Image Guided Venous Sampling for the Localization of Endocrine Tumors

- The source of excess hormone causing diseases such as Conn’s syndrome or ACTH-dependent Cushing’s syndrome cannot be reliably determined using only non-invasive diagnostic tools.
- Bilateral inferior petrosal sinus sampling (IPSS) is the gold standard for determining whether the source of excess adrenocorticotropic stimulating hormone (ACTH) in patients with ACTH-dependent Cushing’s syndrome is from the pituitary or is ectopic.
- Bilateral adrenal vein sampling can demonstrate the location of the aldosterone secreting adenoma.
- IPSS and bilateral adrenal vein sampling are performed by an interventional radiologist under fluoroscopic guidance.

Elevated levels of cortisol production resulting in Cushing’s syndrome can be caused by elevated production of adrenocorticotropic hormone (ACTH) from a pituitary or an ectopic tumor or excessive autonomous production of cortisol from a hyperfunctioning adrenal tumor. Differentiating between ACTH-dependent and ACTH-independent Cushing’s syndrome is generally straightforward and achieved with laboratory testing. However, identifying the source of the excess hormone in cases of ACTH-dependent Cushing’s can be challenging.

A high-dose dexamethasone suppression test can be helpful in distinguishing between pituitary and ectopic tumors because high doses of dexamethasone are more likely to inhibit pituitary secretion of ACTH. However, this test is reported to have 60-80% sensitivity and specificity. Stimulation by corticotropin-releasing hormone (CRH) can also be helpful because pituitary tumors are more likely to respond to stimulation by this hormone; although, in many cases ectopic tumors also respond.

Pituitary gadolinium-enhanced MRI is indicated in patients with ACTH-dependent Cushing’s disease, but interpretation is limited when small or no lesions are detected because of the high prevalence of pituitary tumors.

Figure 1. IPSS venography. Image shows microcatheters in both inferior petrosal sinuses (black arrows) after contrast injection from the left side, which opacified the contralateral sinus via mild reflux, indicative of proper catheter positioning. The black star indicates the expected location of the pituitary gland within the opacified cavernous sinus.
incidentalomas in asymptomatic patients. In addition, false-negative results have been associated with microadenomas that are too small to detect with imaging. Similarly, the accuracy of MRI or CT of the adrenal glands is limited by the high prevalence of non-functioning adrenal nodules.

**Bilateral Inferior Petrosal Sinus Sampling**

Once it has been established that the hypercortisolemia of Cushing’s syndrome is due to excess production of ACTH and a pituitary protocol MRI has demonstrated either pituitary microadenoma (<1 cm) or no pituitary lesion, bilateral inferior petrosal sinus sampling (IPSS) is indicated in most cases. Performed by an interventional radiologist, IPSS can determine whether the source of excess ACTH production is from the pituitary or an ectopic source, thus preventing unnecessary transsphenoidal surgery. Bilateral IPSS may also aid in tumor localization because the secretion of ACTH is often asymmetrical, with higher amounts draining from the ipsilateral side of the adenoma.

The procedure is initiated by placing microcatheters into both inferior petrosal sinuses. Contrast is then injected, and fluoroscopy is used to observe the anatomy of the inferior petrosal veins and the cavernous sinus (Figure 1), which can vary from patient to patient. For example, the position of the anterior condylar vein is important because it joins the inferior posterior sinus (IPS); therefore, the microcatheter must be advanced past this junction to avoid sampling errors. Under fluoroscopic guidance, the microcatheters are placed symmetrically, and intermittent fluoroscopy is used to confirm their correct position during the procedure. Once the positioning of the catheters is confirmed, blood samples are drawn from each IPS as well as a peripheral sample from the femoral sheath. CRH or desmopressin, is then administered peripherally. Blood samples are drawn from each IPS and peripherally at 3, 5,
Cushing's disease is confirmed if the ratio of baseline ACTH levels in the IPS and the periphery is ≥2 or if the ratio is ≥3 after the administration of CRH. The accuracy, as determined by a meta-analysis of 21 studies, has shown the sensitivity and specificity to be 96% and 100% respectively. An intersinus ratio of ≥1.4 has been proposed as evidence of ipsilateral localization of an adenoma, but estimates of the accuracy of the method range from 50-100%, and surgeons routinely perform a full exploration of the pituitary gland if Cushing’s disease is present.

**Adrenal Vein Sampling**

Primary aldosteronism, or Conn’s syndrome, is a potentially curable cause of secondary hypertension with prevalence rates ranging from 5–4.4%. It is detected by measuring the aldosterone-renin ratio and confirmed by a 24-hour urine collection after a sodium load. Once primary aldosteronism has been confirmed, a CT scan of the adrenal glands and their vasculature is recommended to examine adrenal anatomy and position of the adrenal veins, which may vary from patient to patient. CT is not considered reliable for identifying the source of excess hormone production. Just as in the pituitary gland, non-functional adenomas are commonly found in asymptomatic patients. Moreover, hypersecreting adrenal glands may appear to be normal in size in imaging studies. However, if a CT scan shows an adenoma larger than 2.5–4 cm, surgery may be warranted on the basis of the potential for malignancy, unless imaging findings suggest that it is a benign lesion such as a myelolipoma. Additionally, adrenal nodules greater than 1 cm in younger patients are sometimes removed without further localization studies, since incidental adrenal nodules are uncommon in younger patients.

When surgical therapy is being considered to treat primary aldosteronism, bilateral adrenal vein catheterization and venous sampling should also be considered. This test is performed by a vascular interventional radiologist who uses information from a CT scan to catheterize each of the adrenal veins under fluoroscopic guidance. With constant ACTH stimulation, blood samples are taken from each adrenal vein and a peripheral vein. Adrenal veins should have a significantly higher level of cortisol than peripheral blood samples; in fact, a cortisol ratio of 3:1 is required to be confident that the adrenal vein has been successfully sampled. However, the procedure is technically challenging with high reported failure rates associated mainly with difficulty in cannulation of the right adrenal vein. The fusion of CT and angiographic images, a technique now available in the new angiography suite at Massachusetts General Hospital, has been helpful to ensure correct placement. Adrenal adenomas, which produce excess aldosterone, will show a ratio higher than that of the peripheral sample and the normal gland, identifying the adrenal gland for surgical resection to cure the Conn’s syndrome. Therefore, adrenal sampling can confirm that the source of the excess aldosterone is from the adrenal glands and whether it comes from the right or left gland. Similar to IPSS patients, post-procedure patients remain in bed and under observation for four hours before discharge.

**Scheduling**

Appointments for IPSS or adrenal sampling can be made by calling 671-726-8396. The procedures are performed in the Interventional Radiology facilities on the main campus of Massachusetts General Hospital.

**Further Information**

For more information regarding IPSS and adrenal vein sampling, please contact Rahmi Oklu, MD, PhD, Interventional Radiology, Massachusetts General Hospital (617-726-8396).

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References


