

Nicole De La Pena, MD¹; Michael Martini, MD, PhD¹; R. Chase Ransom, MD, PhD¹; Ramin Morshed, MD²; Derek O’Keeffe, MD, PhD³; William Young Jr., MD³; John L. Atkinson, MD¹; Lorenzo Rinaldo, MD, PhD¹; Harry Cloft, MD, PhD⁴; Jamie Van Gompel, MD¹
¹Mayo Clinic Department of Neurologic Surgery, ²University of San Francisco Department of Neurologic Surgery, ³Mayo Clinic Department of Endocrinology, ⁴Mayo Clinic Department of Radiology

Introduction

In MRI-negative Cushing’s disease, inferior petrosal sinus sampling (IPSS) can help confirm the pituitary as the source of excess ACTH. Prior studies have demonstrated that IPSS does not correlate with pituitary adenoma laterality^{1,2}; however, IPSS-guided resection continues to be practiced. This study evaluated different patterns of angiographic cross filling of IPSS venograms to categorize the risk of pituitary adenoma mislateralization.

Methods

A single center, retrospective review of cases between 1998-2017 was performed in which patients underwent IPSS for a presumed ACTH-secreting pituitary adenoma.

IPSS venogram filling patterns were subdivided into three groups (Fig. 1): Group 1: no angiographic cross filling when either IPS was injected; Group 2: angiographic cross filling that occurred with the injection of one IPS but not the other (directional cross filling); Group 3: angiographic cross filling that occurred when either IPS was injected (bilateral cross filling).

Contralateral and ipsilateral ACTH response ratios (ratio of change in ACTH levels measured at 10 minutes compared to 2 minutes after CRH administration) were compared between each group.

A multivariate logistic regression was performed with multiple venogram characteristics to create a model of factors that predicts an increased risk of mislateralization by IPSS.

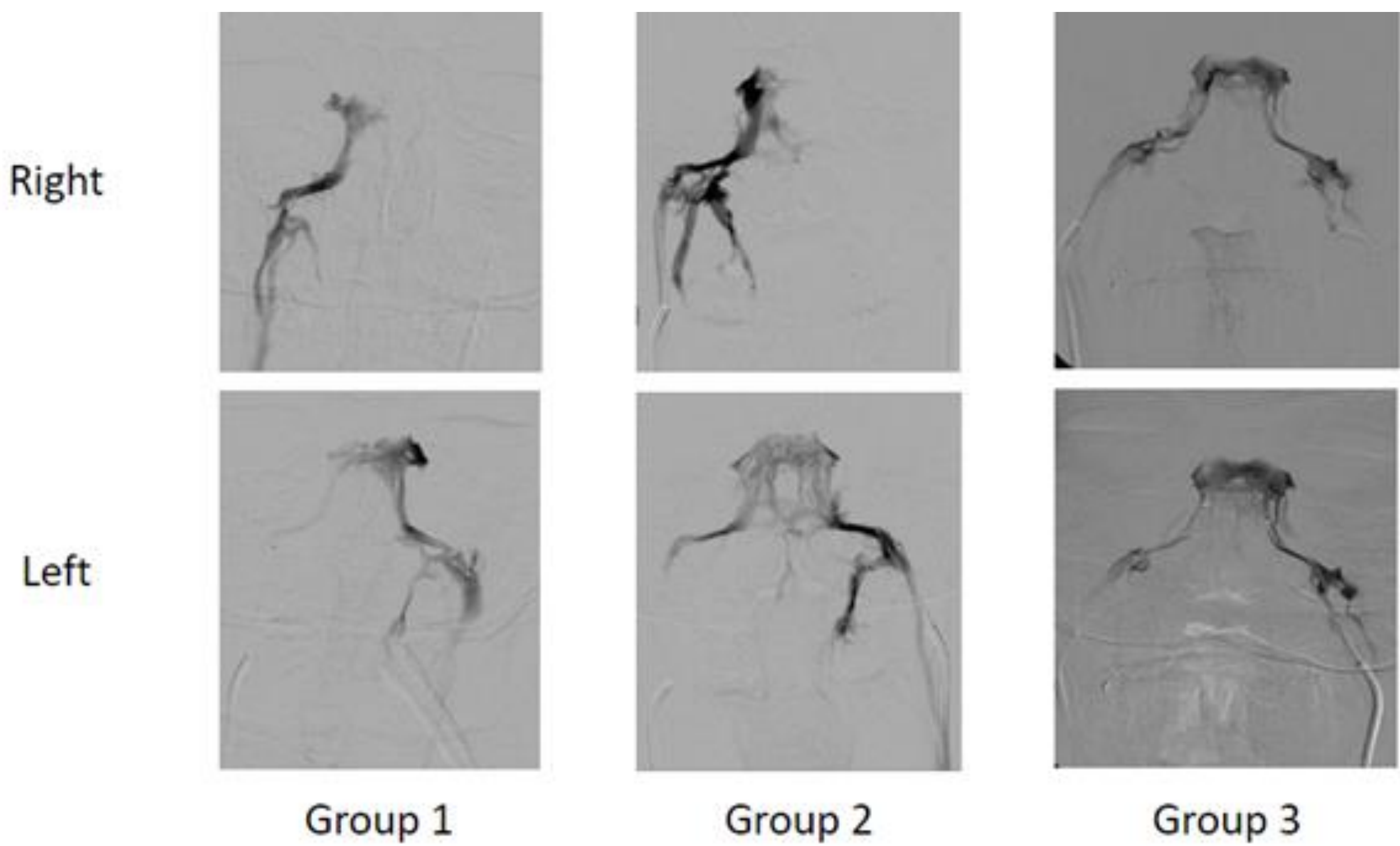


Figure 1. Angiographic examples of group 1 (no cross filling), group 2 (directional cross filling), and group 3 (bilateral cross filling). The left venogram in group 2 also demonstrates basilar venous plexus filling.

Results

Forty-two patients were included in the study, with 9 patients classified in group 1 (21.4%), 17 in group 2 (40.5%), and 16 in group 3 (38.1%).

There was a trend of increasing contralateral and decreasing ipsilateral ACTH response ratio from group 1 to group 3 (Fig. 2).

Patients in group 1 and group 2 had a 77.8% and 94.1% rate of agreement between IPSS and intraoperative lateralization, respectively (positive predictive value), while patients in group 3 only had a 68.8% rate of agreement.

Multivariate analysis revealed that bilateral cross filling had an increased risk of mislateralization by IPSS by 10 times, while directional cross filling had a decreased risk of mislateralization, though this was outside of statistical significance (Table 1). A multivariate logistic regression model designed to predict IPSS mislateralization using angiographic IPS cross filling, basilar venous plexus filling, and the bilateral cross filling pattern achieved an AUC of 0.78 (95% CI 0.61 - 0.95, $p = 0.015$; Fig. 3).

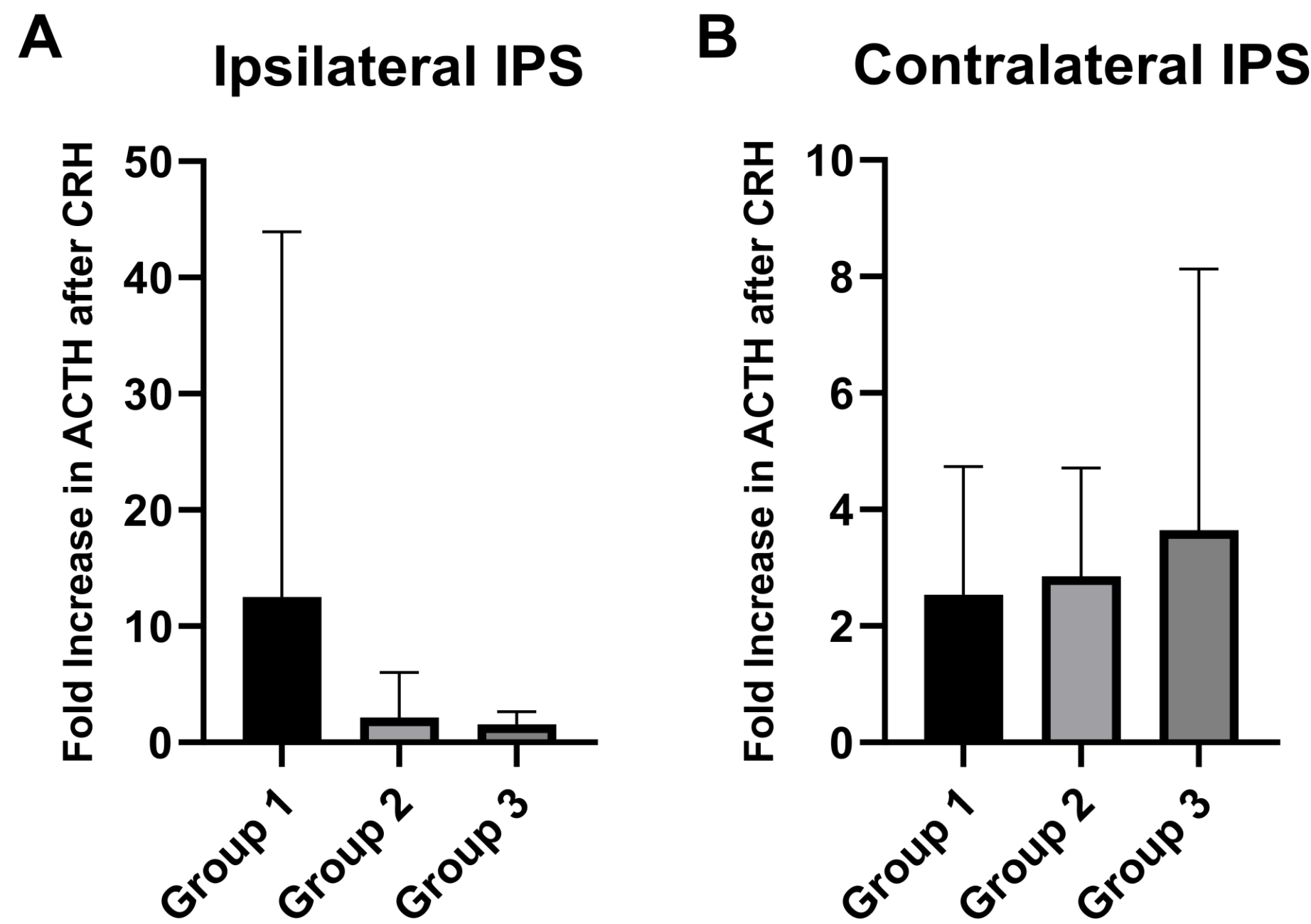


Figure 2. Mean ACTH response ratio for the ipsilateral (A) and contralateral (B) IPS for each group.

	Odds Ratio (95% CI)	P value
Any angiographic cross filling	0.46 (0.02-5.8)	0.55
Basilar venous plexus filling	8.1 (0.96-183.1)	0.09
Directional cross filling	0.96 (0.004-0.8)	0.057
Bilateral cross filling	10.4 (1.25-232.1)	0.057

Table 1. Multivariate analysis of different angiographic cross filling characteristics and mislateralization by IPSS.

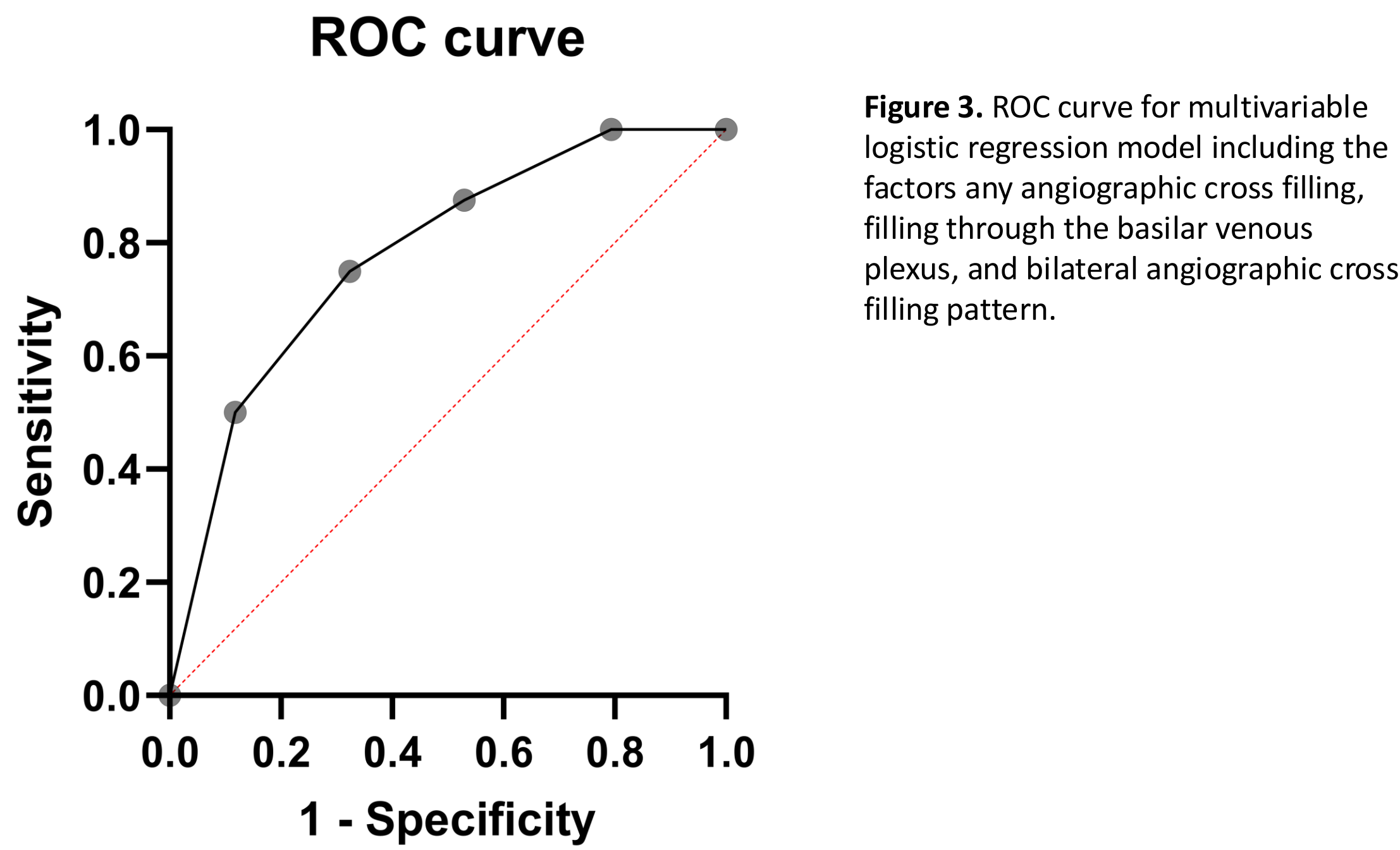


Figure 3. ROC curve for multivariable logistic regression model including the factors any angiographic cross filling, filling through the basilar venous plexus, and bilateral angiographic cross filling pattern.

Discussion

Different patterns of angiographic cross filling across the pituitary via the IPS mediates different levels of risk of mislateralization with IPSS. In cases where there is bilateral cross filling, there may be a dilutional effect that decreases the measured ACTH response on the ipsilateral side and increases this response on the contralateral side, decreasing the reliability of the study to lateralize the adenoma. The presence of basilar venous plexus filling is likely a modifier of this effect, as this adds an additional channel in which dilution can occur and lead to a sampling error³.

The limitations of this study include a small sample size, which portends low power. Additionally, although the procedure is mainly performed by one neurointerventional radiologist at our institution, there are differences in technical characteristics of performing the angiogram that could influence the extent of crossfilling of the contrast during the study, including power of injection into the IPS.

Conclusions

- Bilateral cross filling showed an increased risk of mislateralization with IPSS while directional cross filling showed a decreased risk
- Basilar venous plexus cross filling may mediate the increased risk of mislateralization
- These findings may direct treatment decisions for surgical resection and radiosurgery of these adenomas depending on the pattern of cross filling observed during IPSS

Contact

Nicole De La Peña, MD
Mayo Clinic, Department of Neurologic Surgery
200 1st St SW, Rochester, MN 55902
delapena.nicole@mayo.edu

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