

Following the recent evolution in therapeutic strategies for GH-secreting pituitary adenomas, determining optimal individualized patient management is now crucial.

**Objective:** To determine whether pre-surgical medical treatment (PSMT) in patients with acromegaly improves surgical outcome and to specify thresholds for such a strategy.

**Methods and design:** This retrospective study included 110 newly diagnosed acromegalic patients operated on between 1997 and 2007 at Timone Hospital, Marseille, France. The mean long-term follow-up period was 52 ± 36.6 months (median 41 months). Sixty-four patients (58.4%) received PSMT (long acting Somatostatin Analogs) during 2 to 18 months (mean 6.4 months) and all patients underwent pituitary surgery. Remission was based on updated criteria, associating GH nadir after oral glucose tolerance test <0.4 µg/L and normal IGF-1 for age, sex and gender at early (3 months) evaluation or at the end of follow-up (n=95).

### Results:

At 3 months and at long-term evaluation, **pre-treated and no pre-treated groups were comparable for the main confounding factors** except for IGF-1 at diagnosis which was higher in patients with PSMT at both evaluations.

#### 3 months Evaluation

Data	Patients with PSMT (6.4 +/- 4.1) 5 months median n=64	Patients no PSMT n=46	p
- Age at diagnosis (years)	44.1 ± 10.7	45 ± 14.6	0.7
- GHm at diagnosis (µg/L)	31.4 ± 35.8	30.1 ± 38.6	0.87
- IGF-1 at diagnosis (% ULN)	3.5 ± 1.4	2.9 ± 1.5	<b>0.04</b>
- GH nadir after OGTT (µg/L)	26 ± 32.2	25.7 ± 33.6	0.90
- Pre-surgical adenoma size (mm)	16.6 ± 6.5	18.6 ± 13.3	0.32
- Macro/micro adenoma (% patients)	82.6	81.2	> 0.9
- Local Invasion (% of patients)	54.7	54.4	>0.9
- Visual Field abnormalities (% patients)	26	27	> 0.9
- Hyperprolactinemia (% of patients)	31.2	30.4	>0.9
- Pre-surgical pituitary deficiency (% patients)	48.4	39.1	0.44
- Age at surgery (years)	44.9 ± 10.8	45.2 ± 14.2	0.89
- Delay before surgery (years)	0.9 ± 0.5	0.6 ± 0.9	<b>0.03</b>
- endoscopic surgery (% patients)	21.9	17.4	0.63
- Impression of complete tumor removal (% patients)	46.9	34.8	0.47

#### Long-Term Evaluation

Data	Patients with PSMT (6.5 +/- 4.1) 5 months median n=54	Patients no PSMT n=41	p
- Age at diagnosis (years)	44 ± 10.7	44 ± 14.3	>0.9
- GHm at diagnosis (µg/L)	33.3 ± 36.6	31.6 ± 40.8	0.84
- IGF-1 at diagnosis (% ULN)	3.4 ± 1.3	2.8 ± 1.5	<b>0.03</b>
- GH nadir after OGTT (µg/L)	27.3 ± 33.6	26.4 ± 35.3	0.92
- Pre-surgical adenoma size (mm)	16.9 ± 6.9	19.1 ± 13.9	0.33
- Macro/micro adenoma (% patients)	77.8	80.5	0.8
- Local Invasion (% of patients)	59.3	53.7	0.68
- Visual Field abnormalities (% patients)	28.9	27.3	> 0.9
- Hyperprolactinemia (% of patients)	31.5	29.3	>0.9
- Pre-surgical pituitary deficiency (% patients)	48.1	39	0.41
- Age at surgery (years)	44.9 ± 10.8	44.3 ± 14	0.82
- Delay before surgery (years)	0.9 ± 0.7	0.6 ± 0.9	<b>0.03</b>
- endoscopic surgery (% patients)	22.9	14.9	0.43
- Impression of complete tumor removal (% patients)	44.4	34.1	0.59
- Follow-up (months)	46.5 ± 34.5	57.8 ± 38.3	0.13

In multivariate analysis, PSMT was significantly linked to:

• **Early remission:** 45.3% patients in remission with PSMT vs 26.1% without; [(OR=3.17 (1.15-8.73), p=0.009].

• **Long-term remission:** 61.1% patients in remission with PSMT vs 36.6% without; [(OR=2.74 (1.04-7.26), p=0.022].

Duration of PSMT was **not significantly different** in cured or not-cured patients, at both evaluations:

3 months: 6.3 months +/- 4.3 (C) vs 7.5 months +/- 4.2 (NC), p=0.36  
Long-Term: 5.9 months +/- 4.1 (C) vs 7.3 months +/- 4 (NC), p=0.21

PSMT was more beneficial for patients with somatotroph adenoma **larger than 15 mm:**

Group 1: Size<15 mm + No PSMT

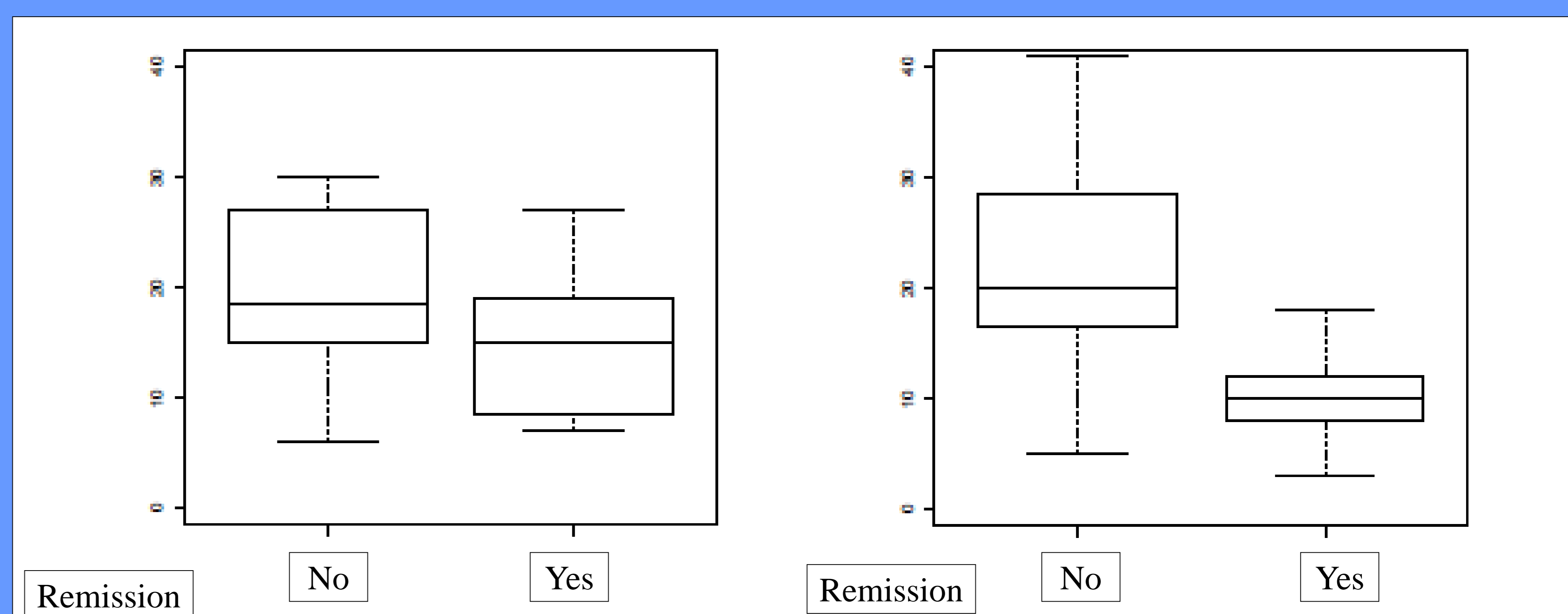
Group 2: Size<15 mm +PSMT

Group 3: Size>15 mm + No PSMT

Group 4: Size>15 mm+ PSMT

In multivariate analysis, group 3 (Size>15 mm, No PSMT) had a significant lower remission rate than the 3 other groups (p<0.01).

Noteworthy, **no patient** with a **more than 18 mm** adenoma or a **mean GH exceeding 35 ng/ml** at diagnosis was cured by surgery without PSMT.



Long Term remission and size of the adenoma in patients with (left) or without (right) PSMT

### Conclusion

Pre-surgical medical treatment (PSMT) significantly improved short and long-term remission in operated acromegalic patients, independently of its duration and main confounding factors, and seemed to be especially interesting in adenomas larger than 15 mm.