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Conclusions
NST could serve as a novel useful parameter for assessment of BC and CVD risk in BT patients.

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AEP478

Uncured acromegaly, the dark side of the moon: a cross- sectional study

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Introduction
Although surgical treatment of acromegaly is the treatment of choice in most patients, a wide therapeutic arsenal is available. Medical treatment can be indicated as primary treatment, complementary and even as pre-operative treatment.
Objectives
To determine the prevalence of uncured acromegaly and the prevalence of controlled disease within this group. To clinically, biochemically and histologically characterize uncured acromegalics. To analyze the predictive factors for non-cure in acromegaly.
Material and methods
Retrospective study of adult patients with uncured acromegaly under follow-up in the Neuroendocrinology Unit of a tertiary hospital in Madrid during the period 2000–2020. Non-cure criteria were considered: elevated IGF-1 according to age and sex and random GH ≥ 1µg/l and/or post OGTT 75 gr ≥ 0.4 or ≥ 1µg/l, according to the analytical method used. Controlled disease criteria were considered: normal IGF-1 according to age and sex and random GH < 2.5µg/l. Continuous variables were expressed as mean and standard deviation and categorical variables as absolute values and percentages. Univariate and multivariate logistic regression models were analyzed to determine predictors of non-healing, significant $P < 0.05$.
Results
Of 97 adult patients with acromegaly, 52.7% ($n = 51$) did not meet cure criteria, of these, 46.5% ($n = 40$) after sphenoidal surgery. 56.9% were women, age 61 ± 18.7 years, BMI 28.4 ± 5 kg/m^2, IGF-1 956.2 ± 677.1µg/l and GH 30.0 ± 42.7µg/l. 75% presented pituitary macroadenoma, 82.1% with extrasellar extension. 50% were somatotropinomas and the rest secreted GH+PRL (35%), GH + PRL + TSH (10%) and PRL (5%). 84.6% and 41.7% had positivity for Ki67 (72.7% < 3% and 27.3% 3–10%) and p53, respectively. 94.1% ($n = 48$) received medical treatment, 20 patients in monotherapy (12 SSAs, 7 carbergoline and 1 pegvisomant) and 28 patients in combined therapy (12 SSAs + cabergoline, 6 SSAs + pegvisomant, 1 pegvisomant + cabergoline and 9 triple therapy). In total, 92% met criteria for controlled disease, 100% of those treated with SSA and pegvisomant in monotherapy and 85.7% with cabergoline in monotherapy (directly proportional to the dose), and 89.2% of those receiving combined therapy. 35.7% also received RT, with 93.3% controlling the disease. Predictive factors of non-cure after surgery were pituitary macroadenoma, initial GH and IGF-1 values and co-secretion of GH + PRL and GH + PRL + TSH.
Conclusions
The surgical remission rate exceeds 50%. Almost all patients who are not cured achieve control of the disease with pharmacological treatment. Medical treatment should be individualized according to the presence of pituitary macroadenoma, co-secreting hormone pituitary adenomas, initial levels of GH and IGF-1 and the clinical and hormonal evolution of the patient.

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AEP479

Metabolic profile in patients with prolactinoma before and on dopamine agonist therapy

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Background
Prolactinomas are the most frequent type of hormone-secreting pituitary adenomas. Prolactin(PRL)-receptor mediates intracellular signaling pathways that contribute to weight gain, dyslipidemia, impaired fasting glucose (IFG), type 2 diabetes mellitus (T2DM) and cardiovascular disease, parameters that improve along with PRL level control on dopamine agonist (DA) therapy.
Aim
To assess metabolic disturbances in prolactinomas at diagnosis and during follow-up.
Methods
Fifty-seven patients with prolactinomas (aged 50.2 ± 17.6 years, 37 M:20 W median PRL 838.45 mg/l) were retrospectively assessed for weight, lipids, fasting glycemia, blood pressure, cardiovascular events. Evaluation was made at baseline, at 6, 12 and 24 months after DA treatment (1–7 mg/week cabergoline/7.5–30 mg/day bromocriptine). Nadir PRL on therapy was 0.2 mg/l. Serum PRL was measured by chemiluminescence.
Results
At the time of diagnosis, 27.3% were overweight and 52.7% obese. Weight excess was significantly more prevalent in men (89.2%) vs. women (55), $P < 0.01$ and in macroprolactinoma (83.7%) vs. microprolactinoma (37.5%), $P < 0.01$. Nine subjects had central hypothyroidism, 46 central hypogonadism and 5 panhypopituitarism. Initial BMI (29.8 ± 5.4 kg/m^2) significantly decrease both at 6-months (29.1 ± 4.6 kg/m^2, $P = 0.04$) and 24-months (28.9 ± 5.6 kg/m^2, $P = 0.01$). Maximum decrease in BMI (0.7 kg/m^2) occurred at 6-months, despite the fact that only 63.2% had achieved disease control. At the time of diagnosis, 65.3% had dyslipidemia. Initial cholesterol level was 208.3 ± 40.7 mg/dl and significantly decreased both at 6-months (185.1 ± 39.6 mg/dl, $P < 0.01$) and 24-months (183.5 ± 44.04 mg/dl, $P < 0.01$). Significant decrease was also observed in LDL-cholesterol and triglyceride levels from 127.3 ± 38.9 mg/dl and 165.3 ± 135.3 mg/dl at baseline to 106.2 ± 28.8 mg/dl($P = 0.05$) and 133.1 ± 77.4 mg/dl($P = 0.01$) at 6-months and to 106.9 ± 31.4 mg/dl and 115.5 ± 72.8 mg/dl, respectively at 24-months ($P < 0.01$). HDL-cholesterol levels were similar at 6-months, but significantly lower at 24-months compared to baseline (42.3 ± 9.9 mg/dl vs. 49.1 ± 44 mg/dl, $P = 0.04$). Nine of 37 dyslipidemic patients (24.3%) received statin. Arterial hypertension (26.31%, $n = 15$) and chronic coronary syndrome (CCS) (10.5%, $n = 6$) prevalence was similar at the time of diagnosis and at 24-months: 29.8% ($n = 17$) patients with hypertension and 12.3% ($n = 7$) patients with CCS. At baseline, 21.8% ($n = 12$) had IFG and 5.3% ($n = 3$) DM. At 24-months evaluation, the prevalence of IFG and DM was 7.3% ($n = 4$) and 3.6% ($n = 2$), respectively.
Conclusion
Two years dopamine agonists treatment improved metabolic parameters in prolactinoma patients, with weight loss, decrease in total and LDL-cholesterol and triglycerides. Long term follow-up, larger studies are necessary to assess cardiovascular risk of patients with PRM, in order to stratify therapeutic intervention and to reduce associated mortality.

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AEP480

What should be the optimal testosterone level to improve the symptoms of hypogonadism in male macroprolactinomas?

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Objectives
Male prolactinoma patients mostly have hypogonadotropic symptoms. While treatment with dopamine agonists (DAs; such as bromocriptine or cabergoline) leads to recovery of sexual glands, it can lead to impulsive control disorders as an undesirable side effect. The aim of this retrospective study is to determine the level of testosterone that eliminates symptoms, provides fertility and does not cause this undesirable side effect regardless of prolactin (PRL) level in macroprolactinomas with long-term follow-up.

Material and Methods
Twenty-seven male patients with macroprolactinoma followed in outpatient Pituitary Clinic were included to the study. There were 16 macro (≥ 1–2.8 cm), 7 large macro (≥ 2.9–3.9 cm) and 4 giant (≥ 4 cm) adenomas. From medical records PRL, LH, FSH, Testosterone (T) were evaluated and a timeline was created to analyze the progress regarding symptoms of hypogonadism and infertility. At each visit, their answers to hypogonadism symptoms and fertility questions were evaluated. PRL and T levels in the period when they were asymptomatic and fertile were recorded. Fertility-induced T levels were compared with age-matched thirty-three controls. Patients with children prior to admission were excluded from fertility statistical analysis.
Results
The mean age of patients was 38.8 ± 11.8 years, and 41.6 ± 10.2 years in the controls. The average delay in diagnosis was 4.3 years. Mean PRL, basal tumor diameter and shrinkage were 2846 ± 3415 ng/ml, 27.2 ± 10.2 mm and 63.4%, respectively. Basal T levels were 1.6 ± 1.0 ng/ml for patients and 4.4 ± 1.5 ng/ml for controls ($P < 0.001$). Mean T level in asymptomatic period was significantly lower than controls (3.2 ± 0.4 ng/ml vs. 4.4 ± 1.5 ng/ml, respectively, $P = 0.002$), and at this time mean PRL was slightly elevated than normal as 27.2 ng/ml. Mean maximum dose of bromocriptine and cabergoline were 11.1 ± 5.1 mg/daily and 1.7 ± 0.6 mg/weekly, respectively. The patients were followed up for an average of 8.3 ± 4.8 years. Fertility was achieved in 6 of the patients who desired fertility, and there was no difference between the T levels of these patients and the controls (3.7 ± 0.8 ng/ml vs. 4.4 ± 1.5 ng/ml, $P = 0.38$). When fertility was achieved mean PRL level was 26.9 ± 23 ng/ml. The highest T levels of the patients under therapy was not significantly different from controls (4.9 ± 1.6 ng/ml vs. 4.4 ± 1.5 ng/ml, respectively). Mean PRL level accompanying these T levels was 12.1 ± 15.2 ng/Ml.
Conclusion
The slightly elevated PRL should not be taken into account in these patients under treatment, when symptoms disappear, or fertility is restored. Therefore, patients should be carefully questioned in terms of their complaints at each visit and the dose of DA should not be increased unnecessarily to avoid possible adverse serious side effects.

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AEP481

Pituitary function after transsphenoidal surgery including measurement of basal morning cortisol as predictor of adrenal insufficiency

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Introduction
Patients with pituitary adenomas undergoing transsphenoidal surgery require pre- and post-surgery examination of pituitary hormones. There is currently no consensus on how to evaluate the adrenal axis post-surgery. The aims of this study were to investigate factors that may predict postoperative adrenal insufficiency (AI) and to investigate the overall effect of transsphenoidal surgery on the pituitary function.
Methods
One-hundred-and-forty-three consecutive patients who had undergone transsphenoidal surgery for pituitary adenomas were included. Data on tumour size, pituitary function pre-surgery, plasma basal cortisol measured within 48 hours post-surgery and pituitary function 6 months post-surgery were collected. Patients with AI prior to surgery, perioperative glucocorticoid treatment, Cushing's disease and no re-evaluation after 1 month were excluded ($n = 93$) in the basal cortisol analysis.
Results
Low plasma basal cortisol post-surgery, tumour size and previous pituitary surgery were predictors of AI (all $P < 0.05$). A basal cortisol cut-off concentration of 300 nmol/l predicted AI 6 months post-surgery with a sensitivity and negative predictive value of 100%, specificity of 81% and positive predictive value of 25%. New gonadal, thyroid and adrenal axis insufficiencies accounted for 2%, 10% and 10%, respectively. The corresponding recovery rates were 17%, 7% and 24%, respectively
Conclusion
Transsphenoidal surgery had an overall beneficial effect on pituitary endocrine function. Low basal plasma cortisol measured within 48 hours after surgery, tumour size and previous surgery were identified as risk factors for AI. We recommend measurement of basal cortisol post-surgery to secure glucocorticoids to patients at risk of AI and to avoid unnecessary glucocorticoid treatment.

Table 1. Association between basal cortisol and adrenal axis six months post-surgery

Basal cortisol level	Sufficient	Insufficient	Total	Cut-off limits	Specificity	Sensitivity	NPV	PPV
0–99 nmol/l	2	2	4	100 nmol/l	96%	67%	98%	50%
100–199 nmol/l	2	0	2	200 nmol/l	92%	67%	98%	33%
200–299 nmol/l	5	1	6	300 nmol/l	81%	100%	100%	25%
300–399 nmol/l	9	0	9	400 nmol/l	62%	100%	100%	14%
400–499 nmol/l	4	0	4	500 nmol/l	53%	100%	100%	12%
500–599 nmol/l	4	0	4	600 nmol/l	45%	100%	100%	10%
> = 600 nmol/l	21	0	21					
Total	47	3	50					

Grouping plasma basal cortisol levels according to sufficiency vs. insufficiency of the adrenal axis assessed by Synacthen-test six months post-surgery. PPV = Positive predictive value. NPV=Negative predictive value.

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AEP482

Factors that contribute to dopamine agonist resistance of prolactinomas

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Introduction
Prolactinomas are the most common hormone-secreting pituitary tumours encountered in the clinic. They are usually treated with dopamine agonists (DA): bromocriptine (BRC) and cabergoline (CAB), which are highly effective in the majority of cases. DA resistance is the failure to achieve normal levels of prolactin and, or reduction of the adenoma with at least 50%.
Aim
to assess the prevalence of the known factors that contribute to DA resistance (male gender, younger age at diagnosis, large tumours, the invasiveness of the tumour) among patients that do not respond to medical treatment.
Materials and methods
222 patients with prolactinoma were retrospectively assessed for treatment responsiveness. Gender, age of the diagnosis, serum prolactin levels, the dimensions of the pituitary adenoma were compared in responsive and resistant patients. Prolactin was measured by chemiluminescence and tumour volume and extension by computed tomography scan or MRI.
Results
there were 188 patients responsive to DA therapy and 34 resistant ones. There is no significant gender differences between the 2 groups (M:F = 83:105 in responsive group vs. 16:18 in resistant group, n = ns, chi square test). Resistant patients tend to be younger (30.5 ± 12.5 years) than responsive ones (35.6 ± 13.6 years), P = ns. Serum median prolactin was similar in responsive patients (650 ng/ml) and in resistant ones (462 ng/ml). Median maximum diameter was also similar (2.1 cm vs.2.12 cm).
Conclusions
In our series, there were no significant differences regarding gender, age at diagnosis, initial prolactin levels or tumour volume between patients responsive or resistant to DA therapy. Attention should be payed to histological and genetic differences between these patients.

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AEP483

Electrolyte disturbances in hospitalized patients with COVID-19

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