Real-Time Super Selective Venous Sampling in Remedial Parathyroid Surgery

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BACKGROUND: Remedial cervical exploration for persistent or recurrent primary hyperparathyroidism can be technically difficult, but is expedited by accurate preoperative localization. We investigated the use of real-time super selective venous sampling (sSVS) in the setting of negative noninvasive imaging modalities.

STUDY DESIGN: We performed a retrospective analysis of a prospective database incorporating real-time sSVS in a tertiary academic medical center. Between September 2001 and April 2014, 3,643 patients were referred for surgical treatment of primary hyperparathyroidism. Of these, 31 represented remedial patients who had undergone one (n = 28) or more (n = 3) earlier cervical explorations and had noninformative, noninvasive preoperative localization studies.

RESULTS: We extended the use of the rapid parathyroid hormone assay in the interventional radiology suite, generating near real-time data facilitating onsite venous localization by a dedicated interventional radiologist. The predictive value of real-time sSVS localization was investigated. Overall, sSVS correctly predicted the localization of the affected gland in 89% of cases. Of 31 patients who underwent sSVS, a significant rapid parathyroid hormone gradient was identified in 28 (90%), localizing specific venous drainage of a culprit gland. All patients underwent subsequent surgery and were biochemically cured, with the exception of one who had metastatic parathyroid carcinoma. Three patients with negative sSVS were also explored and cured.

CONCLUSIONS: Preoperative parathyroid localization is of paramount importance in remedial cervical explorations. Real-time sSVS is a sensitive localization technique for patients with persistent or recurrent primary hyperparathyroidism, when traditional noninvasive imaging studies fail. These results validate the utility and benefit of real-time sSVS in guiding remedial parathyroid surgery. (J Am Coll Surg 2015;220:994−1000. © 2015 by the American College of Surgeons)

Primary hyperparathyroidism (PHPT) is a common endocrine disease affecting 1 in 500 to 1,000 patients.[1-3] Surgical management remains the sole curative treatment option. Index parathyroid operations for PHPT are associated with cure rates exceeding 95% and complication rates ranging between 1% and 2% when performed by experienced surgeons.[4-6] However, a substantial number of patients require remedial cervical exploration for persistent or recurrent PHPT after initial exploration. Such failure rates exist largely because the majority of parathyroid operations in the United States are performed by low-volume surgeons who attain lower operative success rates.[7-9] Remedial cervical exploration can be technically challenging due to scarring and obliteration of tissue planes, is associated with an increased risk of collateral injury, particularly to the recurrent laryngeal nerves, and the operative failure rate is increased. Given the increased complexity, the decision to reoperate is influenced by the ability to localize the culprit gland(s) preoperatively.[10-12]

First-line parathyroid localization studies consist of noninvasive imaging studies, including ultrasound, sestamibi, CT, and MRI scans. Patients with informative, noninvasive localization studies proceed to surgical exploration. However, there remains a subset of patients with non-localizing or discordant studies, who can benefit from

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Abbreviations and Acronyms
PHPT = primary hyperparathyroidism
PTH = parathyroid hormone
sSVS = super selective venous sample
SVS = selective venous sampling

invasive preoperative localization techniques, such as selective venous sampling (SVS) and arteriography. We previously reported our experience with SVS and demonstrated the value of this localization modality in 6 patients in the reoperative setting.[4] Our approach allowed for the extrapolation of the rapid parathyroid hormone (PTH) assay to the interventional radiology suite, which facilitated near real-time data during onsite venous localization. Use of onsite PTH analysis results in immediate feedback, guiding the interventionist and improving the success rate of this localization study. Additionally, the interventional radiologist can obtain samples from areas with a subtle gradient in an effort to increase the resolution by sampling smaller venous branches. Similarly, collecting additional blood samples from the area with the highest PTH gradient also increases the resolution of the study. Some authors refer to this sampling method as "super selective" venous sampling (sSVS), emphasizing the refinement of this modified technique compared with conventional SVS.[13] The current cumulative series represents the experience from 31 patients who underwent real-time sSVS at our institution.

METHODS

Institutional Review Board approval was obtained before the retrospective analyses of our prospective database. The medical records of all patients who underwent sSVS and subsequent surgical exploration for recurrent or persistent PHPT at a single institution between September 2001 and April 2014 were reviewed. A dedicated interventional radiologist (JEA) performed all selective venous localization studies, and there was no change in technique during the study period. After referral, all patients underwent a detailed history and physical examination, followed by confirmatory laboratory testing. Eligible patients had a biochemically confirmed diagnosis of PHPT (serum calcium >10.5 mg/dL [reference range 8.5 to 10.5 mg/dL] and intact PTH >65 pg/mL [reference range 10 to 65 pg/mL]), which persisted or recurred after previous parathyroid surgery. A meticulous review of all operative, imaging, pathologic, and biochemical studies was performed and additional noninvasive preoperative imaging was obtained, if necessary. If an imaging modality demonstrated unequivocal localization of a culprit parathyroid gland, the patients were explored without additional preoperative localization studies. When noninvasive imaging studies were negative or nonconvincing, the patients underwent sSVS in the interventional radiology suite using the rapid PTH assay as an adjunct, before remedial surgery.

Real-time super selective venous sampling and arteriography

The technical details of the procedure have been described previously.[4] All procedures were performed using a standardized protocol. Briefly, after catheterization of the common femoral vein, blood from the iliac vein was obtained (baseline value) before extensive selective venous sampling of small venous branches from the neck and mediastinum. Venography is performed at every site of venous sampling. In addition, in super selective sampling, venograms were obtained in 2 planes to delineate the precise anatomic location of the vessel being sampled. In the setting of equivocal results, the interventional radiologist acquired additional samples in any area that demonstrated a subtle gradient. The investigation continued until a positive assay was obtained or no additional veins could be catheterized to reveal a significant gradient. A 2-fold elevated PTH value, as compared with the baseline PTH level obtained from the iliac vein, defined a positive localizing study.[14] A negative localization study is one in which no useful localization information was obtained before the exploration. The results of sSVS were compared with the results of noninvasive localization methods, including ultrasound, sestamibi, CT, and MRI scans. The decision for initial side sampling takes into account operative records and pathologic findings from initial neck explorations, results from noninvasive imaging tests, and results from the prevenous arterial phase that might show a hypervascular focus. The venous anatomy of these patients is subject to vascular remodeling, as all patients underwent at least one earlier neck exploration. Accordingly, an arterial study precedes venous sampling. In brief, after the arterial injection, which might suggest a culprit gland, imaging is continued until the venous drainage is delineated. Occasionally, the major route of venous drainage from an arterial injection will be to the contralateral side. This information prompts venous sampling from this area.

Remedial parathyroidectomy

All remedial parathyroid operations were performed by the current endocrine surgeons at our institution after a thorough review of the angiography findings and PTH gradients with the interventional radiologist. An intraoperative PTH assay was used adjunctively in all cases, and an adequate reduction in PTH levels (50% drop from baseline), as well as drop into a normal PTH range after parathyroid gland resection allowed for termination