

## Introduction

Accurate diagnosis of patients presenting with prolactinomas and non-functioning adenomas (NFA) can be challenging given that radiographic and biochemical testing is often equivocal. Increased size of NFA can potentially cause increased prolactin levels due to mass effect on the pituitary stalk, often referred to as 'stalk effect'. This study aims to better correlate prolactinoma size with serum prolactin levels to help guide surgical and medical decision making by differentiating the two diagnoses.

## Methods

Retrospective review of patients undergoing transphenoidal surgery (TSS) from 2008 – 2018 was performed. Patients undergoing first-time surgical intervention for histologically confirmed prolactinoma and NFA were included. Pre-treatment MRI scans were reviewed and maximum diameter in orthogonal planes was measured. Radiographic cystic appearance was also noted. Tumors were grouped based on size as follows: <10mm, 11-20mm, and >20mm.

## Results

Seventy-seven prolactinoma patients (28 cystic lesions and 49 non-cystic) and 217 NFA patients (34 cystic lesions and 183 non-cystic) were included in this study. Statistically significant differences ( $p < 0.01$ ) were detected between serum prolactin levels in patients with prolactinomas (mean 731.6ng/dl, range: 7.4ng/dl – 13,579.9ng/dl) compared to patients with NFAs (25.52ng/dl, range 0.25ng/dl – 148ng/dl).

Comparison between cystic prolactinomas and NFAs, as well as non-cystic lesions, revealed statistical significance in tumors between 11-20mm (cystic mean: 133.37ng/dl vs. 23.38ng/dl, non-cystic means: 370.20ng/dl vs. 26.60ng/dl) and >20mm (cystic means: 2,394.42ng/dl vs. 28.42ng/dl, non-cystic means: 1,526.40ng/dl vs. 24.76ng/dl).

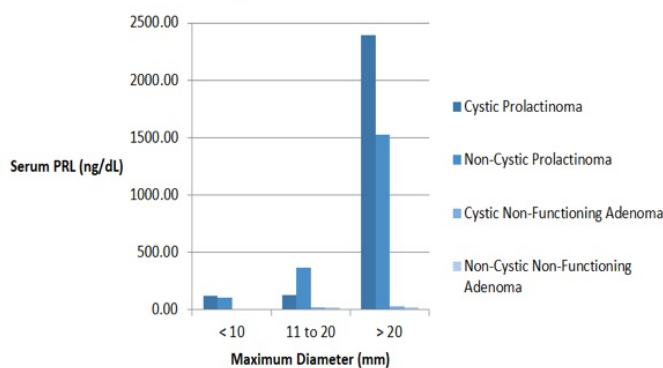
In comparing serum prolactin levels in cystic to non-cystic prolactinomas, there was a statistically significant decrease in serum prolactin comparing across all sizes (means: 613.77ng/dl vs. 937.92ng/dl); however, no differences were found when categorized by size. Analysis was limited by the number of NFA microadenomas in this cohort.

## Conclusions

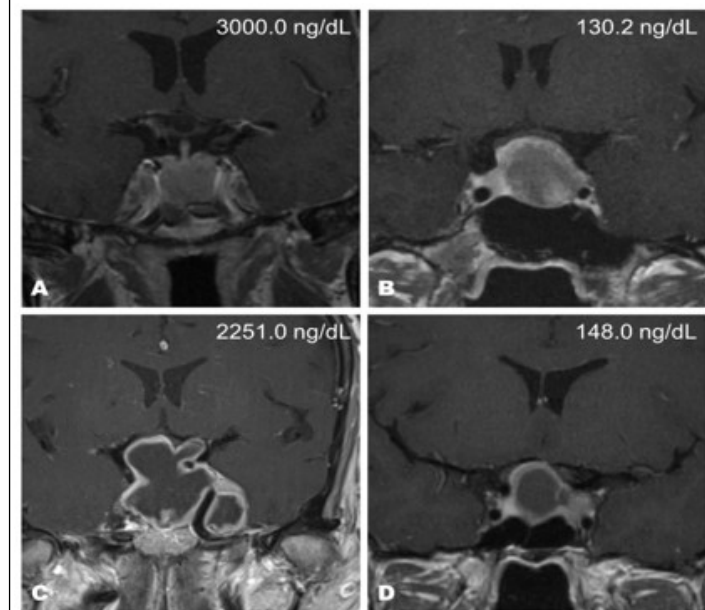
Prolactinoma size and absence of cyst significantly influence serum prolactin levels. Additional studies involving larger cohorts will improve knowledge of their biochemical effects in the setting of equivocal diagnostic work-up, as well as potentially expose more specific identifying characterization of these tumors. Furthermore, this study strengthens the classical teaching that serum prolactin levels below 150ng/dl may represent "stalk effect" as opposed to a functional adenoma.

**Figure 1.**

### Average Serum Prolactin Level



**Figure 2.**



High-resolution, post-contrast, coronal MRI highlighting radiographic equivalence of prolactinoma and NFA.

Corresponding serum prolactin level is indicated in the upper right-hand corner. Panel A and B represent a non-cystic prolactinoma and NFA, respectively. Panel C and D represent a cystic prolactinoma and NFA, respectively.

**Table 1.** Comparison of mean serum prolactin levels among tumor types.

	Non-Cystic Lesions		Cystic Lesions		p-value
	Average	Range	Average	Range	
<b>Prolactinomas</b>					
< 10mm	104.46 ± 98.95	26.1 – 447.0	124.13 ± 130.06	8.0 – 454.2	0.674
10 – 20mm	370.20 ± 670.30	12.0 – 3000.0	133.37 ± 142.43	37.3 – 493.6	0.308
> 20mm	1526.40 ± 1568.31	7.4 – 5704.0	2394.42 ± 4060.30	60.7 – 13579.9	0.472
<b>Non-Functioning Adenomas</b>					
< 10mm	8.70	-	-	-	-
10 – 20mm	26.60 ± 29.81	0.3 – 148	23.38 ± 14.62	2.5 – 56.1	0.717
> 20mm	24.76 ± 22.62	0.25 – 127.6	28.42 ± 28.31	2.2 – 130.2	0.505
< 10mm	-	-	-	-	-
10 – 20mm	< 0.0001		< 0.01		
> 20mm	< 0.0001		< 0.01		