

The Value of Preoperative CT Venography for Inferior Petrosal Sinus Sampling

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Abstract

Introduction: In patients with suspected pituitary adenomas, the inferior petrosal sinus (IPS) provides the main transvenous access route to sample pituitary secretions. On occasion variant anatomy makes access and sampling difficult or even impossible. However, standard of care does not include preoperative imaging and the potential role for image guidance, especially in light of variant anatomy, remains unclear. We aimed to assess to whether pre-procedure CT venography (CTV) can improve the rate of successful sampling and whether the additional radiation dose is justified.

Methods: Nine patients with suspected Cushing's syndrome were referred for IPS between the years of 2010 and 2016. Head CTVs were obtained for each patient prior to the procedure. Venous anatomy was detailed by an experienced neuroradiologist and compared to the anatomy defined by the intra operative digital subtraction angiography (DSA). We assessed the frequency of discordant anatomy between the imaging modalities and analyzed the cases that benefited from road map guidance.

Results: Venous anatomy from CTV were identified as follow: three hypoplastic IPSs, one IPS draining into the IJV inferiorly at the level of C3-C4 (type II), one IPS divided into multiple channels before draining into the IJV (type III), and one non-visualized IPS-IJV connection (Type IV). Findings on DSA were congruent with all but the Type IV connection, which was indeed patent but hypoplastic with slow flow. Roadmap guidance with DSA alone was sufficient for successful catheterization of each IPS. Additionally, the average effective dose for CTV and DSA/Fluoroscopy was 5.4 mSv and 3.0 mSv, respectively.

Conclusions: While preoperative CTV may identify variant IPS venous drainage and accelerate the performance of inferior petrosal sinus sampling, catheterization can be accomplished under DSA and fluoroscopic guidance alone in nearly all patients. CTV guidance may be helpful when confronting complex aberrant anatomy, but its role appears limited to cases where initial attempts are unsuccessful. We recommend against routine preoperative imaging for IPS sampling in light of the rarity of critically aberrant anatomy, minimal intraoperative benefit, and nearly a double dose of radiation.

Keywords: Cushing's Disease; Inferior Petrosal Sinus Sampling; Radiation Dose; Optimization; CTV; DSA

Abbreviations

CTV: Computed Tomographic Venography; DSA: Digital Subtraction Angiography; IPS: Inferior Petrosal Sinus

Introduction

Inferior petrosal sinus (IPS) sampling plays a critical role in the diagnosis and localization of pituitary adenomas in patients with ACTH dependent Cushing's syndrome [1]. The IPS itself drains pituitary secretions from the posterior aspect of the ipsilateral cavernous sinus to the internal jugular vein [2]. Once a catheter is parked in the IPS, venous blood is sampled pre and post systemic administration of CRH or DDAVP [2]. To diagnose Cushing's disease, the ratio of the concentration of ACTH in the IPS sample to that in the contralateral IPS or periphery must be greater than 2:1, or greater than 3:1 after CRH administration [1-5].

Occasionally, navigating the deep venous system using digital subtraction angiography (DSA) proves difficult and requires a deep understanding of variant drainage patterns. Shiu., *et al.* described the appearance and frequency of four common separate types of drainage patterns, listed in table 1 [6].

Drainage Pattern	Description	Distribution, %
Type I	IPS drains directly into Internal Jugular Bulb	45
Type II	IPS Anastomosis with communicating vein or directly to the Anterior Condylar Vein	24%
Type III	IPS exists as plexus of veins	24%
Type IV	IPS drains into the Vertebral Venous Plexus and Anterior Condylar Vein without connection to the Internal Jugular Bulb	7%

Table 1: Distribution of Inferior Petrosal Sinus drainage patterns as originally described by Shiu., *et al* [6].

A typical example of Type 1 drainage patterns is shown in figure 1. Additional morphologic evaluation conducted by Mitsuhashi., *et al.* via novel 3D rotational angiography reported a frequency of 3.6% [7]. Rarely, the IPS does not opacify on DSA prompting the operator to troubleshoot and employ technically challenging maneuvers to find an alternate pathway.



Figure 1: CTV demonstrating Type 1 IPS – Inferior Jugular Bulb drainage pattern, bilaterally.

Image guidance for IPS catheterization has traditionally involved DSA alone [1-4]. While CT venograms and MR venograms provide high resolution road maps, they are seldom obtained before the procedure. This rational is in part due to the reported low frequency of complex variant anatomy. However, there has been no reported data on whether prior knowledge of vascular anatomy improves operative times or decreases radiation exposure. In this retrospective study, we hypothesize the benefit of obtaining a pre procedure high resolution CT venogram (CTV) in facilitating catheterization, and whether the potential increase in technical success and efficiency justifies the risk of increased radiation and contrast exposure.

Methods

We conducted a single-center retrospective observational study involving patients undergoing IPS sampling with suspected Cushing's disease. Data from 9 patients was collected from a period spanning August 2010 to March 2016 from Johns Hopkins Hospital, Baltimore, Maryland. This study was approved by the Johns Hopkins Medicine IRB (IRB00119976).

IPS Sampling Procedure

A total of 9 patients were studied (4 females) with ages ranging from 23 to 64 years of age. Axial contrast-enhanced CT venogram with thin sections [Toshiba Aquilion ONE (0.5 mm)] was obtained for each patient with multiplanar and 3D reconstructions. Intraoperatively, the IPS sampling procedures were performed under local anesthesia with intravenous sedation or general anesthesia, similar to the technique described by Radvany, *et al* [8]. Briefly, operative technique included bilateral femoral venous access with 8 French vascular sheaths, through which 5 French shuttle sheaths (Cook) were advanced into the IJV over 0.035" glidewires (Terumo). 4 French DAV catheters (Cook) were introduced, which were then advanced into both inferior petrosal sinuses under fluoroscopic and/or vascular map guidance. Of note, two patients underwent a slightly different sampling procedure involving use of the 5 French catheter alone for IPS aspiration. Anecdotally, this allowed for a higher rate of aspiration while saving the cost of two 4 French micro catheters.

Anatomical Analysis

Images and reports for each of these patients were reviewed. All original interpretation was done by an experienced and subspecialty trained neuroradiologist. Anatomical drainage patterns involving with IPS were observed and recorded, noting discordance between CTV and DSA reports.

Overcoming Anatomic Variants Intra-procedurally

When access to a given IPS was difficult and not readily obtained, the initial troubleshooting step was to catheterize the contralateral side using the same technique. Typically, at least one IPS was accessible. Contrast injection through the ipsilateral side led to opacification of the cavernous sinus which was often followed by opacification of the contralateral drainage pathway. The resultant DSA roadmap then allowed for guidance through the problematic IPS.

Radiation Analysis

We compared radiation exposure between imaging modalities. Radiation data from the CT venograms (Toshiba Aquilion ONE, slice thickness 0.5 mm) was provided in the form of CTDIvol (mGy) and Dose-Length-Product (mGy-cm). DSA radiation measurements were provided in the form of dose and Kerma-Area-Product.

Due to the technical differences in imaging, reporting of radiation exposure, and irradiation geometries, we used effective dose calculations to provide an approximate comparison between CTV and DSA [9-11]. Effective dose conversion factors for DLP and KAP used in this study were 0.0022 mSv/mGy-cm and 0.07 mSv/Gy-cm², respectively [9]. Differences were evaluated with two tailed student's t-test.

Results

Anatomical Results

Nine patients with suspected Cushing's disease underwent IPS sampling to evaluate for pituitary adenoma. CTV drainage patterns for IPS venous anatomy were carefully scrutinized and compared to previously described variants. The left IPS was hypoplastic in two cases, indicating diminutive caliber compared to the contralateral side. The right IPS was hypoplastic in one case. There was one type II variant which had a single vein draining into the IJV at the level of C3-C4. There was one type III variant. Finally, there was one type IV variant without a visible connection between the left IPS and the internal jugular vein. The remaining twelve IPS drainage connections were visualized at the level of the jugular bulb or just inferior.

In contrast, DSV demonstrated patency of IPS drainage bilaterally in all patients, including those with hypoplastic sinuses and the type IV variant seen on CTV. The type II and type III variant anatomies were confirmed. With the exception of the false positive type IV variant, delineation of venous anatomy was congruent between CTV and DSV. Additionally, catheter placement into each IPS was successful for each patient.

Radiation Results

The average CTV Dose-Length-Product and DSV/Fluoroscopic Dose-Area-Product was 2467.4 mGycm and 43142.2 mGycm², respectively. Due to differences in radiation geometry and dosimetry reporting, we approximated effective doses for each modality using previously published conversion factors [9]. The effective doses for CTV and DSV/Fluoro were 5.43 mSv and 3.02 mSv, respectively.

Discussion

IPS sampling plays a central component in the diagnosis and workup of ACTH dependent Cushing syndrome, [12]. The procedure itself is technically challenging and while complications are rare, cases of vascular damage and hemorrhage been reported [13,14]. Despite previously described variations in IPS venous anatomy and difficulties in catheterization, preoperative imaging is not typically pursued. Intuitively, CTV provides beneficial roadmap guidance and in certain cases can alert the physician to alternate or even impossible venous access. However, in this study we find that the role of routine preoperative CTV is minimal given its marginal benefit in terms of navigation and high dose of added radiation (5.43 mSv).

Preoperative imaging demonstrated bilaterally patent IPS in nine patients with the exception of one IPS where a connection to the internal jugular vein was not visualized. In patients where no normal IPS exists, this feature would be of great help a priori. Three sinus drainage patterns were deemed hypoplastic. We also observed a single type II and type III connection. While catheter navigation without roadmap assistance was not evaluated, the authors note that each positive DSV finding was seen on the preoperative CTV. However, the type IV variant anatomy characterized as non-visualized sinus drainage pattern was actually found to be patent on DSV. We suspect poor specificity of CTV in these cases is due to poor or slow flow in small caliber vessels.

Additionally, certain patients with known hypoplastic IPS drainage on CTV continued to pose difficulty in catheterization despite prior anatomical knowledge. Traditional catheter and fluoroscopic techniques were still required to gain access. One such technique, as described above, includes contrast injection of the contralateral IPS to opacify the cavernous and ipsilateral IPS to visualize the drainage pattern (Figure 2) [13]. This process contributed to visualization of the previously suspected type IV anatomy.



Figure 2: Example of CTV and DSV discrepancy with troubleshooting technique to gain IPS access. A) CTV demonstrating poorly visualized left sided IPS drainage to the Inferior Jugular Bulb. B) DSV showing catheter placement in the right IPS. Contrast injection traverses the cavernous sinus, opacifies the contralateral IPS, and demonstrates patent connection to the left Inferior Jugular Bulb. C) DSV demonstrating successful catheter placement into the left IPS.

Though fluoroscopic techniques are independently able to identify variants and facilitate catheter placement, CTV may still be advantageous for drainage patterns rendering catheterization from the ipsilateral side impossible. However, the frequency of this drainage pattern in the literature is between 0.6 - 7%, suggesting variants that would benefit from imaging are rare [5-7]. In addition to the rarity, similar but patent drainage patterns which are susceptible to slow flow may appear impossible to cannulate on CTV. The low prevalence and poor specificity, especially in these cases, question any role for preoperative imaging in improving procedural efficiency.

Finally, the use of CTV carries significant radiation risk for patients. The risks of radiation exposure have been well documented and have led to numerous statements by the Food and Drug Administration, National Cancer Institute, and American College of Radiology regarding mitigating the risks of radiation [15-18]. In our study, radiation exposure of both CTV and DSV was nearly three times as much as DSV alone (8.43 mSv vs. 3.02 mSv). Considering CT scans of the head have been one of the largest contributors of radiation-related cancer in the United States, head CT scans must be ordered judiciously in patients, and their standard use must be examined. Moreover, the contrast in these scans exposes patients to adverse effects, ranging from pain and nausea to nephrotoxicity and anaphylaxis [19,20]. Lastly, CTVs can unnecessarily add an estimated cost of \$500-600 per examination [21].

The study's limitations include small sample size and retrospective nature. Additionally, while we suspect probable reduction in fluoroscopy time due to pre-op scans, the low prevalence of variant anatomy may render this effect small. Studies directly comparing radiation dosage and procedural times with and without preoperative imaging may provide more definitive evidence. Roadmap guidance may be helpful when confronting complex aberrant anatomy, but its role appears limited to cases where initial attempts are unsuccessful. We recommend against routine preoperative imaging for IPS sampling in light of the rarity of critically aberrant anatomy, minimal intraoperative benefit, and nearly doubled dose of radiation.

Author Statements

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Competing Interests Statement

The Authors declare that there is no conflict of interest.

Contributorship Statement

Vikram Rajpurohit: Corresponding and main author who provided contributions to the conception and design of the work, acquisition and analysis of the data, drafted and revised the manuscript, and provided final approval of the version to be published.

Ankur Doshi: Co-author who provided contributions to the acquisition and analysis of data, drafted portions of the manuscript, and provided final approval of the version to be published.

Ferdinand Hui: Principle investigator who provided substantial contributions to the conception and design for the study, acquisition of the data, and revision of the work to be published. He also provided final approval of the version to be published.

All authors agree to be accountable for all aspects of work.

Data Sharing

Data sharing: Anonymized patient level data set available from the corresponding author on request. Consent was not obtained but the presented data are anonymized and risk of identification is low.

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