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RESEARCH

Real-time intraoperative ultrasound imaging of the posterior pituitary gland during endoscopic endonasal approach

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Abstract

Purpose Pituitary adenomas are amongst the most common benign central nervous system tumors, and often require resection via an endoscopic endonasal approach (EEA). Two of the most common associated complications are central diabetes insipidus (DI) and syndrome of inappropriate antidiuretic hormone secretion (SIADH). Both are thought to be caused by manipulation of the posterior pituitary gland (PPG), making intraoperative visualization and preservation of this structure critical. Intraoperative endoscopic endonasal ultrasound (IEUS) may present an optimal tool for this purpose. This study aims to describe the appearance and morphology of the PPG on IEUS.

Methods This study included all pituitary adenoma surgeries during which IEUS was utilized and the PPG was visualized between 1/1/2022, and 12/31/2023. Demographic, clinical, pathological, and radiological data were retrospectively collected. The PPG was described as either hypoechoic, isoechoic, or hyperechoic as compared to the anterior pituitary gland and adenoma, and the morphology of the PPG was further classified as ellipse or crescent shaped.

Results The PPG was hypoechoic in all 43 cases included in our final cohort (100.0%). Morphologically, the PPG appeared elliptical in 27 cases (62.8%), and crescent shaped in 16 cases (37.2%).

Conclusion The PPG can typically be visualized by IEUS as a hypoechoic structure immediately anterior to the posterior wall of the sella turcica, with elliptical morphology being the most common appearance. These characteristics can be used by the skull base surgeon to more confidently identify the position and morphology of the PPG intraoperatively for its' preservation.

Keywords Endoscopic endonasal approach · Endoscopic ultrasound · Intraoperative imaging · Posterior pituitary gland · Pituitary gland · Ultrasound

Introduction

Pituitary adenomas are the most common pituitary lesion, occurring in up to 10% of the general population [9, 22, 29]. Although often benign, surgical resection may be required in the presence of symptomatic endocrine axis disturbances or neurovascular compression [9, 22, 1, 25, 11, 10]. Resection via an endoscopic endonasal approach (EEA) has emerged as an increasingly popular technique for these lesions [7, 21, 26]. Though refinement of this technique over the last decade has decreased the rates of many major complications, such as CSF leak [32], rates of postoperative central diabetes insipidus (DI) and syndrome of inappropriate antidiuretic hormone secretion (SIADH) remain largely unchanged [22, 15, 20, 2, 30, 14, 33, 6]. DI and SIADH are transient or permanent sodium regulation disorders that increase hospital length of stay and decrease patient quality of life [3, 18]. Both are thought to be caused primarily by intraoperative manipulation of, or injury to, the posterior pituitary gland (PPG) [2, 3, 18, 17, 16, 27]. Therefore, it is critically important to effectively visualize this structure and have a sense of its location during surgery to ensure its preservation.

Intraoperative endoscopic endonasal ultrasound (IEUS) is a relatively new surgical tool that is becoming more

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frequently used in EEA skull base procedures [12]. It has been readily adopted by neurosurgeons due to its ability to identify neurovascular structures encountered during such procedures, allowing for maximal exposure in real-time [12]. However, to the best of our knowledge, no studies to date have described the IEUS characteristics of the PPG, and its potential impact on intraoperative gland preservation. A descriptive analysis of the PPG on IEUS is critical to allow surgeons to accurately identify the gland to define an optimal resection plane and avoid damage during either exposure or resection. Additionally, visualizing the gland after resection, and before closure, may be valuable in determining whether the gland has been affected and predicting the likelihood of postoperative complications including DI and SIADH [16].

Herein, the authors describe the imaging characteristics and morphology of the PPG on IEUS among patients being treated for pituitary adenomas. Additionally, we describe the relationship of the PPG to the anterior pituitary gland and adenoma, the clinical presentation and outcomes of these patients, and discuss the potential benefit of utilizing IEUS to guide safe adenoma resection and preserve the PPG.

Methods and materials

Study design and patient eligibility

This study was conducted at The Ohio State University, Department of Neurosurgery, Skull Base Division. After obtaining institutional review board approval (study #2020H0221), a descriptive study was conducted to report the IEUS imaging characteristics of the PPG. The hospital's electronic medical record system was queried to identify all patients who underwent neurosurgical operations in which IEUS was utilized between January 1st, 2022, and December 31st, 2023. All patients that underwent EEA operations for pituitary adenomas where the IEUS was used to visualize the PPG were included in the final analysis. All cases in which the PPG was not visualized, or the images were not available in the hospital's record were excluded. Patient consent was obtained prior to each procedure.

Variables and data collection

A retrospective chart review of each included patient's electronic medical record was performed to collect demographic, clinical, pathological, and radiological variables. The demographic variables included patients' age and gender. Clinical variables of interest included: primary or recurrent adenoma, symptoms at presentation (headache, visual deficits, cranial nerve palsies, and/or dizziness), pituitary gland associated hormonal dysfunction (adrenocorticotropic hormone (ACTH), prolactin, thyroid stimulating hormone (TSH), luteinizing hormone (LH)/ follicle stimulating hormone (FSH), and/or growth hormone (GH) dysfunction, or panhypopituitarism), extent of resection (gross total, near total, or subtotal), length of follow-up, and postoperative complications (transient or permanent DI/SIADH and transient or permanent new hormonal dysfunction). Extent of resection was evaluated via postoperative MRI images. Pathologic variables analyzed included only final tumor pathology reports (tumors classified as either non-functioning, somatotroph, lactotroph, corticotroph, thyrotroph, gonadotroph, PPG lesion, or plurihormonal).

Radiological variables included maximum tumor diameter, presence or absence of cavernous sinus invasion, PPG US morphology (ellipse vs. crescent shaped) and characteristics of the PPG (hypoechoic, isoechoic, or hyperechoic). PPG morphology and appearance were assessed intraoperatively by two skull base neurosurgeons (D.M.P. and K.C.W) and images were retrospectively reviewed by a licensed clinical neuroradiologist (L.M.P.). Tumor diameter and cavernous sinus invasion were assessed via preoperative MRI images. Preoperative tumor size was based on magnetic resonance imaging (MRI) and classified as macroadenoma or microadenoma, if ≥ 1 cm or < 1 cm, respectively. Compression of the optic apparatus was also visualized based on the MRI (sagittal and coronal views) and by visual field exam.

Intraoperative ultrasound imaging

The IEUS imaging was performed using the Bk 5,000 Ultrasound System with the N20P6 Minimally Invasive 6×7 mm Transducer® (BK Medical, Peabody, Massachusetts). The IEUS was utilized before dural opening to guide the size of the durotomy, ensure adequate exposure, and evaluate the anatomic relationship of the adenoma to the posterior pituitary gland. Both still images and video recordings of the US were evaluated for each patient, if available.

Statistical analysis

Data was collected using Microsoft Excel 2019 software. The characteristics of the cohort were described with numerical variables presented as the mean and standard deviation. Categorical variables were presented as absolute numbers and as a percentage of included patients. Given the descriptive nature of the study, formal statistical analysis was not conducted.

Results

Study population and patient characteristics

During the study period, 117 EEA cases utilizing IEUS were identified. Of these, 93 were for pituitary adenomas. Fifty cases were excluded for not intentionally identifying the PPG, leaving 43 patients in our final sample.

Most patients were female (67.4%) with a mean age of 49.1 years (± 15.9). Patients were followed for an average of 9.16 months (± 6.31). Eight patients (18.6%) had a recurrent adenoma. The most common presenting symptom was headaches (18/43, 41.9%), followed by visual deficits (9/43, 20.9%), oculomotor nerve palsy (4/43, 9.3%), and dizziness (5/43, 11.6%).

Preoperative hormone dysfunction was observed in 31 patients (72.1%). Dysfunction was most often caused by overproduction of ACTH (hypercortisolism) (15/43, 34.9%), prolactin (10/43, 23.3%), LH/FSH (hypergonadism), and GH (both 6/43, 14.0%). Six adenomas were found incidentally (14.0%). No patients presented with preoperative DI/SIADH. Table 1 details the presenting characteristics of all included patients.

Table 1 describes the demographic and presenting characteristics of the included patient population.

Tumor and clinical variables

Table 2 presents tumor and surgical data for all included cases. The mean maximum pituitary adenoma diameter was 1.51 (± 0.81) cm, with 30 cases (69.8%) being macroadenomas, and 13 (30.2%) being microadenomas. Cavernous sinus invasion was identified in 17 cases (39.5%). Gross total resection was achieved in 42 cases (97.7%), with the remaining patient undergoing near total resection due to tumor adherence to the internal carotid artery (1/43, 2.33%).

Table 1 Patient presenting characteristics ($n = 43$)

Variable	# of Patients (%), or Mean ± SD
Male Sex	14 (32.6)
Age	49.1 ± 15.9
Primary Adenoma	35 (81.4)
Recurrent Adenoma	8 (18.6)
Clinical Presentation	
Headache	18 (41.9)
Dizziness	5 (11.6)
Visual Deficit	9 (20.9)
CN3 Palsy	4 (9.30)
CN4 Palsy	1 (2.33)
CN6 Palsy	1 (2.33)
Hormonal Dysfunction	31 (72.1)
ACTH Dysfunction	15 (34.9)
Prolactin Dysfunction	10 (23.3)
TSH Dysfunction	3 (6.98)
LH/FSH Dysfunction	6 (14.0)
GH Dysfunction	6 (14.0)
Panhypopituitarism	1 (2.33)
Found Incidentally	6 (14.0)
Length of Follow-up (mo)	9.16 ± 6.31

Table 2 details the tumor and clinical data for all included cases.

Final pathologic diagnosis revealed 4 non-functioning adenomas (9.30%), 19 (44.2%) corticotrophs, 8 (18.6%) gonadotrophs, 5 (11.6%) lactotrophs, 1 (2.33%) somatotroph, and 6 (14.0%) plurihormonal adenomas. No thyrotrophs, pars intermedia or PPG lesions were identified.

Postoperatively, 7 patients (16.3%) developed transient DI or SIADH, while only 1 patient (2.33%) developed permanent DI (Table 3). Furthermore, 2 patients (4.65%) exhibited new anterior pituitary gland hormonal dysfunction in the postoperative course (both exhibited postoperative ACTH deficiency that was managed medically). This effect was transient (lasting less than 3 months) in both patients.

Table 3 describes the clinical outcomes of the patient population.

Intraoperative ultrasound characterization of the posterior pituitary gland

On intraoperative US imaging, the PPG was hypoechoic compared to the anterior pituitary gland and adenoma in all 43 cases (100.0%). There were no cases in which the PPG was visualized as isoechoic or hyperechoic. Morphologically, the PPG was elliptical in 27 cases (62.8%) (Figs. 1a and c and 2a and c), and crescent-shaped in 16 cases (37.2%) (Figs. 1b and d and 2b and d). An ellipse was the predominant morphology in both micro- (10/13, 76.9%) (Fig. 2) and macroadenomas (17/30, 56.7%) (Fig. 1), but the crescent shape was more often noted in

Table 2 Preoperative tumor/surgical data ($n = 43$)

Variable	# of Patients (%), or mean ± SD
Macroadenoma	30 (69.8)
Max Tumor Diameter (cm)	1.51 ± 0.81
Cavernous Sinus Invasion	17 (39.5)
Gross Total Resection	42 (97.7)
Near Total Resection	1 (2.33)
Subtotal Resection	0 (0)
Pathology	
Null	4 (9.30)
Somatotroph	1 (2.33)
Lactotroph	5 (11.6)
Corticotroph	19 (44.2)
Thyrotroph	0 (0)
Gonadotroph	8 (18.6)
Posterior Gland Lesion	0 (0)
Plurihormonal Adenoma	6 (14.0)

Table 3 Postoperative outcomes ($n=43$)

Variable	# of Patients (%), or Mean ± SD
New Postoperative Anterior Gland Dysfunction	
Transient	2 (4.65)
Permanent	0 (0)
Post-op DI/SIADH	
Transient	7 (16.3)
Permanent	1 (2.33)

macroadenomas (13/30, 43.3%, vs. 3/13, 23.1%). These results are detailed in Table 4.

Table 4 details the imaging characteristics of the posterior pituitary gland on intraoperative endoscopic endonasal ultrasound.

Discussion

DI and SIADH are believed to be caused by manipulation of, or injury to, the PPG during endoscopic endonasal surgery and are associated with decreased postoperative quality of life and longer postoperative hospital stays [2, 3, 18, 17, 16, 27]. Thus, it is critical to identify this structure both during surgical planning and intraoperatively to ensure its preservation.

Magnetic resonance imaging is currently considered the gold standard to identify the PPG in the pre- and postoperative periods [8, 13]. The PPG often appears as the characteristic hyperintense "bright spot" on T1-weighted MR images [8, 13]. Notably, this bright spot is absent in patients with DI whose posterior gland vasopressin content is markedly decreased [8, 13]. Though this information is useful for demonstrating the role of PPG injury in the development of DI, the pitfall in this approach is

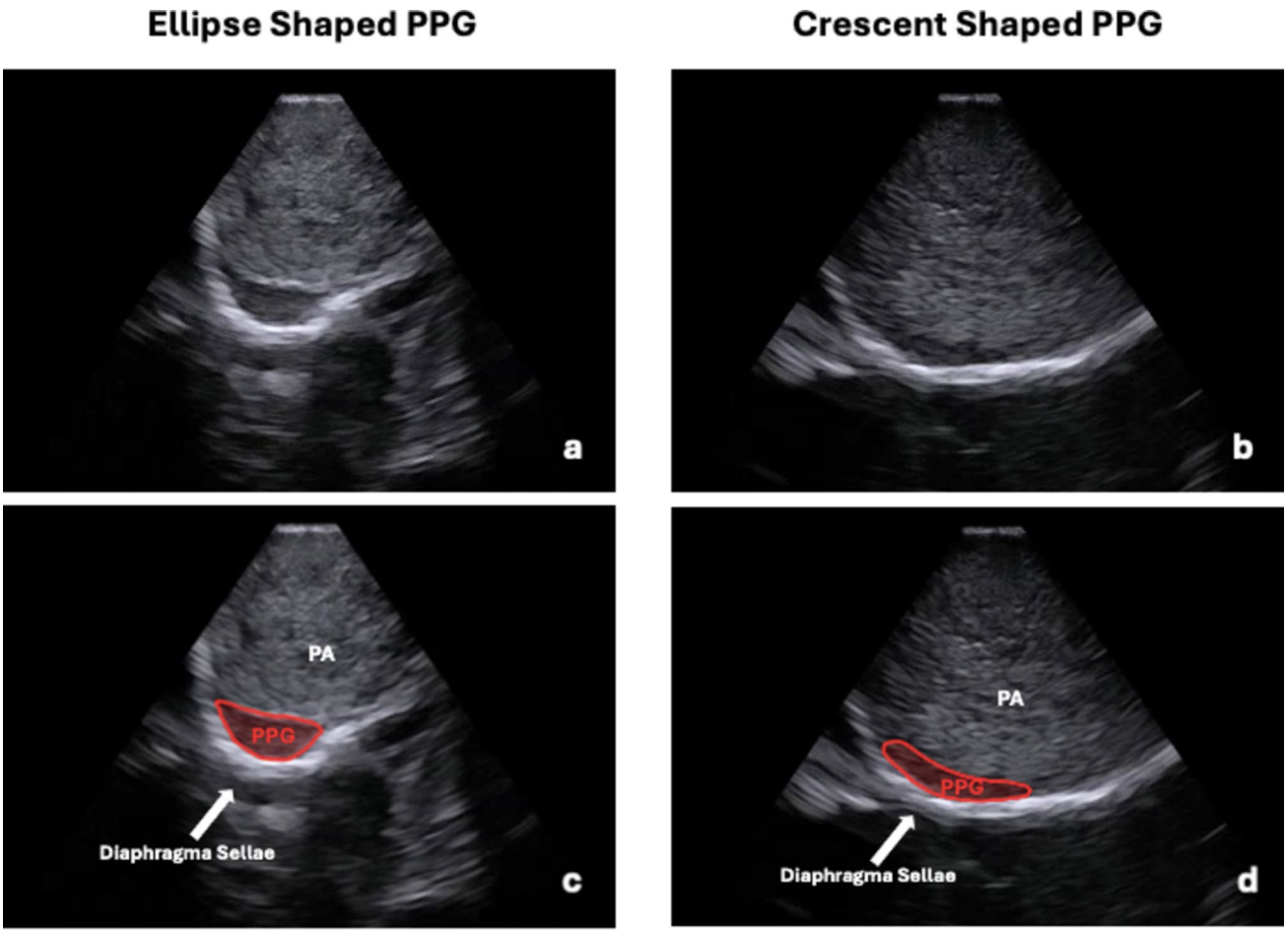

Fig. 1 Intraoperative endonasal ultrasound images of the posterior pituitary gland appearing as either ellipse (**a**, **c**) or crescent (**b**, **d**) shaped during macroadenoma resection. Panels (**c**) and (**d**) show the same images as (**a**) and (**b**), respectively, with the posterior pituitary gland (PPG), pituitary macroadenoma (PA), and diaphragma sellae highlighted. The anterior pituitary gland cannot be visualized in these images due to macroadenoma compression

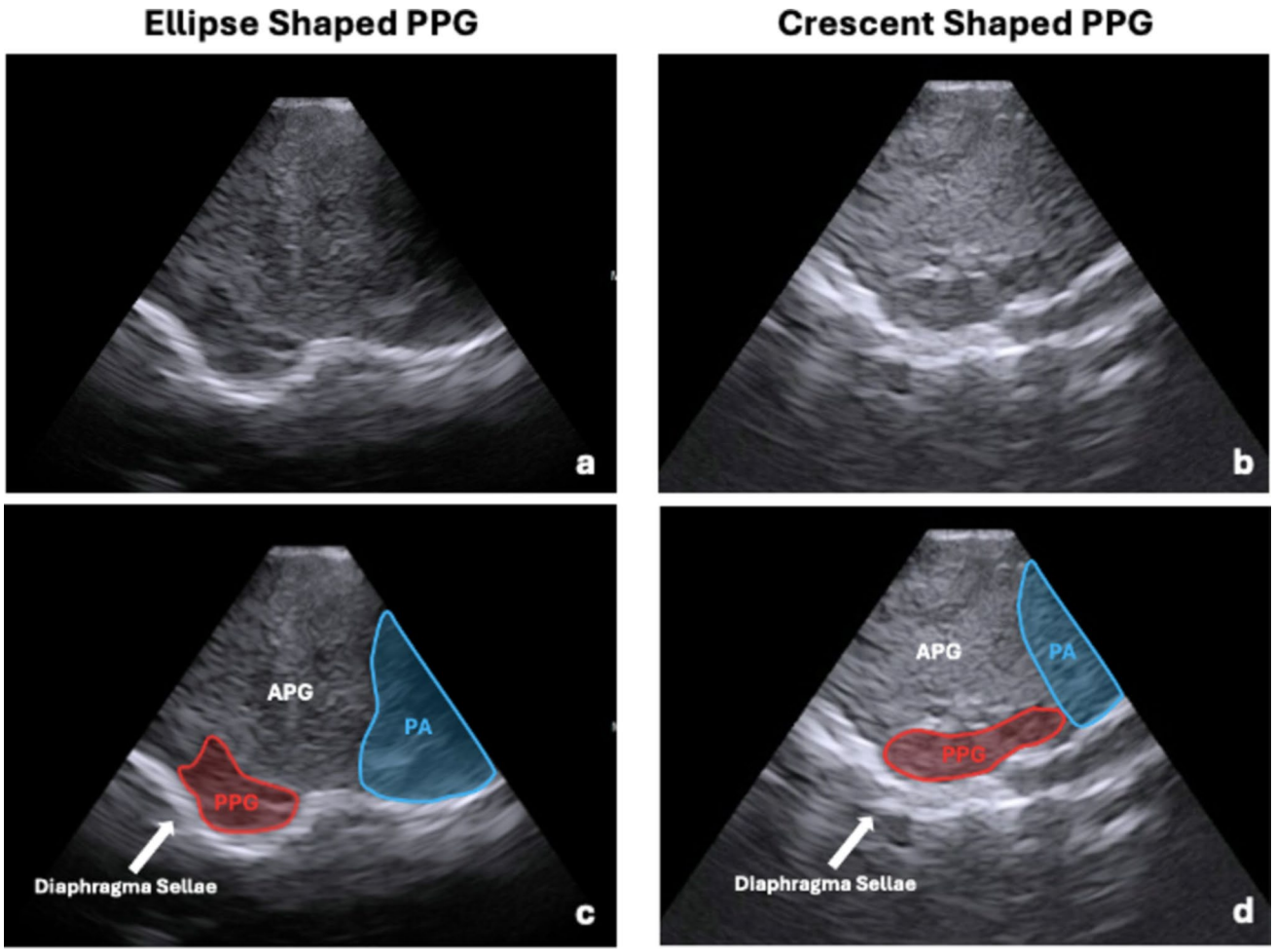

Fig. 2 Intraoperative endonasal ultrasound images of the posterior pituitary gland appearing as either ellipse (**a**, **c**) or crescent (**b**, **d**) shaped during microadenoma resection. Panels (**c**) and (**d**) show the same images as (**a**) and (**b**), respectively, with the posterior pituitary gland (PPG), anterior pituitary gland (APG), pituitary microadenoma (PA), and diaphragma sellae highlighted

that intraoperative visualization of the PPG using MRI is imperfect due to limitations in neuronavigation accuracy and shift. More precise intraoperative visualization of the PPG may provide significant clinical utility in limiting damage to the gland and allowing more prompt diagnosis of complications like DI and SIADH.

IEUS is a rapidly developing surgical tool that has the potential to change the way endoscopic endonasal skull base procedures are performed. It is being adopted by more and more endoscopic skull base neurosurgeons because it allows for real-time imaging, unlike intraoperative MRI, and can be performed several times during the same procedure without disruption to the workflow of the operation [12]. However, because its application is in its infancy, literature regarding the interpretation of the data acquired during surgery is limited [28].

Several recent publications have begun to describe the utility of, and pertinent imaging characteristics for, the use of IEUS to identify anatomical structures in a variety of skull base procedures [12, 23, 4, 5, 19, 31]. These reports focus either on identifying neurovascular structures – such as the internal carotid arteries, anterior cerebral arteries, basilar artery, hypophyseal arteries and the optic nerve, or the lesion itself [12, 23, 4, 5, 19, 31]. No previous study has described the imaging characteristics of the PPG on intraoperative US.

The presented study aimed to describe PPG characteristics on IEUS. The results reliably demonstrated that the PPG appears hypoechoic to the anterior pituitary gland and adenoma (43/43 cases, 100.0%), and is readily identified as the hypoechoic structure immediately anterior to the posterior wall of the sella turcica. The gland appears as either ellipse or crescent shaped, with the ellipse shape being more common (27/43, 62.8%) (Figs. 1 and 2). However, the crescent shape is seen more frequently in macroadenomas (43.3% vs. 23.1%) (Fig. 1), likely due to the mass effect exerted on the PPG by larger tumors within the confines of the sella.

Table 4 Intraoperative appearance of posterior pituitary gland ($n=43$)

Variable	# of Patients (%), or Mean ± SD
Hypoechoic	43 (100)
Isoechoic	0 (0)
Hyperechoic	0 (0)
Shape	
Ellipse	27 (62.8)
Crescent	16 (37.2)
Macroadenoma	
Ellipse	17 (56.7)
Crescent	13 (43.3)
Total	30
Microadenoma	
Ellipse	10 (76.9)
Crescent	3 (23.1)
Total	13

Knowledge of these characteristics will allow surgeons to more confidently identify the relative location of the PPG before, during and after adenoma resection. Considering that intraoperative intradural identification of the PPG is currently based solely on surgeon judgement [24], identification by IEUS stands to provide significant value in helping surgeons define a more optimal approach and resection plane, thereby preserving as much healthy tissue as possible. When applied appropriately, this may help to significantly decrease rates of postoperative DI and SIADH.

Moreover, several recent studies have demonstrated that stretching of the pituitary stalk during or after tumor removal is significantly associated with the onset of DI postoperatively [22, 16]. It was posited that after resection of a large pituitary lesion, the stalk will descend to fill the newly created cavity. This leads to rapid stretching of the stalk that disrupts the axonal pathways connecting the magnocellular neurons of the supraoptic and paraventricular nuclei with the posterior pituitary gland through the infundibulum, precipitating DI [22, 16]. Intraoperative US may also provide utility in predicting DI due to this phenomenon in real-time, as changes in PPG position from pre- to post-resection may act as a reasonable surrogate marker for the extent of stalk stretch that has occurred. Though visualization of the gland will not prevent this from happening, prompt recognition will help determine which patients are at an increased risk for postoperative complications and allow treatment to be administered in a timely fashion, reducing the associated morbidity.

While our study was purely descriptive, it is important to note that complication rates in the patients we analyzed were on par with, and primarily on the lower end of, historically reported ranges for similar procedures. Larger series have shown that transient DI/SIADH occurs in 14–21.2% of cases and permanent DI/SIADH occurs in less than 4.6% of cases [15, 33, 6]. Comparatively, in our cohort, transient postoperative DI/SIADH was noted in 16.3% of cases (7/43), and permanent DI/SIADH was seen in 2.33% of cases (1/43). Future larger, comparative studies are needed to determine if the use of IEUS has a significant impact on complication rates in EEA operations.

Limitations

The presented study has several limitations. The retrospective nature of the study creates inherent limitations due to the possibility of data extraction or entry errors. Furthermore, it is not clear on retrospective review whether the surgeon was intentionally seeking out the PPG on IEUS. Therefore, this study cannot speak to the frequency at which the PPG can be confidently identified, nor can a comparison be made between the complication rates of cases in which the PPG was able to be identified or not. Finally, because pituitary adenomas were the only pathology analyzed in this study, the results cannot necessarily be generalized to all EEA operations. However, the imaging characteristics described are most likely applicable to identifying the PPG in the majority of EEA operations.

Conclusions

IEUS is a useful tool to identify the PPG during pituitary adenoma resection. On imaging, the PPG can be visualized just anterior to the posterior wall of the sella, and it appears hypoechoic compared to the anterior pituitary gland and the pituitary adenoma. Furthermore, the morphology of the PPG can generally be described as either an ellipse or crescent shape, with the ellipse shape being more common. These imaging characteristics can be used by the skull base surgeon to more confidently identify the position and morphology of the PPG intraoperatively, helping to ensure its' preservation and potentially limit complications such as DI and SIADH.

Author contributions Conceptualization: K.C.W., D.M.P., G.F.; Methodology: R.B.J., G.F., D.M.P., K.C.W.; Software: N/A; Validation: N/A; Formal Analysis: R.B.J., G.F., K.C.W.; Investigation: R.B.J., G.F., K.C.W.; Resources: N/A; Data Curation: R.B.J., G.F.; Writing – Original Draft Preparation: R.B.J.; Writing – Review & Editing: R.B.J., G.F., M.A.D., L.M.P., D.M.P., K.C.W.; Visualization: R.B.J., G.F., M.A.D., L.M.P., D.M.P., K.C.W.; Supervision: G.F., M.A.D., L.M.P., D.M.P., K.C.W.; Project Administration: G.F., M.A.D., L.M.P., D.M.P., K.C.W.; Funding Acquisition: N/A.

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Data availability No datasets were generated or analysed during the current study.

Declarations

Ethics approval This study was performed in line with the principles of the Declaration of Helsinki. Approval was granted by the institutional review board/ethics committee of The Ohio State University (study #2020H0221).

Competing interests Dr. Daniel Prevedello is a consultant for Stryker Corp., Medtronic Corp., BK Medical and Integra; he has received an honorarium from Mizuho and royalties from KLS- Martin and ACE Medical. All other authors report no conflict of interest.

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