Rate of Prolactin Suppression Can Predict Future Prolactin Normalization, Tumor Shrinkage and Time to Remission in Men with Macroprolactinomas.

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Introduction

Dopamine agonists (DA) are the mainstay treatment for prolactinomas, but clinical characteristics that predict their effects on prolactin (PRL) suppression and tumor shrinkage are missing.

Our study aimed to identify measures in early follow-up of men harboring macroprolactinomas, that will predict dynamics of PRL decrease and adenoma shrinkage.

Patients and Methods

A single center historical prospective study including a consecutive group of 71 men with pituitary macroadenomas ($\geq$ 10mm) and hyperporlactinemia (> 7xULN) treated medically with cabergoline. Starting dose was 0.5 mg/wk, or 1 mg/wk if PRL >1000 ng/ml, increased every 2 months, as necessary.

Comparisons of PRL normalization rates were performed according to PRL levels achieved at 6 months, maximal adenoma shrinkage during follow-up, and other patient characteristics. Correlations were performed to identify characteristics of PRL suppression dynamics.

Results

Prolactin levels after 6 months of treatment correlated positively with current PRL levels (r=0.74, p<0.001), with time to PRL normalization (r=0.75, p<0.001), and with adenoma diameter following treatment (r=0.38, p=0.01). Adenoma shrinkage depicted by first MRI on treatment correlated with maximal adenoma shrinkage during follow-up (r=0.56, p=0.006).

Five patients had nadir PRL levels $\geq$ x 3 ULN (51 ng/ml), and showed slower response to cabergoline treatment with consistently higher PRL levels compared to responding patients throughout follow-up (mean 6 months PRL levels, 519±403 vs. 59±118 ng/ml, p<0.001).

Baseline clinical characteristics according to PRL levels 6 months following CAB initiation.

|	<17 ng/ml n=30	18-51 ng/ml n=18	>51 ng/ml n=23	p value
Follow up duration (years, mean±SD)	5.6±2.9	6.0±4.5	8.7±5.5	0.034
Maximal cabergoline dose (mg/week, mean±SD)	1.05±0.65	1.4±0.5	2.9±1.6	<0.001
Operated n(%)	3(10.0)	3(16.7)	9(39.1)	0.031
Visual impairment n(%)	8(28.6)	5(45.5)	14(70.0)	0.018
Level at presentation (ng/ml, mean±SD)	2,796±4,608	2,412±2,419	18,739±56,379	NS
Level after 6 months (ng/ml, mean±SD)	5.9±4.8	33.0±11.0	249.6±277.2	<0.001
Long-term nadir (ng/ml, mean±SD)	4.0±4.0	15.6±11.2	63.0±84.9	<0.001
Number normalized n(%)	30(100)	11(61.1)	9(39.1)	<0.001
Time to normalization (months, mean±SD)	3.8±2.4	14.3±5.3	33.0±21.1	<0.001

Probability of PRL normalization over time: All patients (A), patients who were close to normal PRL (<x3 ULN) vs. higher PRL levels 6 month after treatment initiation (B), and patients operated vs.+ those treated medically only (C).
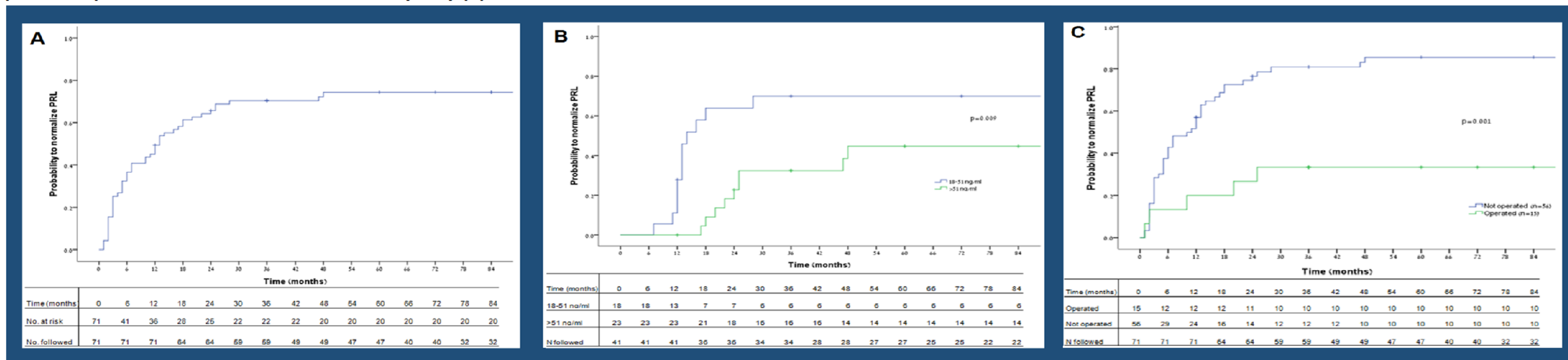
Correlation between PRL levels 6 months on treatment and current PRL levels (A) and treatment duration to PRL normalization (B).
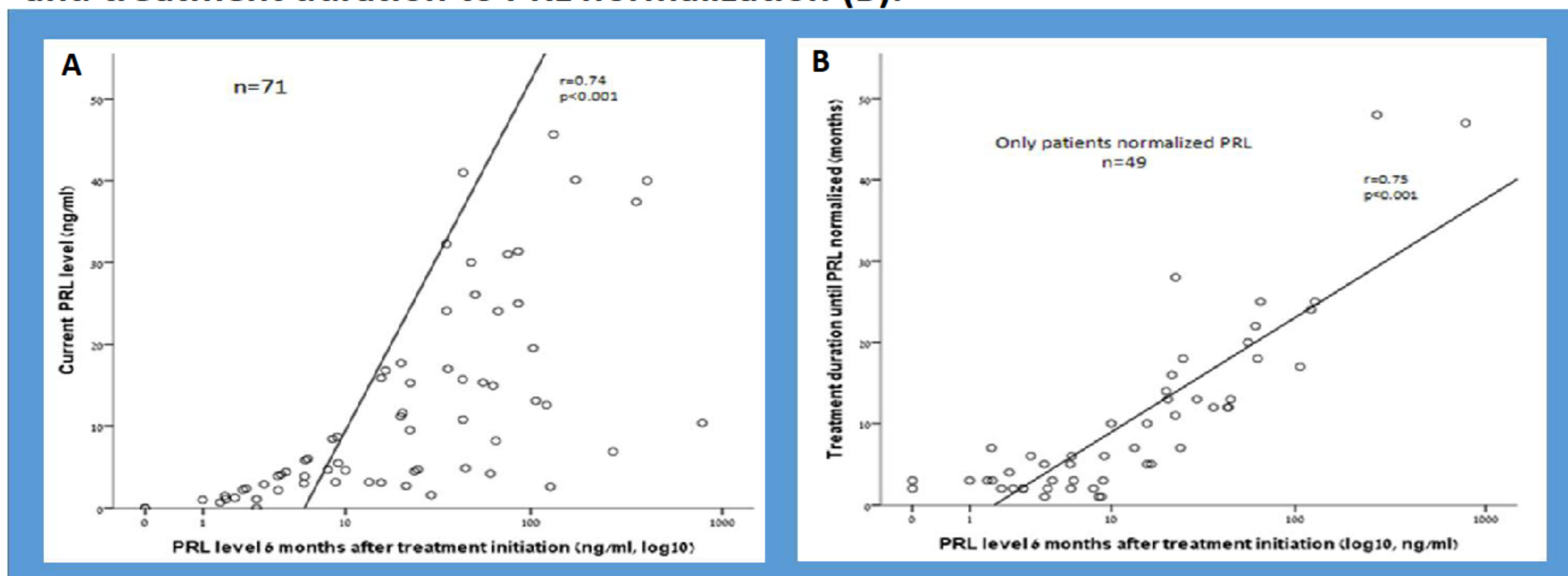
PRL levels in patients with persistent hyperprolactinemia (> x 3 ULN) vs. normal/nearly normal PRL during follow-up.
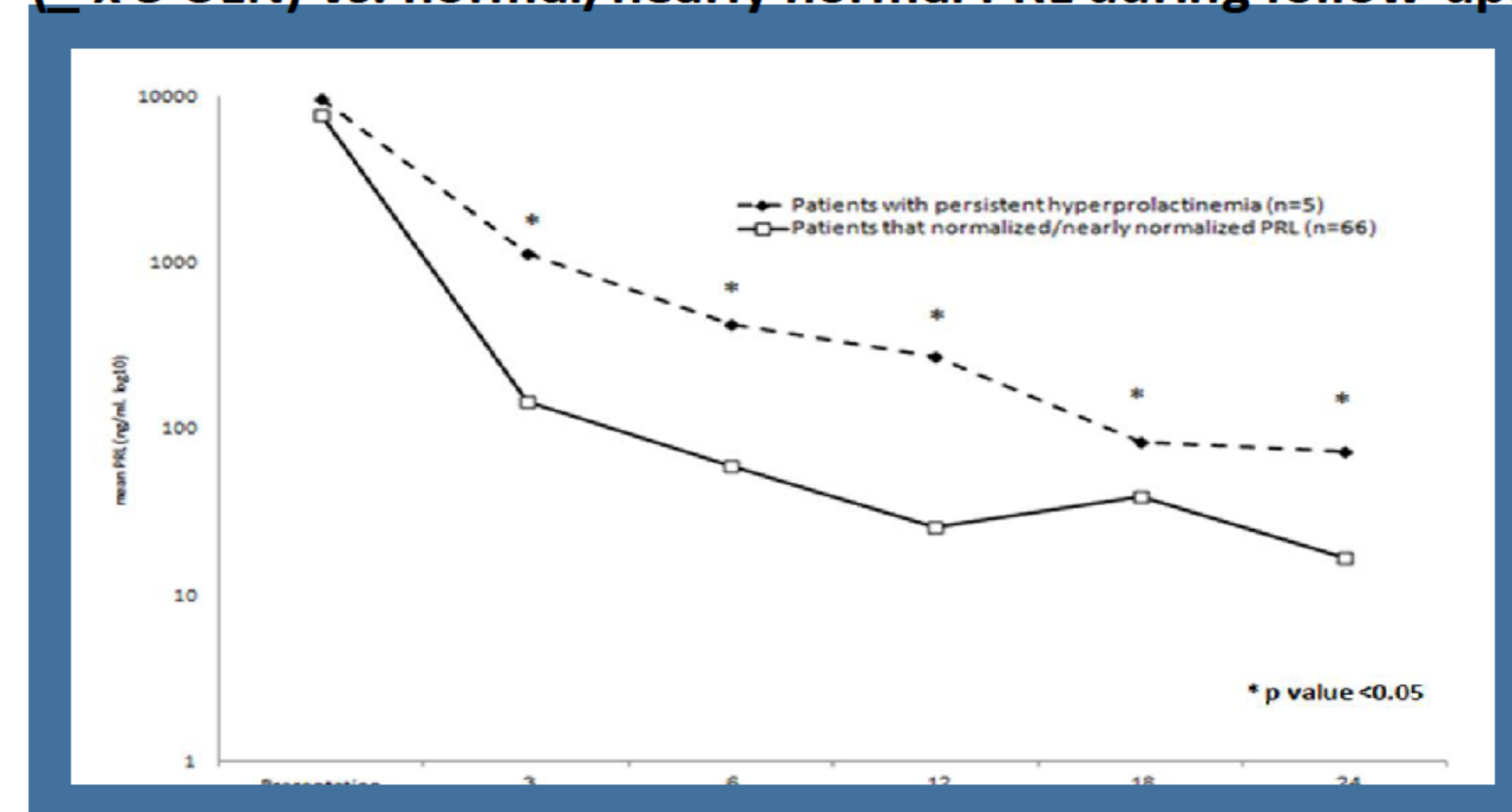
Conclusions

Six months PRL levels might serve as a surrogate marker for PRL normalization and adenoma shrinkage dynamics among men harboring macroprolactinomas.