TÜRKİYE ENDOKRİNOLOJİ VE METABOLİZMA DERNEĞİ BÜLTENİ



Sayı 62 • Nisan – Mayıs – Haziran - 2018

40. TÜRKİYE ENDOKRİNOLOJİ VE METABOLİZMA HASTALIKLARI KONGRESİ TAMAMLANDI

"40. Türkiye Endokrinoloji ve Metabolizma Hastalıkları Kongresi" bu yıl Sueno Hotel Antalya'da 09-12 Mayıs 2018 tarihleri arasında, **1350** kişinin katılımı ile başarı ile tamamlandı. Bu yıl kongre bünyesinde "Temel Tiroid Ultasonografi Kursu", "Diyabet Teknolojileri Kursu" ve "Nöroradyoloji Kursu" olmak üzere 3 kurs ve kongrenin son günü "1. Obezite Sempozyumu" gerçekleştirildi.

40. TEMHK bilimsel programında, 10 konferans, 22 panel, 5 uzmanına danış, 3 Karşıt görüş, 8 sözel bildiri oturumu, 12 uydu sempozyum yer aldı. 7'si yabancı olmak üzere toplam 205 konuşmacı ve oturum başkanı bilimsel programda görev aldı. Bu yıl ilk kez TEMD' nin gerçekleştirdiği çalışmaların sunulduğu "TEMD Paneli" ve genç endokrinologların çalışmalarını sunma fırsatı buldukları "TEMD GENÇ Paneli" bilimsel program içinde yer aldı.

Kongremizde her yıl olduğu bu yıl da Genç Araştırıcı ödülü verildi. Bu yıl "Genç Araştırıcı Ödülü"nü almaya, Dr. Kadriye Aydın hak kazandı. Dr. Kadriye Aydın açılış töreninde "Akromegali ve Komorbiditeleri" başlıklı konferansını verdi.

40. TEMHK'de 53 Sözel, 205 Poster olmak üzere toplam 258 bildiri sunuldu. Bilimsel kurul tarafından yapılan değerlendirmeler sonucunda her yıl olduğu gibi bu yıl da en iyi 3 sözlü ve 3 poster bildiriye ödül verildi.



Ödül alan bildirler

Sözel Bildiri Birincilik Ödülü

Tiroid Kanserinde Klinikopatolojik Karakteristikler ile ABO Kan Grubu ve Rh Faktörü Arasındaki İlişki *Abbas Ali Tam, Didem Özdemir, Sevgül Fakı, Muhammet Cüneyt Bilginer, Reyhan Ersoy, Bekir Çakır*

Sözel Bildiri İkincilik Ödülü

Karsinoid Sendroma Sebep Olan Nöroendokrin Tümör Vakalarının Değerlendirilmesi: Tek Merkez Deneyimi Aslı Sezgin Çağlar, Ender Doğan, Figen Öztürk, Ümmühan Abdülrezzak, Erdoğan Sözüer, Alper Yurci, Metin Özkan, Şebnem Gürsoy, Fahri Bayram

Sözel Bildiri Üçüncülük Ödülü

Hiperoksalüri Oluşturulmuş Sıçanlarda Böbrek Dokusundaki FGF-23/Klotho Ekspresyon Profilinin Ürolitiazis Patogenezindeki Rolünün Araştırılması Hasan Aydın, Ferda Özkan, Cihangir Yavuz Pars

Poster Bildiri Birincilik Ödülü

Türk Toplumunda Papiller Tiroit Kanserlerinde (PTK) BRAFV600E Mutasyon Sıklığının İncelenmesi

Serhat Özçelik, Rıfat Bircan, Şükran Sarıkaya, Aylin Ege Gül, Büşra Aydın, Mehmet Çelik, Akın Dayan, Nimet Karadayı, Yasemin Tütüncü, Hasret Cengiz, Melike Özçelik, Hülya Ilıksu Gözü

Poster Bildiri İkincilik Ödülü

Hiperaktif Tiroid Nodüllerinin Sitoloji ve Histopatoloji Bulguları Hipoaktif Tiroid Nodüllerinden Farklı mıdır? Hüsniye Başer, Oya Topaloğlu, Muhammet Cüneyt Bilginer, Serap Ulusoy, Aydan Kılıçarslan, Elif Özdemir, Reyhan Ersoy, Bekir Çakır

Poster Bildiri Üçüncülük Ödülü

Preoperative Parenteral Ibandronate for Treating Severe Hypercalcemia Associated with Primary Hyperparathyroidism: An Effective and Cheap Drug *Zafer Pekkolay, Faruk Kılınç, Hikmet Soylu, Belma Özlem Tural Balsak, Mehmet Güven, Şadiye Altun Tuzcu, Alpaslan Kemal Tuzcu*











Bildiri Teşvik Ödülü

 40. TEMHK' de bu yıl ilk kez "Bildiri Teşvik Ödülü" başlığı altında bir ödül verildi. Bu yıl "Osteoporoz ve Metabolik Kemik Hastalıkları" alanında kongremize gönderilen bildiriler arasında yapılan değerlendirme sonucu "Türkiye'de Metabolik Kemik Hastalıkları Konusunda Endokrinolojinin Bilimsel Yeri nedir ve ne olmalıdır?" başlıklı çalışması ile Dr. Ceyla Değertekin ve ark. ödülü almaya hak kazandı. Bildiri ödülleri 12 Mayıs günü kapanış töreninde sahiplerine iletildi.

Birincilik Ödülü

Ratio of Thyrotropin to Thyroglobulin as a Novel Marker for Differentiating Between Benign and Malignant Thyroid Nodules within Different Bethesda Categories

Abbas Ali Tam, Didem Özdemir, Cevdet Aydın, Muhammet Cüneyt Bilginer, Mustafa Ömer Yazıcıoğlu*, Nuran Süngü**, Reyhan Ersoy, Bekir Çakır

İkincilik Ödülü

The Role of FTO Gene Alleles on the Diet and Metabolic Risk Factors in the Subjects with Diabetes

Asher Fawwad, Iftikhar Ahmed Siddiqui*, Fariha Shaheen, Rubina Hakeem, Nazish Waris, Syeda Nuzhat Nawab**,

Syed Muhammad Shahid**, Anna Parker***, Abdul Basit

Üçüncülük Ödülü

Cytologic Comparison Between Growing and Nongrowing Benign Thyroid Nodules Evaluated Using Two Different Growth Criteria

Mehmet Muhittin Yalçın, Sena Yeşil*, Barış Akıncı*, Fırat Bayraktar*, Abdurrahman Çömlekçi*, Sinan Ünal**, Aytaç Gülcü***, Sevinç Eraslan*, Tülay Canda****

- Sosyal Faaliyetler
- 40. TEMHK bilimsel açıdan olduğu kadar sosyal program açısından da oldukça zengindi. Kongremiz kapsamında ebru- ritm- taş boyama atölyeleri, satranç turnuvası, kelime yarışması ve konser gecesi düzenlendi.



 Bu yıl ilk kez, TEMD yayını olan "Turkish Journal of Endocrinology and Metabolism - 1. Ödüllü Makale Yarışması" sonuçlandı ve en iyi üç makale ödül almaya hak kazandı. Turk-JEM ödülü açılış töreninde sahiplerine iletildi.







TÜRKİYE ENDOKRİNOLOJİ VE METABOLİZMA DERNEĞİ BÜLTENİ

TİROKURS 23, KAYSERİ TAMAMLANDI

Tüm Türkiye çapında değişik bölgelerimizde yapılan Tiroidoloji Kursu–TİROKURS, 23 Haziran 2018 tarihinde Kayseri Hilton Otel'de endokrinoloji araştırma görevlileri, aile hekimleri ve iç hastalıkları uzmanlarından oluşan 60 hekimin katılımı ile başarı bir şekilde tamamlanmıştır. Emeği geçen tüm üyelerimize teşekkür eder, saygılarımızı sunarız.



ENDOKRİN KONSEY TAMAMLANDI...

Endokrin Konsey toplantımız, 2 Haziran 2018 tarihinde, Swissotel Büyük Efes, İzmir'de 150 meslektaşımızın katılımı ile başarılı bir şekilde tamamlanmıştır.

Emeği geçen tüm üyelerimize teşekkür eder, saygılarımızı sunarız.

Kongre, Kurslar ve Sempozyumlar





Bilimsel Kongreler, Ulusal ve Uluslararası Sempozyumlar

15-18 Temmuz 2018 9th International Congress of Neuroendocrinology Toronto, Canada *http://www.icn2018.org/*

15-18 Eylül 2018 41st Annual Meeting of the ETA Newcastle, England *http://www.eta2018.org*

01-05 Ekim 2018 54th EASD Annual Meeting Berlin, Germany *www.easd.org*

25-28 Ekim 2018

EndoBridge 2018 Regnum Carya Hotel, Antalya www.endobridge.org

1-4 Aralık 2018

18th International Congress of Endocrinology and 53rd SEMDSA Congress Cape Town, South Africa *http://www.ice2018.org*

14-15 Aralık 2018 8. Türkiye Tiroid Hastalıkları Kongresi Ankara *www.temd.org.tr*

Üyelerimizden Literatür Seçmeleri

CLINICAL PRESENTATIONS, METABOLIC ABNORMALITIES AND END-ORGAN COMPLICATIONS IN PATIENTS WITH FAMILIAL PARTIAL LIPODYSTROPHY

Akinci B¹, Onay H², Demir T³, Savas-Erdeve Ş⁴, Gen R⁵, Simsir IY⁶, Keskin FE⁷, Erturk MS⁸, Uzum AK⁹, Yaylali GF¹⁰, Ozdemir NK¹¹, Atik T¹², Ozen S¹³, Yurekli BS⁶, Apaydin T⁷, Altay C¹⁴, Akinci G¹⁵, Demir L¹⁶, Comlekci A³, Secil M¹⁴, Oral EA¹⁷. *Metabolism. 2017 Jul;72:109-119. doi: 10.1016/j.metabol.2017.04.010. Epub 2017 Apr 27.*

Objective: Familial partial lipodystrophy (FPLD) is a rare genetic disorder characterized by partial lack of subcutaneous fat.

Methods: This multicenter prospective observational study included data from 56 subjects with FPLD (18 independent Turkish families). Thirty healthy controls were enrolled for comparison.

Results: Pathogenic variants of the LMNA gene were determined in nine families. Of those, typical exon 8 codon 482 pathogenic variants were identified in four families. Analysis of the LMNA gene also revealed exon 1 codon 47, exon 5 codon 306, exon 6 codon 349, exon 9 codon 528, and exon 11 codon 582 pathogenic variants. Analysis of the PPARG gene revealed exon 3 p.Y151C pathogenic variant in two families and exon 7 p.H477L pathogenic variant in one family. A non-pathogenic exon 5 p.R215Q variant of the LMNB2 gene was detected in another family. Five other families harbored no mutation in any of the genes sequenced. MRI studies showed slightly different fat distribution patterns among subjects with different point mutations, though it was strikingly different in subjects with LMNA p.R349W pathogenic variant. Subjects with pathogenic variants of the PPARG gene were associated with less prominent fat loss and relatively higher levels of leptin compared to those with pathogenic variants in the LMNA gene. Various metabolic abnormalities associated with insulin resistance were detected in all subjects. End-organ complications were observed.

Conclusion: We have identified various pathogenic variants scattered throughout the LMNA and PPARG genes in Turkish patients with FPLD. Phenotypic heterogeneity is remarkable in patients with LMNA pathogenic variants related to the site of missense mutations. FPLD, caused by pathogenic variants either in LMNA or PPARG is associated with metabolic abnormalities associated with insulin resistance that lead to increased morbidity.

SPECTRUM OF CLINICAL MANIFESTATIONS IN TWO YOUNG TURKISH PATIENTS WITH CONGENITAL GENERALIZED LIPODYSTROPHY TYPE 4.

Akinci G¹, Topaloglu H², Akinci B³, Onay H⁴, Karadeniz C⁵, Ergul Y⁶, Demir T³, Ozcan EE⁷, Altay C⁸, Atik T⁹, Garg A¹⁰.

Eur J Med Genet. 2016 Jun;59(6-7):320-4. doi: 10.1016/j.ejmg.2016.05.001. Epub 2016 May 7.

Congenital generalized lipodystrophy type 4 is an extremely rare autosomal recessive disorder. We report our clinical experience on two unrelated Turkish patients with congenital generalized lipodystrophy type 4. A 13-year-old girl (patient-1) presented with generalized lipodystrophy and myopathy. Further tests revealed ventricular and supraventricular arrhythmias, gastrointestinal dysmotility, atlantoaxial instability, lumbosacral scoliosis, and metabolic abnormalities associated with insulin resistance. A 16-year-old girl (patient-2) with congenital generalized lipodystrophy type 4 was previously reported. Here, we report on her long term clinical follow-up. She received several course of anti-arrhythmic treatments for catecholaminergic polymorphic ventricular tachycardia and rapid atrial fibrillation. An implantable cardioverter defibrillator was also placed. A homozygous PTRF mutation, c.259C > T (p.Gln87*), was identified in patient-1. Congenital generalized lipodystrophy type 4 was caused by homozygous PTRF c.481-482insGTGA (p.Lys161Serfs*41) mutation in patient-2. Our data indicate that patients with congenital generalized lipodystrophy type 4 should be meticulously evaluated for cardiac, neuromuscular, gastrointestinal and skeletal diseases, as well as metabolic abnormalities associated with insulin resistance.

CLINICAL SPECTRA OF NEUROMUSCULAR MANIFESTATIONS IN PATIENTS WITH LIPODYSTROPHY: A MULTICENTER STUDY.

Akinci G¹, Topaloglu H², Demir T³, Danyeli AE⁴, Talim B⁵, Keskin FE⁶, Kadioglu P⁷, Talip E³, Altay C⁸, Yaylali GF⁹, Bilen H¹⁰, Nur B¹¹, Demir L¹², Onay H¹³, Akinci B³.

Neuromuscul Disord. 2017 Oct;27(10):923–930. doi: 10.1016/j.nmd.2017.05.015. Epub 2017 Jun 1.

Lipodystrophy is a heterogeneous group of disorders characterized by loss of adipose tissue. Here, we report on clinical spectra of neuromuscular manifestations of Turkish patients with lipodystrophy. Seventy-four patients with lipodystrophy and 20 healthy controls were included. Peripheral sensorimotor neuropathy was a common finding (67.4%) in lipodystrophic patients with diabetes. Neuropathic foot ulcers were observed in 4 patients. Drop foot developed in 1 patient with congenital generalized lipodystrophy type 1. Muscle symptoms and hypertrophy were consistent findings in congenital generalized lipodystrophy (21/21) and familial partial lipodystrophy (25/34); on the other hand, overt myopathy with elevated creatine kinase activity was a distinctive characteristic of congenital generalized lipodystrophy type 4. Muscle biopsies revealed myopathic changes at different levels. Accumulation of triglycerides was observed which contributes to insulin resistance. All patients with congenital generalized lipodystrophy suffered from tight Achilles tendons at various levels. Scoliosis was observed in congenital generalized lipodystrophy type 4 (2/2) and familial partial lipodystrophy type 2 (2/17). Atlantoaxial instability was unique to congenital generalized lipodystrophy type 4 (2/2). Bone cysts were detected in congenital generalized lipodystrophy type 1 (7/10) and congenital generalized lipodystrophy type 2 (2/8). Our study suggests that lipodystrophies are associated with a wide spectrum of neuromuscular abnormalities.

DO VESICULAR MONOAMINE 2 GENOTYPES RELATE TO OBESITY AND EATING BEHAVIOR?

Avsar O¹, Kuskucu A², Sancak S³, Genç E⁴. Neuropsychiatry (London) (2017) 7(6), 1020-1025.

Genetic factors contribute to development of obesity and eating behavior. Vasicular monoamine transporter 2 (VMAT2, SLC18A2) gene is a dopaminergic system gene that regulates dopamine neurotransmission, and may be a part of the pathogenesis of obesity and eating behavior. No previous studies have analyzed VMAT2 polymorphisms about obesity and eating behavior. In the current study, we investigated the association of rs363399 and rs4752045 with adult obesity and eating behavior in 448 subjects. No genetic association was found for VMAT2 polymorphisms and obesity. On the other hand, the C/C genotype of rs363399 and the C/G genotype of rs4752045 were significantly associated with eating behavior, particularly 'eating for reward' and significantly higher in obesity group (p < 0.001). These results suggested that C/C and C/G genotypes might have an effect on eating behavior ('eating for need' vs 'eating for reward') and might be involved in the development of obesity in an indirect way. Future studies are needede to replicate these findings in other populations.

FEMALE GONADAL FUNCTIONS AND OVARIAN RESERVE IN PATIENTS WITH ACROMEGALY: EXPERIENCE FROM A SINGLE TERTIARY CENTER.

Dogansen SC¹, Tanrikulu S², Yalin GY², Yarman S². Endocrine. 2018 Apr;60(1):167–174. doi: 10.1007/s12020-018-1540-5. Epub 2018 Feb 5.

Purpose: To evaluate the gonadal functions and related factors in female patients with acromegaly at the time of diagnosis, the course of gonadal dysfunctions and pregnancies during the follow-up period, and the investigation of ovarian reserve with serum anti-Mullerian hormone (AMH) levels in patients with reproductive age.

Methods: Patients who were not menopausal at the time of acromegaly diagnosis (n = 47) were included in this study. Baseline gonadal status was evaluated retrospectively. Patients were divided into three groups: normal gonadal function (group 1), gonadal dysfunction without central hypogonadism (group 2), and central hypogonadism (group 3). Group 1 and group 2 were compared in terms of clinical and laboratory findings. AMH levels were studied in patients who were \leq 45 years old (n = 14) at the time of the study. Data related to pregnancies (n = 13) were evaluated retrospectively.

Results: Group 1 included 18 patients (38%), group 2 included 18 patients (38%), and group 3 included 11 patients (24%). The estimated duration of acromegaly was longer, and baseline PRL levels were higher, in group 2 than group 1 (p=0.002 and p=0.015, respectively). Gonadal functions recovered in 66% of patients. AMH levels were low in 64% of patients. The frequency of maternal diabetes and hypertension was 7.7%, and there was no tumoral growth in any of the pregnancies.

Conclusion: The most important factors affecting gonadal functions, excluding central hypogonadism, are hyperprolactinemia and the duration of the indolent period before diagnosis of acromegaly. AMH levels in the majority of patients were found to be lower than the expected age. Despite the decreased ovarian reserve, fertilization and normal birth can be achieved with careful surveillance.

CLINICOPATHOLOGICAL SIGNIFICANCE OF BASELINE T2-WEIGHTED SIGNAL INTENSITY IN FUNCTIONAL PITUITARY ADENOMAS.

Dogansen SC¹, Yalin GY², Tanrikulu S², Tekin S², Nizam N², Bilgic B³, Sencer S⁴, Yarman S².

Pituitary. 2018 Aug;21(4):347-354. doi: 10.1007/s11102-018-0877-3.

Purpose: To assess baseline T2-weighted signal intensity (T2-WSI) of functional pituitary adenomas (FPA), and to investigate the relationship of baseline T2-WSI with clinical features, histopathological granulation patterns, and response to treatment in patients with acromegaly, prolactinoma and Cushing's disease (CD).

Methods: Somatotroph adenomas (n = 87), prolactinomas (n = 78) and corticotroph adenomas (n = 29) were included in the study. Baseline T2-WSI findings (grouped as hypo-, iso- and hyperintense) were compared with hormone levels, tumor diameter, granulation patterns and response to treatment.

Results: Somatotroph adenomas were mostly hypointense (53%), prolactinomas were dominantly hyperintense (55%), and corticotroph adenomas were generally hyperintense (45%). Hyperintense somatotroph adenomas were larger in size with sparsely granulated pattern and tumor shrinkage rate was lower after somatostatin analogues (SSA) (p = 0.007, p = 0.035, p = 0.029, respectively). T2 hypointensity was related with higher baseline IGF-1% ULN (upper limit of normal) levels and a better response to SSA treatment (p = 0.02, p = 0.045, respectively). In female prolactinomas, hyperintensity was correlated with a smaller adenoma diameter (p = 0.001). Hypointense female prolactinomas were related to younger age at diagnosis, higher baseline PRL levels and dopamine agonist (DA) resistance (p = 0.009, p = 0.022, p < 0.001, respectively). Hyperintense corticotroph adenomas were related to larger adenoma size and sparsely granulated pattern (p = 0.04, p = 0.017, respectively). There was no significant difference in the recurrence with T2WSI in CD.

Conclusion: Baseline hypointense somatotroph adenomas show a better response to SSA, whereas hypointensity was related to DA resistance in female prolactinomas.

EXENATIDE TREATMENT CAUSES SUPPRESSION OF SERUM FASTING GHRELIN LEVELS IN PATIENTS WITH TYPE 2 DIABETES MELLITUS.

Guclu M¹, Kiyici S², Gul Z³, Cavun S³. Endocr Connect. 2018 Jan;7(1):193–198. doi: 10.1530/EC-17-0242. Epub 2017 Dec 7.

Aim: In the present study, we investigated the long-term effects of exenatide treatment on serum fasting ghrelin levels in patients with type 2 diabetes mellitus.

Methods: Type 2 diabetic patients, who were using metformin with and without the other antihyperglycemic drugs on a stable dose for at least 3 months, were enrolled in the study. BMI>35 kg/m² and HbA1c>7.0% were the additional inclusion criteria. Oral antihyperglycemic drugs, other than metformin, were stopped, and metformin treatment was continued at 2000 mg per day. Exenatide treatment was initiated at 5 µg per dose subcutaneously (sc) twice daily, and after one month, the dose of exenatide was increased to 10 µg twice daily. Changes in anthropometric variables, glycemic control, lipid parameters and total ghrelin levels were evaluated at baseline and following 12 weeks of treatment.

Results: Thirty-eight patients (male/female = 7/31) entered the study. The mean age of patients was 50.5 ± 8.8 years with a mean diabetes duration of 8.5 ± 4.9 years. The mean BMI was 41.6 ± 6.3 kg/m2 and the mean HbA1c of patients was $8.9 \pm 1.4\%$. The mean change in the weight of patients was -5.6 kg and the percentage change in weight was $-5.2 \pm 3.7\%$ following 12 weeks of treatment. BMI, fasting plasma glucose and HbA1c levels of patients were decreased significantly (P < 0.001 and P < 0.001; respectively), while there was no change in lipid parameters. Serum fasting ghrelin levels were significantly suppressed following 12 weeks of exenatide treatment compared with baseline values (328.4 ± 166.8 vs 245.3 ± 164.8 pg/mL) (P = 0.024).

Conclusion: These results suggest that the effects of exenatide on weight loss may be related with the suppression of serum fasting ghrelin levels, which is an orexigenic peptide.

EVALUATION OF CHROMOSOMAL DNA DAMAGE, CYTOTOXICITY, CYTOSTASIS, OXIDATIVE DNA DAMAGE AND THEIR RELATIONSHIP WITH ENDOCRINE HORMONES IN PATIENTS WITH ACUTE ORGANOPHOSPHATE POISONING.

Gundogan K¹, Donmez-Altuntas H², Hamurcu Z³, Akbudak IH¹, Sungur M¹, Bitgen N⁴, Baskol G⁵, Bayram F⁶.

Mutat Res. 2018 Jan;825:1-7. doi: 10.1016/j.mrgentox.2017.11.005. Epub 2017 Nov 9.

Pesticides are commonly used compounds in agriculture. Especially, organophosphates (OPs) are among the extensively used pesticides. Therefore, OPs poisoning is common, especially in underdeveloped and developing countries. Primary aim of this study was to research the effects of acute OPs poisoning on genome instability in the individuals' lymphocytes with acute OPs poisoning both by using the cytokinesis-block micronucleus cytome (CBMN-cyt) assay to examine chromosome/genome damage, cell proliferation index and cell death rate and by using the plasma 8-hydroxy-2'-deoxyguanosine (8-OHdG) levels to determine oxidative DNA damage. Secondary aim of this study was also to assess whether a relation exists between endocrine hormones and the genome damage in acute OPs poisoning. In the study, blood samples were analysed of 13 patients before and after treatment admitted to the Department of Intensive Care Unit with acute OPs poisoning and of 13 healthy subjects of similar age and sex. The present study demonstrates that genome damage (micronucleus; MN and nucleoplasmic bridges; NPBs frequencies), apoptotic and necrotic cell frequencies increased in lymphocytes of patients with acute OPs poisoning before treatment and decreased after treatment. The present study also show that CBMN cyt assay parameters and 8-OHdG levels could be affected by some endocrine hormones such as E2, fT3, fT4, GH, IGF-1, FSH, LH, TSH, PRL, but not be related to ACTH and tT levels in acute OPs poisoning. In conclusion, it is believed that this is the first study to evaluate the chromosomal/oxidative DNA damage, cell proliferation, cell death and their associations with endocrine hormones in acute OPs poisoning. These preliminary findings need to be supported by further studies with larger sample sizes.

CONSTITUTIVE STIMULATORY G PROTEIN ACTIVITY IN LIMB MESENCHYME IMPAIRS BONE GROWTH.

Karaca A¹, **Malladi** VR¹, **Zhu** Y¹, **Tafaj** O¹, **Paltrinieri** E¹, **Wu** JY², **He** Q¹, **Bastepe** M³. *Bone.* 2018 *May*;110:230-237. *doi:* 10.1016/j.bone.2018.02.016. *Epub* 2018 *Feb* 20.

GNAS mutations leading to constitutively active stimulatory G protein alpha-subunit (Gsa) cause different tumors, fibrous dysplasia of bone, and McCune-Albright syndrome, which are typically not associated with short stature. Enhanced signaling of the parathyroid hormone/parathyroid hormone-related peptide receptor, which couples to multiple G proteins including Gsa, leads to short bones with delayed endochondral ossification. It has remained unknown whether constitutive Gsa activity also impairs bone growth. Here we generated mice expressing a constitutively active Gsa mutant (Gsa-R201H) conditionally upon Cre recombinase (cGsaR201H mice). Gsa-R201H was expressed in cultured bone marrow stromal cells from cGsqR201H mice upon adenoviral-Cre transduction. When crossed with mice in which Cre is expressed in a tamoxifen-regulatable fashion (CAGGCre-ER™), tamoxifen injection resulted in mosaic expression of the transgene in double mutant offspring. We then crossed the cGsaR201H mice with Prx1-Cre mice, in which Cre is expressed in early limb-bud mesenchyme. The double mutant offspring displayed short limbs at birth, with narrow hypertrophic chondrocyte zones in growth plates and delayed formation of secondary ossification center. Consistent with enhanced Gsa signaling, bone marrow stromal cells from these mice demonstrated increased levels of c-fos mRNA. Our findings indicate that constitutive Gsa activity during limb development disrupts endochondral ossification and bone growth. Given that Gsa haploinsufficiency also leads to short bones, as in patients with Albright's hereditary osteodystrophy, these results suggest that a tight control of Gsa activity is essential for normal growth plate physiology.

RELATION OF PARAOXONASE 1 ACTIVITY WITH BIOCHEMICAL VARIABLES, BRACHIAL ARTERY INTIMA-MEDIA THICKNESS IN PATIENTS WITH DIABETES WITH OR WITHOUT OBESITY.

Karakaya P¹, Ozdemir B, Mert M, Okuturlar Y. Obes Facts. 2018;11(1):56-66. doi: 10.1159/000486513. Epub 2018 Feb 14.

Aim: The sodium-sparing effect of insulin leads to increase in total sodium pool of the body which is a chronic stimulus for atrial natriuretic peptide (ANP). In our study we aimed to determine the relationship between ANP and microvascular complications of diabetes.

Methods: 60 patients, 30-70 years old, with the diagnosis of type 2 diabetes mellitus (DM) are enrolled into the study. Patients with a chronic disease other than DM are excluded. Blood samples for routine biochemical tests are taken after at least 12 h fasting at 8-9 am. Blood samples for glucose and insulin levels are taken 2 h after a standard meal. Blood tubes with EDTA are used for ANP levels. The microvascular complications of the patients are evaluated.

Results: 32 of the patients had microvascular complications. Age, BMI, waist and hip circumferences, and ANP levels were significantly higher in the group with microvascular complications. There were no significant differences in waist-to-hip ratio, blood glucose, HbA1c, fasting insulin, postprandial insulin, fasting HOMA, postprandial HOMA as well as sodium, potassium, magnesium, calcium and lipid levels between the two groups. When the relationship between ANP and obesity, retinopathy, neuropathy, nephropathy, diabetes time, HbA1c, or sex are evaluated separately, the only significant parameters related to ANP were obesity and retinopathy.

Conclusion: In our study we have found that there was a significant relationship between ANP levels and microvascular complications of diabetes. Future studies are needed to show if ANP is the stimulus of microvascular complication development/progression or only an epiphenomenon.

HOMOZYGOUS MUTATION IN HUMAN SERUM ALBUMIN AND ITS IMPLICATION ON THYROID TESTS.

Mimoto MS¹, Karaca A², Scherberg N¹, Dumitrescu AM¹, Refetoff S^{1,3,4}. *Thyroid.* 2018 Jun;28(6):811–814. doi: 10.1089/thy.2017.0564. Epub 2018 May 24.

An individual with familial dysalbuminemic hyperthyroxinemia (FDH) due to a homozygous mutation (c.653G>A, p.R218H) in the human serum albumin (HSA) gene is reported. The patient was identified during evaluation of abnormal thyroid tests in a large family with multiple levels of consanguinity. He showed a greater increase in total thyroxine (T4) relative to that observed in heterozygous family members. The higher affinity of mutant HSA for T4, together with the large molar excess of HSA relative to thyroid hormones in serum, results in preferential association of T4 with the mutant rather than wild-type HSA in heterozygous individuals. The twofold greater amount of T4 bound to the mutant HSA in the homozygote, relative to heterozygotes, is an adaptive requirement to maintain a normal free T4 concentration.

THE RESULTS OF PARATHYROID HORMONE ASSAY IN PARATHYROID ASPIRATES IN PRE-OPERATIVE LOCALIZATION OF PARATHYROID ADENOMAS FOR FOCUSED PARATHYROIDECTOMY IN PATIENTS WITH NEGATIVE OR SUSPICIOUS TECHNETIUM-99M-SESTAMIBI SCANS

Ozderya A, Temizkan S, Cetin K, Ozugur S, Gul AE, Aydin K. *Endocr Pract. 2017 Sep;23(9):1101-1106. doi: 10.4158/EP171921.0R. Epub 2017 Jul 6.*

Objective: This study aimed to evaluate the results of parathyroid hormone (PTH) assay in parathyroid aspirates to determine uniglandular disease by an endocrinologist-performed ultrasound (US) in patients with discordant or negative technetium-sestamibi scans and to evaluate whether this procedure increases the number of focused parathyroidectomies (FPs).

Methods: We analyzed the data of 65 patients who underwent an endocrinologist-performed US-guided parathyroid fine-needle aspiration (FNA) with PTH wash-out, retrospectively. The results of PTH wash-out procedure and the reports of parathyroid surgery and pathology were reviewed.

Results: Of 65 patients, 54 had positive PTH wash-out results. The median serum PTH level of patients with positive and negative PTH wash-out results was 143 (25 and 75% interquartile range [IQR], 114 to 197) versus 154 (IQR, 115 to 255) pg/mL (P = .45), and the median PTH in FNA was 3,533 (IQR, 1,481 to 3,534) versus 6.0 (IQR, 1 to 6) pg/mL (P < .001), respectively. Forty-five patients underwent surgery. Of the operated patients, 42 had positive PTH wash-out results and had successful FP. Four patients with redo surgery had positive PTH wash-out results and were successfully re-operated with FP. Of 11 patients with negative PTH wash-out results, 3 had bilateral neck exploration (BNE) surgery and 2 patients were successfully operated, while surgery was unsuccessful in 1 patient, despite BNE.

Conclusion: Our study results suggest that endocrinologist-performed US and parathyroid FNA with PTH wash-out increases the number and success of FPs. In particular, patients with redo surgery may benefit from this procedure.

Abbreviations: 4D-CT = four-dimensional computed tomography BNE = bilateral neck exploration FNA = fine-needle aspiration FNAB = fine-needle aspiration biopsy FP = focused parathyroidectomy IQR = 25 and 75% inter-quartile range PHPT = primary hyperparathyroidism PPV = positive predictive value PTH = parathyroid hormone 99mTc = technetium US = ultrasound.

PREGO (PRESENTATION OF GRAVES' ORBITOPATHY) STUDY: CHANGES IN REFERRAL PATTERNS TO EUROPEAN GROUP ON GRAVES' ORBITOPATHY (EUGOGO) CENTRES OVER THE PERIOD FROM 2000 TO 2012.

Perros P¹, Žarković M², Azzolini C³, Ayvaz G⁴, Baldeschi L⁵, Bartalena L⁶, Boschi A⁵, Bournaud C⁷, Brix TH⁸, Covelli D⁹, Ćirić S², Daumerie C¹⁰, Eckstein A¹¹, Fichter N¹², Führer D¹³, Hegedüs L⁸, Kahaly GJ¹⁴, Konuk O¹⁵, Lareida J¹², Lazarus J¹⁶, Leo M¹⁷, Mathiopoulou L¹⁸, Menconi F¹⁷, Morris D¹⁹, Okosieme O¹⁶, Orgiazzi J²⁰, Pitz S²¹, Salvi M⁹, Vardanian-Vartin C²², Wiersinga W²³, Bernard M²⁴, Clarke L²⁵, Currò N²⁶, Dayan C¹⁶, Dickinson J²⁵, Knežević M²⁷, Lane C¹⁹, Marcocci C¹⁷, Marinò M¹⁷, Möller L¹³, Nardi M²⁸, Neoh C²⁵, Pearce S¹, von Arx G¹², Törüner FB⁴.

Br J Ophthalmol. 2015 Nov;99(11):1531-5. doi: 10.1136/bjophthalmol-2015-306733. Epub 2015 May 7.

BACKGROUND/AIMS: The epidemiology of Graves' orbitopathy (GO) may be changing. The aim of the study was to identify trends in presentation of GO to tertiary centres and initial management over time.

METHODS: Prospective observational study of European Group On Graves' Orbitopathy (EUGOGO) centres. All new referrals with a diagnosis of GO over a 4-month period in 2012 were included. Clinical and demographic characteristics, referral timelines and initial decisions about management were recorded. The data were compared with a similar EUGOGO survey performed in 2000.

RESULTS: The demographic characteristics of 269 patients studied in 2012 were similar to those collected in the year 2000, including smoking rates (40.0% vs 40.2%). Mild (60.5% vs 41.2%, p<0.01) and inactive G0 (63.2% vs 39.9%, p<0.01) were more prevalent in 2012. The times from diagnosis of thyroid disease to being seen in EUGOGO centres (6 vs 16 months) and from first symptoms of G0 (9 vs 16 months) or from diagnosis of G0 (6 vs 12 months) to first consultation in EUGOGO centres were shorter in 2012 (p<0.01). The initial management plans for G0 were no different except surgical treatments for patients with mild inactive disease were more frequently offered in the 2012 cohort than in 2000 (27.3% vs 17%, p<0.05), and selenium supplements were offered only in the 2012 cohort (21.2% vs 0%, p<0.01).

Conclusions: These findings suggest that the clinical manifestations of patients with GO may be changing over time in Europe.

GRAVES' ORBITOPATHY AS A RARE DISEASE IN EUROPE: A EUROPEAN GROUP ON GRAVES' ORBITOPATHY (EUGOGO) POSITION STATEMENT.

Perros P^{1,2}, Hegedüs L³, Bartalena L⁴, Marcocci C⁵, Kahaly GJ⁶, Baldeschi L⁷, Salvi M⁸, Lazarus JH⁹, Eckstein A¹⁰, Pitz S¹¹, Boboridis K¹², Anagnostis P¹³, Ayvaz G¹⁴, Boschi A⁷, Brix TH³, Currò N¹⁵, Konuk O¹⁶, Marinò M⁵, Mitchell AL¹⁷, Stankovic B¹⁸, Törüner FB¹⁴, von Arx G¹⁹, Zarković M²⁰, Wiersinga WM²¹. Orphanet J Rare Dis. 2017 Apr 20;12(1):72. doi: 10.1186/s13023-017-0625-1.

Background: Graves' orbitopathy (GO) is an autoimmune condition, which is associated with poor clinical outcomes including impaired quality of life and socio-economic status. Current evidence suggests that the incidence of GO in Europe may be declining, however data on the prevalence of this disease are sparse. Several clinical variants of GO exist, including euthyroid GO, recently listed as a rare disease in Europe (ORPHA466682). The objective was to estimate the prevalence of GO and its clinical variants in Europe, based on available literature, and to consider whether they may potentially qualify as rare. Recent published data on the incidence of GO and Graves' hyperthyroidism in Europe were used to estimate the prevalence of GO. The position statement was developed by a series of reviews of drafts and electronic discussions by members of the European Group on Graves' Orbitopathy. The prevalence of GO in Europe is about 10/10,000 persons. The prevalence of other clinical variants is also low: hypothyroid GO 0.02-1.10/10,000; GO associated with dermopathy 0.15/10,000; GO associated with acropachy 0.03/10,000; asymmetrical GO 1.00-5.00/10,000; unilateral GO 0.50-1.50/10,000.

Conclusion: GO has a prevalence that is clearly above the threshold for rarity in Europe. However, each of its clinical variants have a low prevalence and could potentially qualify for being considered as a rare condition, providing that future research establishes that they have a distinct pathophysiology. EUGOGO considers this area of academic activity a priority.

ASSOCIATION BETWEEN PREOPERATIVE THYROTROPHIN AND CLINICOPATHOLOGICAL AND AGGRESSIVE FEATURES OF PAPILLARY THYROID CANCER.

Tam AA¹, Ozdemir D², Aydın C², Bestepe N², Ulusoy S³, Sungu N⁴, Ersoy R², Cakir B².

Endocrine. 2018 Mar;59(3):565-572. doi: 10.1007/s12020-018-1523-6. Epub 2018 Jan 27.

Purpose: We aimed to investigate the relation between preoperative serum thyrotrophin (TSH) and clinicopathological features in patients with papillary thyroid carcinoma (PTC) and microcarcinoma (PTMC).

Methods: Patients who underwent thyroidectomy and diagnosed to have benign nodular disease or PTC/PTMC in our clinic were evaluated retrospectively. Patients with a previous history of thyroid surgery, patients using antithyroid medications or thyroid hormone and patients with tumors known to be unresponsive to TSH were excluded.

Results: Data of 1632 patients were analyzed. Histopathological diagnosis was benign in 969 (59.4%) and malignant in 663 (40.6%) patients. Preoperative median serum TSH was significantly higher in malignant compared to benign group (1.41 IU/dL vs. 0.98 IU/dL, p < 0.001). Malignancy risk increased gradually as going from hyperthyroidism to euthyroidism and hypothyroidism (20, 40.6, and 59.1%, respectively, p < 0.05). Serum TSH was lowest in benign nodular disease, higher in PTMC and highest in PTC (p < 0.001). This was also true when patients with positive antithyroid peroxidase/antithyroglobulin and with lymphocytic thyroiditis were excluded from the analysis (p < 0.001). Serum TSH was higher in patients with bilateral tumor, capsular invasion and lymph node metastasis (LNM) compared to patients with unilateral tumor, without capsule invasion and without LNM, respectively (p = 0.036, p = 0.002, and p = 0.001, respectively). Patients with aggressive variant PTC had higher serum TSH than nonaggressive ones (p < 0.05).

Conclusion: Preoperative serum TSH is associated with PTMC, PTC and LNM. Serum TSH seems to be related with thyroid cancer regardless of autoimmunity. With the present study, for the first time, we showed an association between serum TSH and aggressive variants of PTC.

AIRWAY AND SLEEP DISORDERS IN PATIENTS WITH ACROMEGALY

Turan 0¹, Akinci B², Ikiz AO³, Itil O⁴, Oztura I⁵, Ada E⁶, Akdeniz B⁷, Yener S², Kaya M⁸, Gedik A⁹, Comlekci A².

Clin Respir J. 2018 Mar;12(3):1003-1010. doi: 10.1111/crj.12618. Epub 2017 Mar 14.

Objective: Acromegaly is a multisystemic disorder caused by excessive secretion of growth hormone (GH). Sleep-disordered breathing (SDB) such as sleep apnea syndrome (SAS) may occur in acromegaly. The aim of study was to assess the presence of sleep disorders and evaluate the systemic complications on respiratory, cardiovascular, and upper airway systems in acromegalic patients.

Methods: The study group consisted of 30 acromegaly outpatients. GH and insulin-like growth factor 1 (IGF-1) measurements were obtained; body pletysmography, arterial blood gas analysis, tissue-doppler imaging, echocardiography, polysomnography, otorhinolaryngologic examination, and head-neck computed tomography were performed.

Results: Sixteen female (53.3%) and 14 male (46.7%) acromegalic patients had a mean age of 51.1 ± 13.2 . GH was supressed in 19 patients (63.3%) when 11 had active acromegaly (36.7%). There were 17 patients with SAS (62.9%) (7: mild, 3:intermediate, 7:severe SAS) and average AHI was 16/h. Sixteen patients had predominantly obstructive SAS while one patient had predominantly central SAS. SAS was statistically more frequent in males than females (P = .015). The mean neck circumference was significantly longer in patients with SAS (P = .048). In SAS patients,the soft palate was elongated and thickened,which was statistically significant (P = .014 and P = .05).Vallecula-to-tongue distance was statistically longer in acromegalic patients with SAS (P = .007). There was a positive correlation between tonsil size,vallecula-to-tongue distance and AHI (r = 0.432, P = .045 and r = 0.512, P = .021, respectively).

Conclusion: SDB seems to be common and clinically important in patients with acromegaly, particularly in men. The most frequent type of apnea in acromegalics is obstructive. Hormonal activity of acromegaly does not seem to have an effect on the development of SAS. Despite its high prevalence, SAS is frequently under-assessed in patients with acromegaly. Systemic complications and SDB should be researched in acromegalics.

AUTONOMOUS CORTISOL SECRETION IN ADRENAL INCIDENTALOMAS AND INCREASED VISCERAL FAT ACCUMULATION DURING FOLLOW-UP.

Yener S¹, Baris M², Peker A², Demir O³, Ozgen B¹, Secil M². Clin Endocrinol (Oxf). 2017 Nov;87(5):425-432. doi: 10.1111/cen.13408. Epub 2017 Aug 2.

Objective: Autonomous cortisol secretion of adrenal incidentalomas (Als) is associated with poor cardiovascular outcome. Because centripetal obesity is a cardiovascular risk factor, we aimed to investigate whether autonomous cortisol secretion is associated with increased visceral fat accumulation.

Design: Retrospective cohort study.

Patients: Patients with Als who attended for follow-up between January 2014 and December 2016 were evaluated. Autonomous cortisol secretion was diagnosed when 1 mg overnight dexamethasone (post-DST) cortisol was >50 nmol/L at baseline and follow-up. Follow-up duration was 34 (12-105) months. Thirty patients with nonfunctioning Als and 44 patients with autonomous cortisol secretion were included. Adrenalectomy was performed in five patients. Six patients with Cushing's syndrome were also recruited.

Measurements: Hormonal evaluation and assessment of total (T), visceral (V) and subcutaneous (S) fat area by computed tomography and calculation of V:S and V:T ratios at baseline and follow-up.

Results: V, V:S and V:T increased (P<.001 for each comparison, Wilcoxon signed rank test for repeated measures) in patients with autonomous cortisol secretion while did not change significantly in patients with nonfunctioning adenomas. Linear regression models including post-DST cortisol, gender, concomitant treatments and follow-up duration showed that both baseline and follow-up DST significantly predicted Δ (V:S) and Δ (V:T) (P<.01 for all models).

CONCLUSIONS: In patients with Als, a post-DST cortisol >50 nmol/L at both baseline and follow-up, was associated with a significant increase in visceral fat after a follow-up duration of ~3 years. This may be of importance to explain the link between autonomous cortisol secretion and poor cardiovascular outcome.

INTERFERENCE IN ACTH IMMUNOASSAY NEGATIVELY IMPACTS THE MANAGEMENT OF SUBCLINICAL HYPERCORTISOLISM.

Yener S¹, Demir L², Demirpence M³, Mahmut Baris M⁴, Simsir IY⁵, Ozisik S⁶, Comlekci A⁶, Demir T⁶.

Endocrine. 2017 May;56(2):308-316. doi: 10.1007/s12020-017-1268-7. Epub 2017 Feb 28.

Purpose: Low plasma corticotropin is considered a useful parameter for the diagnosis of subclinical hypercortisolism in patients with an adrenal incidentaloma. However, immunoassays are vulnerable to interference from endogenous antibodies. In this study, subjects who underwent Hypothalamus-pituitary-adrenal axis evaluation for the assessment of subclinical hypercortisolism were evaluated. The objective of the study was to ascertain whether antibody interference in corticotropin immunoassay affected the diagnostic work-up and clinical decisions.

Methods: The 437 consecutive patients with incidentally discovered adrenal adenomas were included in this single centre study. Patients who had a combination of a nonsuppressed corticotropin concentration (>4.4 pmol/L) and a non-suppressed cortisol concentration after 1 mg overnight dexamethasone suppression test (>50 nmol/L) were selected. Eight eligible subjects without specific features of Cushing's syndrome were identified and recruited for interference studies and follow-up. Nine controls including one patient with unilateral adrenalectomy and one patient with Cushing's disease were recruited as well.

Measurements: Eligible subjects and controls were subjected to hormonal tests and investigations for suspected interference. Interference studies included measurement of corticotropin on a different analytical platform, serial dilutions, polyethylene glycol precipitation and heterophilic antibody analysis. Patients were followed with clinical and laboratory parameters for a median duration of 30 (12-90) months.

Results: Antibody interference was identified in four patients. Rheumatoid factor was responsible for the interference in one patient. Clinical management of the patients was affected by the erroneous results. Interference tests were negative in control subjects.

Conclusions: Erroneous results associated with analytical interference negatively impacted on clinical decision making in this patient group. This should be considered particularly in conditions such as subclinical hypercortisolism which decisions depend on laboratory investigations mainly. Analytical interference could explain the high variability observed both in field measurements from patients who were expected to have lower corticotropin concentrations and in subclinical hypercortisolism prevalence reported by different studies. Many problems can be resolved by ensuring good communication between clinical and laboratory staff.

METABOLIC SYNDROME, HYPERTENSION, AND HYPERLIPIDEMIA IN MOTHERS, FATHERS, SISTERS, AND BROTHERS OF WOMEN WITH POLYCYSTIC OVARY SYNDROME: A SYSTEMATIC REVIEW AND META-ANALYSIS.

Yilmaz B¹, Vellanki P², Ata B³, Yildiz BO⁴.

Fertil Steril. 2018 Feb;109(2):356-364.e32. doi: 10.1016/j.fertnstert.2017.10.018. Epub 2018 Jan 11.

Objective: To provide an evidence-based assessment of metabolic syndrome, hypertension, and hyperlipidemia in first-degree relatives of women with polycystic ovary syndrome (PCOS).

Design: Systematic review and meta-analysis.

Setting: Not applicable.

Patient(s): Mothers, fathers, sisters, and brothers of women with and without PCOS.

Intervention(s): An electronic-based search with the use of PubMed from 1960 to June 2015 and cross-checked references of relevant articles.

Main outcome measure(s): Metabolic syndrome, hypertension and dyslipidemia, and surrogate markers, including systolic blood pressure (BP), diastolic BP, total cholesterol, low-density lipoprotein cholesterol, high-density lipoprotein cholesterol, and triglycerides.

Result(s): Fourteen of 3,346 studies were included in the meta-analysis. Prevalence of the following was significantly increased in relatives of women with PCOS: metabolic syndrome (risk ratio [RR] 1.78 [95% confidence interval 1.37, 2.30] in mothers, 1.43 [1.12, 1.81] in fathers, and 1.50 [1.12, 2.00] in sisters), hypertension (RR 1.93 [1.58, 2.35] in fathers, 2.92 [1.92, 4.45] in sisters), and dyslipidemia (RR 3.86 [2.54, 5.85] in brothers and 1.29 [1.11, 1.50] in fathers). Moreover, systolic BP (mothers, sisters, and brothers), total cholesterol (mothers and sisters), low-density lipoprotein cholesterol (sisters), and triglycerides (mothers and sisters) were significantly higher in first-degree relatives of PCOS probands than in controls.

Conclusion(s): Our results show evidence of clustering for metabolic syndrome, hypertension, and dyslipidemia in mothers, fathers, sisters, and brothers of women with PCOS.

KİTAP BÖLÜMÜ

- Physiopathology, diagnosis, and treatment of GH Deficiency F. Tanriverdi and F. Keleştimur
- Hypothalamic –Pituitary Diseases, Endocriology *F.F. Casanueva*, *E. Ghigo (eds)* https://doi.org/10.1007/978-3-319-38681-2_2-1

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