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AEP776

To optimize the acute octreotide suppression test in predicting the efficacy of long acting somatostatin analogues in acromegaly

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A 6-hour octreotide suppression test (OST) is useful in the selection of patients with acromegaly for chronic somatostatin depot analogues treatment. However, it is time consuming and that brings inconvenience to patients. We aim to simplify the blood sampling of OST, and determine the reliability of a short version of the classic 6-hour OST. The data provided in the supplementary tables of the primary manuscript were used to re-analyze the efficacies of the simplified OST tests. SPSS Software Version 25 was used for data analyses. To find the best receiver operating characteristic (ROC) curve, several analysis of the shorten-test (including 2-hour, 3-hour, 4-hour and, 6-hour's tests) were performed, and compared the parameters of ROC with that of 2-day's examination to find a proper shorten test period. After calculating, □GH (0–3 h) more than 80.51% and 91.84% provided the best predictors of a good GH response (sensitivity 96.9%, specificity 85.7%) and a good IGF-1 response (sensitivity 86.7%, specificity 81.3%). □AUC (0–3 h) more than 71.07% provided the best predictor of a good tumor size response (sensitivity 81.8%, specificity 90.6%). From these results, we conclude that OST could be simplified as the 3-hour measurements. The □GH (0–3 h) is the best optimistic parameter to predict a good GH, or IGF-1, response, while the □AUC (0–3 h) is the best for a good tumor size response to short-term efficacy of SSA in acromegaly.

Keywords: acromegaly, somatostatin analogues, remission prediction, octreotide suppression test.

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AEP777

Acromegaly is associated with reduced socioeconomic status and more so in female patients: A nationwide population-based study

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Context
Acromegaly is a rare and insidious disease associated with severe somatic morbidity but data on socioeconomic status are scarce.
Objective
To study the socioeconomic status in acromegaly in a population based, nationwide follow-up study.
Patients and methods
All incident cases of acromegaly (n=576) during the period 1997–2010 were included, representing 10.116 years at risk. For every patient, 100 persons were sampled from the general population matched on date of birth and gender (comparison cohort). Cox regression and hazard ratios (HR) or conditional logistic regression with 95% confidence intervals (CI) were used.
Main outcome measures
Annual income, allocation of cash benefits, retirement, cohabitation, separation, parenthood and education level.
Results
The proportion of retirement was significantly increased in patients with acromegaly after the time of diagnosis (HR 1.43, CI95% 1.26–1.62) and also during the 5-year pre-diagnostic period (HR : 1.15, CI95% 1.03–1.28). The utilisation of cash benefits was increased in patients with acromegaly in the period preceding the time of diagnosis. Among patients who maintain a paid job, the annual income was similar to the reference population. Compared with the background population, cohabitation was less prevalent (HR : 0.69, CI : 0.50–0.95) as was parenthood (HR : 0.56, CI : 0.39–0.80), whereas neither educational level (HR: 0.61, CI : 0.35–1.06) nor the prevalence of separation (HR : 1.13, CI : 0.86–1.47) weredifferent in acromegaly. A reduced socioeconomic status was present before the diagnosis of acromegaly. Female gender was associated with a significantly worse socioeconomic status (Table 1).

Tabel 1 Hazard ratios of the various outcomes.

After diagnosis	Female	*P*-value	Male	*P*-value
Mortality	1.56 (1.27–1.91)	< 0.01	1.32 (1.09–1.61)	< 0.01
Retirement	1.58 (1.33–1.87)	< 0.01	1.30 (1.08–1.55)	< 0.01
Education	0.65 (0.34–1.25)	0.19	0.52 (0.17–1.63)	0.26
Separation	1.28 (0.89–1.83)	0.18	0.99 (0.67–1.47)	0.95
Cohabitaion	0.62 (0.38–1.00)	0.05	0.76 (0.50–1.16)	0.20
Parenthood	0.33 (0.17–0.67)	< 0.01	0.74 (0.48–1.12)	0.16
5-years pre-diagnosis				
Retirement	1.14 (0.98–1.33)	0.08	1.16 (0.99–1.36)	0.07
Cohabitaion	0.75 (0.53–1.06)	0.10	1.06 (0.79–1.41)	0.71
Parenthood	0.55 (0.34–0.87)	0.01	0.82 (0.60–1.13)	0.23

Conclusion
1. Socioeconomic status is impaired in patients with acromegaly even before diagnosis. 2. Females and patients without disease remission have significantly worse outcomes. 3. Early diagnosis and effective treatment are essential not least in female patients.

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Reproductive and Developmental Endocrinology

AEP778

Case-control study on ACE2 expression in children with short stature

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Background
Short stature is one of the most common presentations to paediatric endocrinologists. It is estimated that despite all the exams, in 50–90% of cases, children are labelled as having idiopathic short stature. It has been recently reported that genetic ACE2 deficiency is associated with reduced body weight as well as with impaired gestational weight gain and fetal growth restriction in pregnancy. It has been argued that ACE2 deficiency, which is usually associated with an increase of tissue Angiotensin II, could be associated with prenatal as well as postnatal changes leading to reduced growth (such as uterine artery dysfunction and IGF-1 reduction, respectively). Based on these premises, the aim of our study was to evaluate whether there was a difference of ACE2 expression in children with short stature as compared to age-matched controls.
Methods
We designed an exploratory case-control study aiming at recruiting consecutively 40 children with short stature (cases) and 40 controls presenting at the Endocrinology Service, aged 2–13 years, excluding those with acute intercurrent diseases, diabetes, renal insufficiency, syndromes and/or on medications. After signing the informed consent to participating in the study, children underwent a medical visit and a fasting blood sampling. Peripheral blood mononuclear cells (PBMC) were isolated to extract mRNA for gene expression analyses. Sera were collected for protein measurements.
Results
Children with short stature (n=17) presented with lower height and body weight as compared to controls (n=18). Our preliminary data show that children with short stature exhibited a significant reduction of ACE2 gene expression, and a significant increase of ACE/ACE2 ratio in PBMC. This was associated with a modest increase of Angiotensin II/Angiotensin 1–7 ratio. Our multivariate analysis showed that across the groups ACE2 was independently associated with height but not with body weight.
Conclusions
To our knowledge, this is the first study investigating ACE2 expression ina paediatric population. Our preliminary results, showing that ACE2

expression is significantly reduced in children with short stature, are in line with the literature. This study could representthe basis for further investigations aiming at establishing the presence of a causal relationship between ACE2 deficiency and growth reduction, with further diagnostic and therapeutic perspectives

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AEP779

Coagulation abnormalities in patients with klinefelter syndrome compared to age-matched healthy controls: Cross-sectional assessment by thrombin generation test

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Introduction
Klinefelter syndrome (KS) is known to be associated with an increased risk of venous thromboembolism and arterial thrombosis, but the aetiology behind this prothrombotic status has not been fully elucidated. The aim of this study was to cross-sectionally investigate the coagulative state in subjects with KS compared to age-matched healthy males.
Methods
Coagulation factors assessment, clinical characteristics collection and thrombin generation test (TGT) were performed in 58 consecutive KS patients and 58 controls. TGT is based on the continuous registration of thrombin generation (mediated by procoagulants) and decay (mediated by anticoagulants) using a fluorogenic substrate. The curve of thrombin concentrations (vertical axis) by time (horizontal axis) is called *thrombogram* and is described by the following parameters: *lag-time* (time from coagulation ignition to the formation of the first amounts of thrombin); *thrombin-peak* and *time-to-peak*; *endogenous thrombin potential (ETP*, the area under the thrombin curve, measured with and without the addition of thrombomodulin); the *ETP-ratio* (ETP with/ETP without thrombomodulin), that may be considered the best parameter through which *in vivo*subtle procoagulant imbalance can be detected.
Results
No statistically significant difference was found between KS patients and healthy subjects in lag-time, thrombin-peak, time-to-peak or ETP; however, the ETP-ratio was significantly higher in KS compared to controls (0.73 and 0.66 respectively, $P<0.001$). KS patients had higher circulating concentrations of Factor VIII ($P=0.001$) and Fibrinogen ($P<0.001$) and a higher Factor VIII/Protein C ratio ($P=0.018$), while platelet count, PT ratio, aPTT ratio, Factor II, Protein C and Antithrombin were similar in the two groups. ETP-ratio was positively correlated with Factor VIII concentrations ($P=0.007$, $\rho=0.355$) and showed a trend of association with impaired fasting glucose ($P=0.069$) and Factor VIII/Protein C ratio ($P=0.072$, $\rho=0.240$). Fibrinogen levels were positively associated with age ($P=0.004$, $\rho=0.401$), body mass index ($P=0.001$, $\rho=0.468$) and fasting plasma glucose ($P=0.049$, $\rho=0.356$), while FVIII did not show any correlation with metabolic parameters as well as age. Testosterone replacement therapy and smoke were not associated with any of the coagulation parameters.
Conclusion
As clinically suggested, a procoagulant imbalance is present in KS subjects and is possibly related to higher Factor VIII concentrations here demonstrated. While testosterone replacement therapy and smoking habit did not show a significant impact, other typical factors associated with thrombotic risk such as advanced age, BMI and altered glucose metabolism could further increase this imbalance by determining hyperfibrinogenemia.

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AEP780

Radioidine (RAI) as a new therapy for the treatment of ovarian cancer through the sodium/iodide symporter (NIS)

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Introduction
Ovarian cancer is the most lethal gynecological malignancy. Early diagnosis has a survival rate of 90%. Unfortunately, more than 70% of cases are diagnosed when the cancer has already metastasized, and survival rates do not exceed 30% in these cases. The sodium iodide symporter (NIS) is an integral plasma membrane glycoprotein expressed in the basolateral surface of the thyroid gland, where it mediates active transport of iodide. Radioiodide therapy (RAI) through NIS is the most effective therapy in thyroid cancer. Our group has demonstrated that NIS is expressed in ovarian surface epithelium and is overexpressed in human epithelial ovarian cancer, establishing NIS as a tumor marker. The aim of this study is to determine whether endogenous expression of NIS in ovarian cancer can be used as therapeutic tool using-RAI in ovarian tumors.
Materials and methods
serous ovarian cancer cell line (SKOV3) was transfected permanently with exogenous NIS (SKOV3-hNIS) and in vitro characterized by different techniques (western-blot, PCR, flow cytometry, immunofluorescence, iodide uptake). In vivo, NIS-transfected and not transfected cells were injected into flanks of nude and NSGs mice. NIStumor expression was analyzed by different techniques and NIS functionality in animal models was measured by SPECT-CT.^{131}I treatment was tested in subcutaneous nude female mice. Human ovarian tumors samples received from the Mostoles Hospital were disaggregated and used to produce primary cultures and PDX animals.
Results
PCR and western-blot show NIS expression in both in vitro (cancer cells) and in vivo (xenotransplanted cells in animal models and human samples). Immunofluorescence and immunohistochemistry show that NIS expression occurs in plasma membrane. In vitro and in vivo (SPECT-CT) Iodide uptake assays show that the expression of NIS in plasma membrane is functional. ^{131}I treatment in subcutaneous tumors show an overall decrease in tumor size of 71% vs a 632% increase in not treated tumors. We observed that more than 37% of tumors disappear in 25 days with just a single ^{131}I dose.
Conclusion
NIS expression in human ovarian cancer cell lines is functional in vitro and in vivo, targeted to the plasma membrane, and able to accumulate iodide. A single dose of ^{131}I reduces ovarian tumor growth in NIS-expressing tumors and is more effective than conventionally chemotherapy. Patient tumors are expressing NIS in the plasma membrane, which leads us to propose NIS as a therapeutic approach to the treatment of ovarian cancer through radio iodine.

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AEP781

Luteinizing hormone/choriogonadotropin receptor (LHCGR) mediates different kinetics of G proteins, β-arrestins and cAMP activation

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Pituitary luteinizing hormone (LH) and placental human choriogonadotropin (hCG) are two heterodimeric glycoprotein hormones regulating reproduction. They bind the same receptor (LHCGR) expressed in gonadal cells, activating hormone-specific G protein- and β-arrestins-dependent signaling cascades, before LHCGR internalization. LH induces preferential proliferative signals, while hCG activates mainly the steroidogenic pathway,