TÜRKİYE ENDOKRİNOLOJİ VE METABOLİZMA DERNEĞİ BÜLTENİ

Üç ayda bir yayımlanır • Üyelere ücretsiz olarak gönderilir

Sayı 59 • Temmuz – Ağustos – Eylül - 2017

TİROİDOLOJİ KURSU (TİROKURS - 19) TAMAMLANDI

Tüm Türkiye çapında değişik bölgelerimizde yapılan *"Tiroid hastalıklarının tanı ve tedavisi ile ilgili güncel bilgilerin interaktif bir ortamda paylaşıldığı"* TİROKURS'un ondokuzuncusu 23 Eylül'de Samsun Anemon Otel'de endokrinoloji araştırma görevlileri, aile hekimleri ve iç hastalıkları uzmanlarından oluşan 60 hekimin katılımı ile başarı bir şekilde tamamlanmıştır.

ENDOKRİN ACİLLER KURSU (DİYARBAKIR) TAMAMLANDI

8. Endokrin Aciller Kursu 70 Hekimin katılımı ile 23 Eylül'de Diyarbakır'da başarılı bir şekilde gerçekleştirilmiştir. Interaktif olarak geçen kursumuz 8 ilde 1000 den fazla hekime ulaşmıştır.

Kongre, Kurslar ve Sempozyumlar

Bilimsel Kongreler, Ulusal ve Uluslararası Sempozyumlar

19. Ulusal İç Hastalıkları Kongresi
11-15 Ekim 2017
Sueno Deluxe Hotel & Kongre Merkezi, Belek, Antalya
http://ichastaliklari2017.org/

EndoBridge 2017
19-22 Ekim 2017
Regnum Carya Hotel, Antalya
http://www.endobridge.org/

87th Annual Meeting of the ATA
18-22 Ekim 2017
The Fairmont Empress & Victoria Conference Centre
Victoria, BC, Canada
http://www.thyroid.org/87th-annual-meeting-ata/

Hipertansiyon ve Lipid Metabolizması Bozuklukları Eğitim Sempozyumu
27-29 Ekim 2017
DoubleTree by Hilton Hotel Avanos, Kapadokya
www.temdkapadokya.org

13. Hipofiz Sempozyumu
10-11 Kasım 2017
Sheraton Otel, Ankara
http://hipofiz2017.org/

Endokrinologlar için İleri Tiroid ve Boyun Ultrasonografisi Kursu
18 Kasım 2017
Mövenpick Otel - Zurih Salonu, Ankara
www.temd.org.tr

40. Türkiye Endokrinoloji ve Metabolizma Hastalıkları Kongresi
09-13 Mayıs 2018
Sueno Hotel, Antalya
http://temhk2018.org/
http://www.temd.org.tr

Üyelerimizden Literatür Seçmeleri

ASSOCIATION OF NECK CIRCUMFERENCE AND PULMONARY FUNCTION IN CHILDREN.

Akın O[1], Arslan M[2], Haymana C[3], Karabulut E[4], Hacihamdioglu B[5], Yavuz ST[6].
Ann Allergy Asthma Immunol 2017 Jul;119(1):27-30. doi: 10.1016/j.anai.2017.04.018. Epub 2017 May 17.

Background: Childhood obesity leads to many complications including impaired respiratory function. There are various anthropometric parameters related to obesity.

Objective: To investigate the correlation between anthropometric indices and pulmonary function test results in children without asthma.

Methods: Children without any respiratory disorders were enrolled in this study. Anthropometric measurements, such as height, weight, neck circumference (NC), and waist circumference, were obtained from the enrollees and body mass index was calculated. Afterward, pulmonary function tests were performed using spirometry.

Results: A total of 178 children (106 boys, 59.5%) with a mean age of 9.7 years were included the study. NC was above the 90th percentile in 65 children. Importantly, pulmonary parameters, such as forced expiratory volume during the first second (FEV_1) and the ratio of FEV_1 to forced vital capacity (FVC), were lower in subjects with a large NC. Similarly, waist circumference was above the 90th percentile in 67 children, and FEV_1/FVC was significantly lower in children with a large waist circumference. Moreover, there was a statistically significant negative correlation among FEV_1, FEV_1/FVC, and body mass index SD score. Also, multivariable linear regression analysis showed that an NC above the 90th percentile was associated with lower FEV_1 and FEV_1/FVC values.

Conclusion: We identified NC as a novel anthropometric index that is strongly correlated with respiratory functions in children. Therefore, close monitoring of respiratory symptoms, particularly in children with obesity and a large NC, could help with early and prompt determination of respiratory complications of obesity.

ARE DOPAMINERGIC GENOTYPES RISK FACTORS FOR EATING BEHAVIOR AND OBESITY IN ADULTS?

Avsar O[1], Kuskucu A[2], Sancak S[3], Genc E[4]. Neurosci Lett.
2017 Jul 27;654:28-32. doi: 10.1016/j.neulet.2017.06.023. Epub 2017 Jun 16.

Dopamine (DA) is the main modulator of the brain reward system and significantly regulates food intake. The idea that obesity is a neurobiological disease rather than a metabolic disorder, is the basis of the study. Changes in dopamine neurotransmission affect the brain reward system in a direct way. Furthermore, changes in the reward system influence the eating behavior in human. The enzymes monoamine oxidase A (MAOA) and catechol-O-methyltransferase (COMT) terminate the DA function by metabolizing it. In our study, the control group which included 214 individuals and 234 subjects with obesity were investigated for MAOA-u VNTR and COMT (rs4680) polymorphisms. In our study, statistical analysis has showed that in control group Val/Met COMT genotype was significantly higher compared with the patient group (p=0.04). When the groups were compared in terms of eating behavior, the number of the subjects who ate for reward was significantly higher in patient group (p=0.03). Our findings demonstrated that eating behavior might have an effect on obesity and dopaminergic polymorphisms could be risk factors for the development of obesity in Turkish population.

POLYCYSTIC OVARY SYNDROME

Azziz R[1,2], Carmina E[3], Chen Z[4,5], Dunaif A[6], Laven JS[7], Legro RS[8], Lizneva D[1,9], Natterson-Horowtiz B[10], Teede HJ[11], Yildiz BO[12]
Nat Rev Dis Primers. 2016 Aug 11;2:16057. doi: 10.1038/nrdp.2016.57.

Polycystic ovary syndrome (PCOS) affects 5-20% of women of reproductive age worldwide. The condition is characterized by hyperandrogenism, ovulatory dysfunction and polycystic ovarian morphology (PCOM) - with excessive androgen production by the ovaries being a key feature of PCOS. Metabolic dysfunction characterized by insulin resistance and compensatory hyperinsulinaemia is evident in the vast majority of affected individuals. PCOS increases the risk for type 2 diabetes mellitus, gestational diabetes and other pregnancy-related complications, venous thromboembolism, cerebrovascular and cardiovascular events and endometrial cancer. PCOS is a diagnosis of exclusion, based primarily on the presence of

hyperandrogenism, ovulatory dysfunction and PCOM. Treatment should be tailored to the complaints and needs of the patient and involves targeting metabolic abnormalities through lifestyle changes, medication and potentially surgery for the prevention and management of excess weight, androgen suppression and/or blockade, endometrial protection, reproductive therapy and the detection and treatment of psychological features. This Primer summarizes the current state of knowledge regarding the epidemiology, mechanisms and pathophysiology, diagnosis, screening and prevention, management and future investigational directions of the disorder.

ASSESSMENT OF DIASTOLIC DYSFUNCTION, ARTERIAL STIFFNESS, AND CAROTID INTIMA-MEDIA THICKNESS IN PATIENTS WITH ACROMEGALY.

Cansu GB, Yılmaz N, Yanıkoğlu A, Özdem S, Yıldırım AB, Süleymanlar G, Altunbaş HA

Endocr Pract. 2017 May;23(5):536-545. doi: 10.4158/EP161637.OR. Epub 2017 Feb 3.

Objective: Early diagnosis and treatment of cardiovascular diseases, the most frequent cause of morbidity and mortality in acromegaly, may be an efficient approach to extending the lifespan of affected patients. Therefore, it is crucial to determine any cardiovascular diseases in the subclinical period. The study objectives were to determine markers of subclinical atherosclerosis and asses heart structure and function.

Methods: This was a cross-sectional, single-center study of 53 patients with acromegaly and 22 age- and sex-matched healthy individuals. Carotid intima-media thickness (CIMT), pulse-wave velocity (PWV), and echocardiographic data were compared between these groups.

Results: CIMT and PWV were higher in the acromegaly group than in the healthy group (P = .008 and P = .002, respectively). Echocardiography showed that left ventricular diastolic dysfunction was present in 11.3% of patients. Left ventricular mass index and left atrial volume index were higher in the patients (P = .016 and P<.001, respectively). No differences in the CIMT, PWV, or echocardiographic measurements were identified between the patients with biochemically controlled and uncontrolled acromegaly and the control group.

Conclusion: Our results showed that subclinical atherosclerosis (i.e., CIMT and PWV markers) and heart structure and function were worse in patients with acromegaly than in healthy individuals. Because there were no differences in these parameters between patients with controlled and uncontrolled acromegaly, our results suggest that the structural and functional changes do not reverse with biochemical control.

Abbreviations: AA = active acromegaly BSA = body surface area CA = biochemically controlled acromegaly CH = concentric hypertrophy CIMT = carotid intima-media thickness DBP = diastolic blood pressure DM = diabetes mellitus ECHO = echocardiography EDV = enddiastolic volume EF = ejection fraction ESV = endsystolic volume GH = growth hormone HC = healthy control HL = hyperlipidemia HT = hypertension IGF-1 = insulin-like growth factor 1 LA = left atrial LAV = left atrial volume LAVI = left atrial volume index LV = left ventricular LVDD = left ventricular diastolic dysfunction LVEF = left ventricular ejection fraction LVH = left ventricular hypertrophy LVMI = left ventricular mass index PWV = pulse-wave velocity RWT = relative wall thickness.

NON-CLASSIC CONGENITAL ADRENAL HYPERPLASIA DUE TO 21-HYDROXYLASE DEFICIENCY REVISITED: AN UPDATE WITH A SPECIAL FOCUS ON ADOLESCENT AND ADULT WOMEN.

Carmina E[1], Dewailly D[2], Escobar-Morreale HF[3], Kelestimur F[4], Moran C[5], Oberfield S[6], Witchel SF[7], Azziz R[8]

Hum Reprod Update. 2017 Sep 1;23(5):580-599. doi: 10.1093/humupd/dmx014.

Background: Non-classic congenital hyperplasia (NCAH) due to 21-hydroxylase deficiency is a common autosomal recessive disorder characterized by androgen excess.

Objective and rationale: We conducted a systematic review and critical assessment of the available evidence pertaining to the epidemiology, pathophysiology, diagnosis and management of NCAH. A meta-analysis of epidemiological data was also performed.

Search methods: Peer-reviewed studies evaluating NCAH published up to October 2016 were reviewed. Multiple databases were searched including MEDLINE, EMBASE, Cochrane, ERIC, EBSCO, dissertation abstracts, and current contents.

Outcomes: The worldwide prevalence of NCAH amongst women presenting with signs and symptoms of androgen excess is 4.2% (95% confidence interval: 3.2-5.4%). The clinical consequences of NCAH expand from infancy, i.e. accelerated growth, to adolescence and adulthood, i.e. premature pubarche, cutaneous symptoms and oligo-ovulation in a polycystic ovary syndrome (PCOS)-like clinical picture. The diagnosis of NCAH relies on serum 17-hydroxyprogesterone (17-OHP) concentrations. A basal 17-OHP concentration ≥2 ng/ml (6 nmol/l) should be used for screening if more appropriate in-house cut-off values are not available. Definitive diagnosis requires a 17-OHP concentration ≥10 ng/ml (30 nmol/l), either basally or after cosyntropin-stimulation. Molecular genetic analysis of the CYP21A2 gene, which is responsible for 21-hydroxylase activity, may be used for confirmation purposes and should be offered to all patients with NCAH along with genetic counseling because these patients frequently carry alleles that may result in classic CAH, the more severe form of the disease, in their progeny. Treatment must be individualized. Glucocorticoid replacement therapy may benefit pediatric patients with accelerated growth or advanced bone age or adult women seeking fertility, whereas adequate control of menstrual irregularity, hirsutism and other cutaneous symptoms is best served by the use of oral contraceptive pills and/or anti-androgens. Some women may need ovulation induction or assisted reproductive technology to achieve pregnancy. Patients with NCAH have a higher risk of miscarriage and may benefit from glucocorticoid treatment during pregnancy.

Wider implications: Evidence-based diagnostic and treatment strategies are essential for the proper management of women with NCAH, especially considering that these patients may need different therapeutic strategies at different stages during their follow-up and that appropriate genetic counseling may prevent the occurrence of CAH in their children.

FAS/FASL GENE POLYMORPHISM IN PATIENTS WITH HASHIMOTO'S THYROIDITIS IN TURKISH POPULATION.

Erdogan M[1], Kulaksizoglu M[2], Ganidagli S[3], Berdeli A[4].

J Endocrinol Invest. 2017 Jan;40(1):77-82. doi: 10.1007/s40618-016-0534-5. Epub 2016 Aug 30.

Objective: Hashimoto's disease is a polygenic disorder with complex etiopathogenesis. Apoptosis is proposed as one of its mechanisms. The Fas/Fas ligand cascade represents a major pathway initiating apoptosis. This study aims to evaluate the influence of Fas and FasL gene polymorphism in Hashimoto's thyroiditis in Turkish population.

Materials and methods: A total of 112 patients with Hashimoto's thyroiditis and 112 cases of healthy control people were included in this study. The evaluation of genotype for Fas -670 A/G and FasL 843 C/T gene polymorphism was performed by using PCR-RFLP method.

Results: The FAS genotype and gene allele frequency distribution did differ between the control group (AA 36.6 %, AG 50.0 %, GG 13.4 %, A 61.6 %, G 38.4 %) and the Hashimoto's thyroiditis patients (AA 21.4 %, AG 50.9 %, GG 27.7 %, A 46.9 %, G 53.1 %) ($p < 0.01$). The evaluation of FasL genotype and gene allele frequency did not show statistically significant difference between the patient group (CC 27.7 %, CT 45.5 %, TT 26.8 %, C 50.4 %, T 49.6 %) and control group (CC 33.9 %, CT 44.6 %, TT 21,4 %, C 56.3 %, T 43.8 %) ($p > 0.05$).

Conclusions: Gene polymorphism of Fas and G allele frequency may play a role in the regulation of apoptosis in thyroid autoimmune disorders. There is a need for further studies to clarify the genetic role of apoptosis in HT.

POLYCYSTIC OVARY SYNDROME AND THE RISK OF OBSTRUCTIVE SLEEP APNEA: A META-ANALYSIS AND REVIEW OF THE LITERATURE.

Helvaci N[1], Karabulut E[2], Demir AU[3], Yildiz BO[4].

Endocr Connect. 2017 Oct;6(7):437-445. doi: 10.1530/EC-17-0129. Epub 2017 Jul 24.

Background and objective: Polycystic ovary syndrome (PCOS) has been reported to be associated with the development of obstructive sleep apnea (OSA). The objective of this meta-analysis is to assess the relationship between PCOS and OSA.

Methods: A literature search was conducted to identify studies linking PCOS with the risk of OSA. Studies in which the presence of OSA was confirmed with overnight polysomnography were included. Random effects models were used to calculate pooled relative risks.

Results: Eight studies conducted in adults and five studies conducted in adolescents were identified. The pooled OSA prevalence was 0.22 (95% confidence interval (CI): 0.08-0.40)

in PCOS patients. The pooled prevalence of OSA was higher in adults (0.32, 95% CI: 0.13-0.55) than adolescents (0.08, 95% CI: 0.00-0.30). Risk of OSA was significantly increased in adult patients with PCOS (odds ratio (OR) 9.74, 95% CI: 2.76-34.41). Risk of OSA was not significantly increased in adolescents (OR: 4.54, 95% CI:0.56-36.43).

Conclusions: These findings demonstrate a significant association between PCOS and OSA in adult patients. Considering the increased risk for long-term cardiometabolic disorders associated with both PCOS and OSA, it is important to diagnose and treat OSA in patients with PCOS.

MATRIX METALLOPROTEINASE 2 (MMP-2) LEVELS ARE INCREASED IN ACTIVE ACROMEGALY PATIENTS.

Karci AC[1], Canturk Z[2], Tarkun I[2], Cetinarslan B[2].

Endocrine. 2017 Jul;57(1):148-155. doi: 10.1007/s12020-017-1283-8. Epub 2017 Mar 22.

Purpose: During follow-up of acromegaly patients, there is a discordance rate of 30% between the measurements of growth hormone and insulin-like growth factor-1 levels. Further tests are required to determine disease activity in patients with discordant results. This study was planned to investigate an association of serum levels of matrix metalloproteinase-2, matrix metalloproteinase-9, and cathepsin B with disease activity in acromegaly patients.

Methods: In this study, 64 acromegaly patients followed in our clinic were divided into two groups according to the 2010 consensus criteria for cure of acromegaly as patients with active disease (n = 24) and patients with controlled disease (n = 40). Serum matrix metalloproteinase-2, matrix metalloproteinase-9, and cathepsin B levels were measured by the enzyme-linked immunosorbent assay method.

Results: The mean serum matrix metalloproteinase-2 level was significantly higher in the active acromegaly patients than in the controlled acromegaly patients (150.1 ± 54.5 ng/mL vs. 100.2 ± 44.6 ng/mL; $p < 0.0001$). There was no significant difference between the active and controlled acromegaly patients regarding serum matrix metalloproteinase-9 and cathepsin B levels ($p = 0.205$ and $p = 0.598$, respectively). Serum matrix metalloproteinase-2 levels of 118.3 ng/mL and higher had a sensitivity of 75% and a specificity of 77.5% in determining active disease. The risk of active acromegaly was 3.3 fold higher in the patients with a matrix metalloproteinase-2 level of >118.3 ng/mL than in the patients with a matrix metalloproteinase-2 level of <118.3 ng/mL.

Conclusions: In this study, serum matrix metalloproteinase-2 level is increased in the active acromegaly patients and a threshold value in determining active disease was defined for serum matrix metalloproteinase-2 level. This study is the first to compare acromegaly patients having active or controlled disease in terms of matrix metalloproteinase-2 and matrix metalloproteinase-9 levels. The results need to be confirmed by a study that will be conducted in a larger patient group also including a healthy control group to demonstrate the value of this novel marker in disease activity.

PENTRAXIN 3 AS A NEW CARDIOVASCULAR MARKER IN ADRENAL ADENOMAS.

Kizilgul M, Beysel S, Ozcelik O, Kan S, Apaydin M, Caliskan M, Ucan B, Sencar E, Ozdemir S, Cakal E.

Endocr Pract. 2017 Jun;23(6):662-668. doi: 10.4158/EP161713.OR. Epub 2017 Mar 23.

Pentraxin 3 (PTX3) is an acute-phase glycoprotein, which is increased in patients with cardiovascular disease (CVD) and considered as a predictor of CVD in the general population. Both functional and nonfunctional adrenal tumors are associated with a higher risk of cardiovascular events and mortality. We aimed to investigate plasma PTX3 levels in patients with functioning and nonfunctioning adrenal tumors and determine its relationship with cardiovascular risk factors.

Methods: Twenty-one patients with functional adrenal tumors (11 pheochromocytomas, 9 Cushing syndrome, and 1 primary hyperaldosteronism), 28 patients with nonfunctional adrenal incidentalomas, and 40 healthy controls were enrolled in the study. Serum PTX3 levels were measured using a human PTX3 enzyme-linked immunosorbent assay.

Results: PTX3 concentrations were significantly higher in the adrenal tumor group compared with the control group (3,001.64 ± 374.64 pg/mL vs. 1,173.59 ± 168.89 pg/mL; P<.001). PTX3 concentrations were positively correlated with carotid intima media thickness (CIMT) (r^2, 0.464; P<.001), high-sensitivity C-reactive protein (hsCRP) (r^2, 0.551; P<.001), diastolic blood pressure (r^2, 0.334; P = .003), systolic blood pressure (r^2, 0.312; P = .006), and urinary metanephrine concentrations (r^2, 0.320; P = .041). Serum PTX3 concentrations in patients with functional adrenal tumors and comorbidities including hypertension, diabetes mellitus, or CVD were higher than in those without comorbidities (3,654.54 ± 447 pg/mL vs. 1,026.96 ± 447.97 pg/mL; P = .008).

Conclusion: We found that serum PTX3 concentrations increased in both functional and nonfunctional adrenal tumors. PTX3 levels were correlated with cardiovascular risk factors such as CIMT, hsCRP, and blood pressure.

Abbreviations: BMI = body mass index; CIMT = carotid intima-media thickness; CRP = C-reactive protein; CT = computed tomography; CVD = cardiovascular disease; FGF2 = fibroblast growth factor 2; hsCRP = high-sensitivity C-reactive protein; PA = primary hyperaldosteronism; PTX3 = pentraxin 3.

EFFECT OF ALTERATIONS IN APOPTOTIC PATHWAY ON DEVELOPMENT OF METABOLIC SYNDROME IN PATIENTS WITH PSORIASIS VULGARIS.

Korkmaz S[1], Korkmaz H[2]

Br J Dermatol. 2017 Jun;176(6):1549-1557. doi: 10.1111/bjd.15185. Epub 2017 Apr 10.

Background: An increase in the incidence of metabolic syndrome (MetS) has been identified in patients with psoriasis.

Objectives: To evaluate the role of changes in expression of apoptosis activators [B-cell lymphoma (Bcl)-2-like protein 4 (BAX), cytochrome c (cytC) and caspase-3 (CASP3)] and apoptosis inhibitors [Bcl-2, survivin, cyclin D1 (CCND1), superoxide dismutase (SOD), catalase 3 (CAT), glutathione synthetase (GS), heat shock protein (Hsp)27, Hsp60, Hsp70 and Hsp90] on development of MetS in patients with psoriasis vulgaris.

Methods: Fifty patients with psoriasis were enrolled; 25 had MetS. Twenty-five healthy people and 25 people with only MetS were included as a control group. Serum fasting blood glucose, urea, creatinine, total cholesterol, high-density lipoprotein cholesterol, low-density lipoprotein cholesterol, triglycerides, thyroid-stimulating hormone, fraction of thyroxine, fasting insulin and highly sensitive C-reactive protein levels were measured. Expression of BAX, cytC, CASP3, Bcl-2, survivin, CCND1, SOD, CAT, GS, and Hsp27, Hsp60, Hsp70 and Hsp90 were measured in peripheral blood. Clinical activation of patients with psoriasis was calculated using Psoriasis Area and Severity Index scores.

Results: In patients with MetS there was an increase in expression of genes for cytC, survivin and Hsp27, Hsp60 and Hsp90, and a decrease in expression of CCND1. Furthermore, expression levels of CCND1 were identified to be an independent risk factor for MetS development in patients with psoriasis.

Conclusions: The increase in expression of survivin and Hsp27, Hsp60 and Hsp90, and the decrease in CCND1 expression may be important mechanisms in the development of MetS in patients with psoriasis.

A NOVEL DELETION INVOLVING GNAS EXON 1 CAUSES PHP1A AND FURTHER REFINES THE REGION REQUIRED FOR NORMAL METHYLATION AT EXON A/B.

Reyes M[1], Karaca A[2], Bastepe M[1], Gulcelik NE[2], Jüppner H[3].

Bone. 2017 Oct;103:281-286. doi: 10.1016/j.bone.2017.07.013. Epub 2017 Jul 12.

GNAS exons 1-13 encode the biallelically expressed alpha-subunit of the stimulatory G protein (Gαs). Additional transcripts derived from this locus use alternative first exons that undergo parent-specific methylation, thus allowing transcription only from the non-modified allele. Pseudohypoparathyroidism type Ia (PHP1A) is characterized by Albright's Hereditary Osteodystrophy (AHO) and resistance to multiple hormones; this disorder is caused by maternal inactivating mutations involving Gαs exons. In contrast, pseudohypoparathyroidism type Ib (PHP1B) is characterized mostly by resistance to PTH and often mild TSH resistance, usually without AHO features. The autosomal dominant variant of PHP1B (AD-PHP1B) is caused by maternal deletions in GNAS or STX16 that reduce Gαs expression through loss-of-methylation at GNAS exon A/B alone or at multiple differentially methylated regions (DMR). Several large maternal deletions involve not only GNAS exons 1-13, but also one or several GNAS DMRs, thus causing PHP1A combined with apparent GNAS epigenetic changes that are indistinguishable from those observed in PHP1B. Some of these deletions include a large CpG island extending from exon A/B to the intron between GNAS exons 1 and 2, but there is no evidence for parent-specific exon 1 methylation. We now describe a family in which

the female proband and her daughter presented with hypocalcemia, elevated PTH levels, shortened metacarpals, and obesity, but without obvious neurocognitive abnormalities. A maternally inherited 2015-bp deletion that includes GNAS exon 1 was identified thereby establishing the diagnosis of PHP1A. The centromeric deletion breakpoint is located 178bp upstream of exon 1, yet no methylation changes were observed at exon A/B. This novel deletion therefore refines further the region between exon A/B and exon 1 that is critical for establishing or maintaining normal methylation at GNAS exon A/B.

SHOULD MULTIFOCAL PAPILLARY THYROID CARCINOMAS CLASSIFIED AS T1A WITH A TUMOR DIAMETER SUM OF 1 TO 2 CENTIMETERS BE RECLASSIFIED AS T1B?

Tam AA, Ozdemir D, Ogmen BE, Fakı S, Dumlu EG, Yazgan AK, Ersoy R, Cakır B.
Endocr Pract. 2017 May;23(5):526-535. doi: 10.4158/EP161488.OR. Epub 2017 Feb 3.

Objective: Considering the diameter of the largest tumor while determining T stage in multifocal papillary thyroid microcarcinomas (PTMCs) might cause underestimation of tumoral stage. We aimed to investigate the effect of total tumor diameter (TTD) on tumor node metastasis (TNM) classification in multifocal T1a PTMCs.

Methods: T1 tumors were grouped as T1a or T1b according to 7th TNM edition. For patients with multifocal T1a, TTD (the sum of the maximal diameter of each focus) was calculated, and these patients were further subgrouped as TTD ≤1 cm or TTD 1 to 2 cm.

Results: There were 724 patients with T1 tumors. Multifocality was observed in 150 (28.5%) of 527 patients with T1a and 84 (42.6%) of 197 patients with T1b tumors (P<.001). Lymph node metastasis (LNM), thyroid capsule invasion, and lymphovascular invasion were significantly higher in T1b compared to T1a (P<.001, P<.001, and P = .015, respectively). There were 8 (1.5%) patients with persistence but not any with recurrence in the T1a group. Persistence and recurrence were observed in 3 (1.5%) and 5 (2.5%) patients in the T1b group, respectively. Among 150 T1a patients with multifocal tumors, TTD was ≤1 cm in 89 (59.3%) and 1 to 2 cm in 61 (40.7%) patients. Number of tumor foci, LNM, and thyroid capsule invasion were significantly higher in multifocal T1a patients with TTD 1 to 2 cm compared to with TTD ≤1 cm (P<.001, P = .032, P = .014, respectively).

Conclusion: TTD might be used as a parameter to determine patients at higher risk for persistence, and T1a multifocal PTMCs with TTD 1 to 2 cm can be reclassified as T1b.

Abbreviations: ETE = extrathyroidal extension LNM = lymph node metastasis PTC = papillary thyroid carcinoma PTMC = papillary thyroid microcarcinoma RAI = radioactive iodine TNM = tumor, node, metastasis TTD = total tumor diameter.

CLASSICAL AND NON-CLASSICAL CAUSES OF GH DEFICIENCY IN ADULTS.

Tanriverdi F[1], Kelestimur F[2].
Best Pract Res Clin Endocrinol Metab. 2017 Feb;31(1):3-11. doi: 10.1016/j.beem.2017.02.001. Epub 2017 Feb 23.

Growth hormone deficiency (GHD) can develop due to a variety of conditions, and may occur either as isolated or multiple pituitary hormone deficiencies. It has been previously demonstrated that GH is one of the most frequent hormonal deficiencies in adult patients with hypopituitarism. The most frequent classical causes of adult-onset GHD (AO-GHD) are pituitary adenomas and/or their treatment. However, during the last decade an increasing number of studies from different parts of the world have revealed that non-tumoural causes of hypopituitarism are more common than previously known. Therefore, in this review our aim is to briefly summarize the classical and non-classical acquired causes of GHD in adults.

GDF-15 AND HEPCIDIN LEVELS IN NONANEMIC PATIENTS WITH IMPAIRED GLUCOSE TOLERANCE.

Yalcin MM[1], Altinova AE[1], Akturk M[1], Gulbahar O[2], Arslan E[1], Ors Sendogan D[3], Yetkin I[1], Toruner FB[1].
J Diabetes Res. 2016;2016:1240843. doi: 10.1155/2016/1240843. Epub 2016 Aug 25.

Aims. Growth Differentiation Factor-15 (GDF-15) has been suggested as one of the regulators of hepcidin, an important regulatory peptide for iron deposition. Current data is conflicting about the relationship between hepcidin and disorders of glucose metabolism. We aimed to investigate serum hepcidin and GDF-15 concentrations and their associations with each other, in nonanemic subjects with impaired glucose tolerance (IGT) in comparison with the nonanemic subjects with normal glucose tolerance (NGT). Methods. Thirty-seven subjects with IGT and 32 control subjects with NGT, who were age-, gender-, and body mass index-(BMI-) matched, were included in the study. Results. Serum GDF-15 levels were significantly higher in IGT compared to NGT. There were no differences in hepcidin, interleukin-6, and high sensitive C-reactive protein levels between the groups. We found a positive correlation between GDF-15 and hepcidin levels. There were also positive correlations between GDF-15 and age, uric acid, creatinine, and area under the curve for glucose (AUC-G). Hepcidin was correlated positively with ferritin levels. In the multiple regression analysis, GDF-15 concentrations were independently associated with age, uric acid, and AUC-G. Conclusions. Impaired glucose tolerance is associated with increased GDF-15 levels even in the absence of anemia, but the levels of hepcidin are not significantly altered in prediabetic state.

UTILITY OF BASELINE SERUM PHOSPHORUS LEVELS FOR PREDICTING REMISSION IN ACROMEGALY PATIENTS.

Yalin GY[1], Tanrikulu S[2], Gul N[2], Uzum AK[2], Aral F[2], Tanakol R[2].
J Endocrinol Invest. 2017 Aug;40(8):867-874. doi: 10.1007/s40618-017-0657-3. Epub 2017 Mar 29.

Purpose: High GH and IGF I levels increase tubular phosphate reabsorption in patients with acromegaly. We aimed to investigate the utility of serum phosphorus levels as an indicator for predicting chance of remission in acromegaly patients.

Design: Fifty-one patients (n: 51; F: 24, M: 27) with diagnosis of acromegaly were included in the study. Plasma IGF-1, Phosphorus (P) and nadir GH levels on oral glucose tolerance test (OGTT) at the time of diagnosis were analysed retrospectively. Patients were classified into two groups according to their plasma P levels; P ≤ 4.5 mg/dl (Group-1, n: 23, 45.1%), P > 4.5 mg/dl (Group-2, n: 28, 54.9%). Two groups were compared according to remission status; remission (n: 27) and non-remission (n: 24). Remission was defined with absence of clinical symptoms, normal plasma IGF-1 (adjusted for age and gender) and GH levels (<1 mcg/dl) at least 3 months after initial treatment.

Results: Serum P levels decreased significantly after treatment in both groups (p < 0.001). There was a significant correlation between baseline phosphorus levels and remission rates, nadir GH in OGTT, pituitary adenoma size and Ki-67 scores (p = 0.001, r: -0.51; p = 0.01, r: 0.44; p = 0.001, r: 0.52; p = 0.02, r: 0.71, respectively). Mean baseline P levels were significantly higher in patients with non-remission (4.8 vs 4.2, P < 0.001). Logistic regression analysis did not reveal an independent effect on remission with any of these risk factors.

Conclusion: High serum P levels may be an indicator for a low likelihood of onset of remission in acromegaly patients. Further studies with wider spectrum are needed to make specific suggestions.

ÜYELERİMİZDEN HABERLER

Literatürde PKOS ile Obstrüktif Uyku Apnesi ilişkisini değerlendiren ilk meta-analiz olma özelliğini taşıyan ve *Avrupa Endokrinoloji Derneği*'nin *Endocrine Connections* isimli dergisinde yeni yayınlanan '***Polycystic ovary syndrome and the risk of obstructive sleep apnea: a meta-analysis and review of the literature"*** adlı makale ile ilgili **Prof. Dr. Bülent Okan Yıldız** ile yaptıkları ve derginin haber olarak paylaştığı röportaj aşağıdadır.

Prof. Dr. Bülent Okan Yıldız'ı tebrik eder, başarılarının devamını dileriz.

POLYCYSTIC OVARY SYNDROME & SLEEP APNEA - RESEARCH BY ESE TREASURER

Professor Bulent Yildiz, M.D.

We spoke to European Society of Endocrinology (ESE) treasurer Professor Bulent Yildiz, M.D. from Hacettepe University School of Medicine, Turkey regarding his recent free publication in Endocrine Connections entitled 'Polycystic ovary syndrome and the risk of obstructive sleep apnea: a meta-analysis and review of the literature'. Endocrine Connections 2017 6:437-445 doi: 10.1530/EC-17-0129.

"Polycystic Ovary Syndrome (PCOS) is a very common endocrine disorder affecting up to 1 in 7 women. Patients present initially with androgen excess (hirsutism, acne, alopecia), irregular menses and infertility but this is a lifelong syndrome associated with obesity, type 2 diabetes, dyslipidemia and potentially cardiovascular disease. A growing body of literature suggests that PCOS might also be associated with obstructive sleep apnea (OSA) which itself is known to contribute to the development of cardiovascular disease and diabetes. The purpose of this meta-analysis was to examine the relation between PCOS and OSA. It is important to know whether OSA is more common in PCOS considering both disorders are associated with cardiometabolic disease.

We have identified eight studies conducted in adults and five studies conducted in adolescents. The pooled prevalence of OSA was 22% (32% in adults and 8% in adolescents). Risk of OSA was increased 10-fold in adult patients with PCOS (OR:9.74, 95% CI: 2.76-34.41) whereas adolescents did not show a significantly increased risk for OSA (OR:4.54, 95% CI: 0.56-36.43).

Adult patients with PCOS need to have a high suspicion of OSA particularly if they snore and feel tired or sleepy during daytime. It would be helpful to tell their doctors about these symptoms. Considering the fact that successful treatment of OSA improves cardiometabolic function, it is important to diagnose OSA in adult patients with PCOS who already face a lifelong risk of diabetes and cardiovascular disease.

In order to confirm findings of the current meta-analysis, further studies focusing on community-based cohorts, and free from clinical referral bias, would be useful to determine whether PCOS is an independent risk factor for OSA. Longitudinal studies, ideally with a large number of cases and controls, are needed to determine when OSA develops and which factors are involved in pathogenesis of OSA in patients with PCOS."

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