outcomes in endoscopic transsphenoidal pituitary surgery. This is a case series based on the experience of a single surgeon. They address an important question of balance between academic and clinical practice in MD-PhD curriculum.*

### **Comment (1)**

*L 107-108 “They did not be asked to assess the burden of the intervention and time required to participate in the research”: This sentence is not clear. Who are the authors talking about? Please rephrase.*

### **Author response**

A sentence stating “These patients were not asked to assess the burden of the intervention and time required to participate in the research.” has been revised in the modified manuscript (lines 107-108).

### **Comment (2)**

*What was the amount experience of the surgeon before academic leave? Do he performed pituitary surgery since his board certification or later? How old was him?*

### **Author response**

Before full-time PhD study, surgeon had 84 cases of endoscopic endonasal transsphenoidal surgery experience. The initial 28 cases are excluded due to not completely done by the single surgeon. Finally, we included 56 cases in the Phase 1. Among them, the initial 9 cases were done in the senior residence period, 10 cases were done in the chief residence period, and 37 cases were done after the board certification (January 2013) (31 years old). In addition, 56 cases in the Phase 2 were done after the board certification.

**Comment (3)**

*The topic of PhD was different from pituitary surgery. Did the surgeon participated to lectures / workshops / cadaver labs on pituitary surgery before returning to clinical practice?*

**Author response**

During the Phase 2 period, surgeon did not participate in workshops/cadaver labs again. Nevertheless, he actively participates in Taiwan Pituitary society meetings and observes other doctors' surgeries 2-3 times.

**Comment (4)**

*Table 1: Given the relative low number of procedures studied, the difference in surgical approach between the two periods didn't reached significancy. However, the proportions are quite different. The authors conducted a subgroup analysis based on the surgical approach. They stated (L195-197) "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 ( $p<0.05$ )". In my opinion, the academic leave allowed the surgeon to gain perspective on his practice so he had a better selection of surgical technique.*

**Author response**

The change in the selection of surgical technique is not due to the PhD study. Because the topic of PhD was different from pituitary surgery. However, during and after the PhD study, surgeon continuously participated in multiple international neurosurgical societies and hence think and develop different surgical techniques. Therefore, surgeon do want to develop different surgical techniques when he came back from the academic leave.

**Comment (5)**

*The authors should also discuss the number of cases per year, as there is some variations between the 2 periods. In the first period, he practiced less than 10 cases per year in 2010-2011 period, which may lengthen the learning curve of pituitary surgery.*

**Author response**

In order to address reviewer's concern, the sentences stating "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.” has been added into the *Limitation* section of the modified manuscript (lines 268-271).

### **Comment (6)**

*Regarding this point (learning curve), again we lack information on the past experience of the surgeon. Did the authors exclude the first cases in the period 1? Otherwise, the period 1 should be considered as the learning curve phase, and the period 2 as “cases beyond the learning curve”.*

### **Author response**

Before full-time PhD study, surgeon had 84 cases of endoscopic endonasal transsphenoidal surgery experience. The initial 28 cases were excluded due to not completely done by the single surgeon. Finally, we included 56 cases in the Phase 1. Among them, the initial 9 cases were done in the senior residence period, 10 cases were done in the chief residence period, and 37 cases were done after the board certification. After full-time PhD study, we consecutively included 56 cases in the Phase 2. A survey questionnaire found a significant drop in all morbidity and mortality after 200 cases experience (Ciric et al., 1997), with another study reporting a continued improvement in the rate of post-operative CSF leaks up to 100 cases experience, and operative time up to 120 cases (Shikary et al., 2017). These suggest that a sustainable surgical volume is required in learning endoscopic resection of pituitary tumors, with up to 100 cases experience. Thus, the cases in the Phase 1 and 2 should be considered as the learning curve phase.

### **References**

1. Ciric I, Ragin A, Baumgartner C, Pierce D. Complications of transsphenoidal surgery: results of a national survey, review of the literature, and personal experience. *Neurosurgery*. 1997;40. 225-36; discussion 36-7.
2. Shikary T, Andaluz N, Meizen-Derr J, Edwards C, Theodosopoulos P, Zimmer LA. Operative Learning Curve After Transition to Endoscopic Transsphenoidal Pituitary Surgery. *World Neurosurg*. 2017;102. 608-12.

### **Comment (7)**

*Most of papers dealing with learning curve in endoscopic pituitary surgery report the case series of experienced surgeons moving from microscopy to endoscopy and may explain the important range of cases required to acquire skills. Nowadays, most of surgeons are only trained in endoscopic surgery, which may shorten the learning curve. Please discuss this point thoroughly,*

*with more recent references (see for example 10.3389/fsurg.2022.959440).*

### **Author response**

A paragraph stating “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 (Smith et al., 2010; Shikary et al., 2017). 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 (Boetto et al., 2022). 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.” has been revised in the *Discussion* section of the modified manuscript (lines 232-257).

### **Comment (8)**

*The references 13-15 seems related to the PhD topic of the surgeons, have no link with the rest of the manuscript, and sound like self-citation process (and are not cited in the text!). Please delete them.*

**Author response**

The references 13-15 has been removed (line 119).

**Reviewer B**

**Comment (1)**

*The authors present an interesting study considering the outcome of endonasal pituitary surgery affected by academix leave of a surgeon. The results revealed that there is no impact of outcome and complication rate if a surgeon is leaving daily surgical routine for academic studies for some months to years.*

*The manuscript is well written. the statitics are adequate.*

*The authors should improve the content of the manuscript by illustration und more detailes description of their surgical technique. Beside this, I suggest to accept.*

**Author response**

One-hand/two-hand technique surgical views and illustration of surgical approach have been added to the modified manuscript, as showed in our previous study (Yan et al., 2021) (line 141).

**Reference**

Jiun-Lin Yan, Chen-Nen Chang, Pin-Yuan Chen. Endoscopic transsphenoidal surgery for resection of pituitary macroadenoma: a retrospective study. PLoS One. 2021;16(8):e0255599.