

TÜRKİYE ENDOKRİNOLOJİ VE METABOLİZMA DERNEĞİ BÜLTENİ



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Sayı 61 • Ocak – Şubat – Mart - 2018

7. Adrenal Gonad Sempozyumu

7. Adrenal Gonad Sempozyumu, 23-24 Şubat 2018 tarihlerinde İstanbul Bilim Üniversitesi, Florence Nightingale Hastanesi'nde, 130 meslektaşımızın katılımı ile başarılı bir şekilde tamamlanmıştır.

Emeği geçen tüm üyelerimize teşekkür eder, saygılarımızı sunarız.



A'dan Z'ye Diyabet Klinik Araştırmalar Eğitimi

A'dan Z'ye Diyabet Klinik Araştırmalar Eğitimi, 17-18 Şubat 2018 tarihlerinde İzmir'de 75 meslektaşımızın katılımı ile başarılı bir şekilde tamamlanmıştır.

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ENDOKRİN ACİLLER KURSU

Endokrin Aciller Kursu, 20 Ocak 2018 tarihinde Akra Barut Hotel, Antalya'da ve 24 Şubat 2018 tarihinde Zorlu Grand Hotel, Trabzon'da meslektaşımızın katılımı ile başarılı şekilde tamamlanmıştır.

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TİROİDOLOJİ KURSU

Tiroidoloji Kursu - TİROKURS 21", 31 Mart 2018 tarihinde Trabzon'da 80 meslektaşımızın katılımı ile başarılı bir şekilde tamamlanmıştır.

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KALITSAL METABOLİZMA HASTALIKLARI KURSU

Derneğimiz Nadir Hastalıklar Çalışma Grubu tarafından "Hiçbir hastalık sahipsiz, hiçbir hasta tanısız kalmasın" konseptiyle başlattığı bölgesel Erişkin Kalıtsal Metabolizma Hastalıkları kursunun ilki 24 Mart 2018'de Ankara'da başarıyla gerçekleştirildi. Erişkin kliniklerinde rastlanan nadir metabolizma hastalıklarının gözden geçirildiği kurs kapsamında 80 meslektaşımızın, konuya olan ilgi ve hakimiyetlerinin arttığı görüldü.

Emeği geçen tüm üyelerimize teşekkür eder, saygılarımızı sunarız.



16. HİPERTANSİYON EĞİTİM KURSU

TEMD Obezite, Lipid Metabolizması, Hipertansiyon Çalışma Grubu 16. Hipertansiyon Eğitim Kursu, 31 Mart - 01 Nisan 2018 tarihlerinde Hilton Garden Inn Hotel, Çorlu'da 70 meslektaşımızın katılımı ile başarılı bir şekilde tamamlanmıştır.

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40

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Üyelerimizden Literatür Seçmeleri

THE 2016 EUROPEAN THYROID ASSOCIATION/EUROPEAN GROUP ON GRAVES' ORBITOPATHY GUIDELINES FOR THE MANAGEMENT OF GRAVES' ORBITOPATHY.

Bartalena L¹, Baldeschi L², Boboridis K³, Eckstein A⁴, Kahaly GJ⁵, Marcocci C⁶, Perros P⁷, Salvi M⁸, Wiersinga WM⁹; European Group on Graves' Orbitopathy (EUGOGO). Adamidou F, Anagnostis P, Ayvaz G, Azzolini C, Boschi A, Bournaud C, Clarke L, Currò N, Daumerie C, Dayan C, Fuhrer D, Konuk O, Marinò M, Morris D, Nardi M, Pearce S, Pitz S, Rudovsky G, Vannucchi G, Vardanian C, von Arx G. *Eur Thyroid J.* 2016 Mar;5(1):9-26. doi: 10.1159/000443828. Epub 2016 Mar 2.

Graves' orbitopathy (GO) is the main extrathyroidal manifestation of Graves' disease, though severe forms are rare. Management of GO is often suboptimal, largely because available treatments do not target pathogenic mechanisms of the disease. Treatment should rely on a thorough assessment of the activity and severity of GO and its impact on the patient's quality of life. Local measures (artificial tears, ointments and dark glasses) and control of risk factors for progression (smoking and thyroid dysfunction) are recommended for all patients. In mild GO, a watchful strategy is usually sufficient, but a 6-month course of selenium supplementation is effective in improving mild manifestations and preventing progression to more severe forms. High-dose glucocorticoids (GCs), preferably via the intravenous route, are the first line of treatment for moderate-to-severe and active GO. The optimal cumulative dose appears to be 4.5-5 g of methylprednisolone, but higher doses (up to 8 g) can be used for more severe forms. Shared decision-making is recommended for selecting second-line treatments, including a second course of intravenous GCs, oral GCs combined with orbital radiotherapy or cyclosporine, rituximab or watchful waiting. Rehabilitative treatment (orbital decompression surgery, squint surgery or eyelid surgery) is needed in the majority of patients when GO has been conservatively managed and inactivated by immunosuppressive treatment.

Keywords: Cyclosporine; Eyelid surgery; Glucocorticoids; Graves' orbitopathy; Orbital decompression; Orbital radiotherapy; Rituximab; Selenium; Squint surgery

IS ULTRASONOGRAPHICALLY DETECTED NODULE DIAMETER CONCORDANT WITH PATHOLOGICAL TUMOR SIZE?

Bilginer MC¹, Ozdemir D², Baser H³, Dogan HT⁴, Yalcin A⁵, Ersoy R², Cakir B². *Int J Surg.* 2017 Jun;42:95-102. doi: 10.1016/j.ijsu.2017.04.054. Epub 2017 Apr 29.

INTRODUCTION: We aimed to compare preoperative ultrasonographical and postoperative histopathological diameters of differentiated thyroid cancer (DTC) lesions and investigate possible factors that can predict the discordance between two measurements.

METHODS: Data of patients with histopathologically confirmed DTC were reviewed retrospectively. Nodules evaluated by preoperative US were matched with histopathologically examined nodules. Incidental tumors and nodules that can not be matched in US and histopathology reports were excluded. Preoperative US diameter and postoperative histopathological size were compared and percentage difference between two measurements was calculated for each lesion.

RESULTS: There were 607 DTC foci in 562 patients. Mean US diameter was significantly higher than histopathological diameter (21.0 ± 15.6 mm vs 17.3 ± 13.6 , $p < 0.001$). US diameter was higher than tumor size in 444 (73.1%), equal in 15 (2.5%) and lower in 148 (24.4%) nodules. Marginal irregularity was observed in 253 (57%) lesions with US diameter > tumor size and 108 (73%) lesions with US diameter < tumor size ($p = 0.010$). Rate of nodules with peripheral halo was higher in lesions with US diameter > tumor size (30.6% vs 20.3%, $p = 0.015$). In nodules with US diameter > tumor size, percentage difference was lower in nodules with microcalcification ($p = 0.020$) and higher in cytologically benign nodules ($p < 0.001$). Among nodules with US diameter < tumor size, <1 cm nodules had significantly higher percentage difference compared to 1-1.9, 2-3.9 and ≥ 4 cm nodules ($p = 0.005$).

CONCLUSION: Ultrasonographically determined diameter is higher than histopathologically determined size in a considerable ratio of DTCs. It might be helpful to consider this discordance while deciding surgical extent in these patients.

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Keywords: Differentiated thyroid cancer; Percentage difference; Tumor size; Ultrasonography diameter

THE EFFECTS OF HOME BLOOD PRESSURE MONITORING ON BLOOD PRESSURE CONTROL AND TREATMENT PLANNING.

Erden S¹, Mefkure Ozkaya H², Banu Denizeri S³, Karabacak E⁴.

Postgrad Med. 2016 Aug;128(6):584-90. doi: 10.1080/00325481.2016.1189303. Epub 2016 May 30.

OBJECTIVES: Blood pressure monitoring is essential in hypertension, which is an important public health issue. Our objective was to compare the rates of blood pressure control and to investigate factors that affect blood pressure control in patients with hypertension.

METHODS: The records of 1006 patients with hypertension were examined retrospectively. The blood pressure control rates of the 394 patients who measured their blood pressure at home (group 1) and those who did not (group 2) were compared.

RESULTS: In group 1, the mean systolic and diastolic blood pressure was $123.91 \pm 12.63/78.64 \pm 8.92$ mmHg measured at home, whereas it was $140.31 \pm 20.56/85.76 \pm 11.55$ mmHg in the office setting ($p < 0.0001$). In the total group ($N=1006$), the blood pressure control achievement rate was 56.1%. The number of cardiovascular events, hypertension duration, and the rate of being employed was higher in group 1 ($p < 0.0001$, $p < 0.0001$ and $p = 0.0001$, respectively), while heart rate and grade 3-4 retinopathy was lower in group 1 ($p < 0.0001$ for both). Occupational status, geographical origin, BMI and the use of angiotensin converting enzyme (ACE) inhibitors were found to be the determinants of office BP control ($p < 0.05$, $p < 0.05$, $p = 0.001$ and $p < 0.05$, respectively), and BMI and grade 3-4 retinopathy findings were found to be the determinants of home BP control ($p < 0.05$ for both).

CONCLUSION: Home blood pressure monitoring is useful in preventing complications and achieving therapy compliance and is essential in diagnosis and treatment planning of hypertension.

Keywords: Blood pressure; home monitoring; hypertension

GENERAL HEALTH STATUS AND INTELLIGENCE SCORES OF CHILDREN OF MOTHERS WITH ACROMEGALY DO NOT DIFFER FROM THOSE OF HEALTHY MOTHERS.

Haliloglu O1, Dogangun B2, Ozcabi B3, Kural HU2, Keskin FE1, Ozkaya HM1, Pamukcu FC2, Bektas E2, Poyraz BC4, Buber H1, Evliyaoglu O3, Kadioglu P5,6.

Pituitary. 2016 Aug;19(4):391-8. doi: 10.1007/s11102-016-0717-2.

PURPOSE: To determine the physical status and intelligence scores of children of acromegalic mothers and to compare them with those of children from mothers without acromegaly.

METHODS: Six women with acromegaly who became pregnant under follow-up between 2010 and 2014 and their 16 children (group A) were assessed and compared with 16 children of healthy women (group B) and 15 children of women with prolactinoma (group C). The physical examinations of children were performed by the department of pediatric endocrinology and intelligence quotient (IQ) testing was undertaken by adult and pediatric psychiatry departments, using appropriate scales for their ages.

RESULTS: Six of the 16 children (girls/boys: 7/9) were born after the diagnosis of acromegaly. Five of the 6 pregnancies occurred when the patients were taking somatostatin analogs, none continued taking the drugs during pregnancy. The mean IQ of groups A, B, and C were 106.4 ± 12.5 , 105.3 ± 12.5 , and 103.2 ± 16.1 respectively ($p > 0.05$). The mean ages, birth percentiles, recent weight and height standard deviation scores were similar between groups ($p > 0.05$). Two siblings from group A and 1 child from group B were large for gestational age at birth. At recent follow-up, two children from group A were found tall for their age and one from group C was short for his age and was placed under the care of pediatric endocrinology clinic.

CONCLUSIONS: Pregnancies in acromegaly seems to be uneventful and the general health status and IQ scores of children from women with and without acromegaly were found similar.

Keywords: Acromegaly; Children; Intelligence quotient; Pregnancy

OUTCOMES OF PRIMARY TRANSSPHEOIDAL SURGERY IN CUSHING DISEASE: EXPERIENCE OF A TERTIARY CENTER.

Keskin FE¹, Ozkaya HM¹, Bolayirli M², Erden S³, Kadioglu P⁴, Tanriover N⁵, Gazioglu N⁶.

World Neurosurg. 2017 Oct;106:374-381. doi: 10.1016/j.wneu.2017.07.014. Epub 2017 Jul 13.

BACKGROUND: To report the initial and long-term remission rates and related factors, secondary treatments, and outcomes of a series of patients with Cushing disease (CD).

METHODS: We included 147 consecutive adult patients with CD who underwent primary transsphenoidal surgery (TSS) between 1998 and 2014 in this study. Eighty-two were followed up in the Cerrahpasa Medical Faculty Endocrinology and Metabolism outpatient clinic. Patients were requested to attend a long-term remission assessment; 55 could be contacted, and data for the remaining 27 patients' last visit to the outpatient clinics were reviewed for early and late remission. Six patients were excluded from the study. Magnetic resonance imaging (MRI) findings and pathologic results including mitosis, Ki-67 levels, and P53 in immunostaining of all patients were evaluated.

RESULTS: Data of 82 patients with CD with an average age of 36 years [interquartile range: 29-47] were analyzed with a mean follow-up of 7.5 years [interquartile range: 5-10]. Overall initial remission rates were 72.3% after TSS. Among the 82 patients, 16 patients had Gamma Knife radiosurgery and 7 patients underwent adrenalectomy. After these additional treatments, the long-term remission rate was found as 69.7%. The highest remission rates were with microadenomas. Recurrence was most frequently seen in patients without tumor evidence on MRI. Patients with high Ki-67 levels had higher recurrence rates in long-term follow-up (P = 0.02).

CONCLUSION: Life-long follow-up for patients with CD seems essential. Undetectable tumors on MRI before TSS and high Ki-67 immunopositivity were found as risk factors for tumor recurrence.

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SCREENING FOR CELIAC DISEASE IN POORLY CONTROLLED TYPE 2 DIABETES MELLITUS: WORTH IT OR NOT?

Kizilgul M^{1,2}, Ozcelik O³, Beysel S³, Akinci H⁴, Kan S³, Ucan B³, Apaydin M³, Cakal E³.

BMC Endocr Disord. 2017 Oct 6;17(1):62. doi: 10.1186/s12902-017-0212-4.

BACKGROUND: Recent studies have demonstrated that immune factors might have a role in the pathophysiology of insulin resistance and type 2 diabetes mellitus (T2DM). Inappropriate glycemic control in patients with T2DM is an important risk factor for the occurrence of diabetes complications. The prevalence of celiac disease (CD) is high in type 1 diabetes mellitus however, there are scarce data about its prevalence in T2DM. Our aim was to investigate the prevalence of celiac disease among insulin-using type 2 diabetes patients with inappropriate glycemic control.

METHODS: IgA tissue transglutaminase antibodies (tTGA IgA) test was performed as a screening test. A total of 135 patients with T2DM whose control of glycemia is inappropriate (HbA1c value >7%) in spite of using insulin treatment for at least 3-months (only insulin or insulin with oral antidiabetic drugs) and 115 healthy controls were enrolled in the study. Upper gastrointestinal endoscopy with duodenal biopsy was performed to all patients with raised tTGA IgA or selective IgA deficiency.

RESULTS: Gender, age, body mass index (BMI) and tTGA IgA, kreatinin, calcium, LDL-cholesterol (LDL-C), total cholesterol, 25-OH vitamin D3 levels were similar between groups. Systolic and diastolic blood pressure, waist circumference, fasting plasma glucose, postprandial plasma glucose, urea, sodium, HbA1c, LDL-C, triglyceride, vitamin B12 levels were significantly higher in DM group (p < 0.0001). BMI, high-sensitive CRP, microalbuminuria, and AST, ALT, potassium, phosphorus levels were significantly higher in the T2DM group (p < 0.05). HDL-cholesterol and parathormone levels were significantly lower in the T2DM group (p < 0.05). Two of the 135 patients with T2DM were diagnosed with CD (1.45%).

CONCLUSIONS: The prevalence of celiac disease among patients with type 2 diabetes, with poor glycemic control despite insulin therapy, is slightly higher than the actual CD prevalence in general population. Type 2 diabetic patients with inappropriate control of glycemia in spite of insulin treatment might be additionally tested for Celiac disease especially if they have low C-peptide levels.

Keywords: Celiac disease; Tissue transglutaminase antibody; Type 2 diabetes mellitus

DIABETOGENIC EFFECTS OF OCHRATOXIN A IN FEMALE RATS.

Mor F¹, Sengul O², Topsakal S³, Kilic MA⁴, Ozmen O⁵.

Toxins (Basel). 2017 Apr 19;9(4). pii: E144. doi: 10.3390/toxins9040144.

In this study, the diabetogenic effects of long term Ochatoxin A (OTA) administration in rats were investigated, and its role in the etiology of diabetes mellitus (DM) was examined utilizing 42 female Wistar rats for these purposes. The rats were divided into three different study and control groups according to the duration of the OTA administration. The rats received 45 µg OTA daily in their feed for 6, 9 and 24 weeks, respectively. Three control groups were also used for the same time periods. Blood and pancreatic tissue samples were collected during the necropsy at the end of the 6, 9 and 24 weeks. The plasma values of insulin, glucagon and glucose were determined for the study and control groups. Pancreatic lesions were evaluated via histopathological examination and insulin and glucagon expression in these lesions was subsequently determined using immunohistochemical methods. Statistically significant decreases in insulin levels were observed, in contrast to increases in blood glucagon and glucose levels. Histopathological examinations revealed slight to moderate degeneration in Langerhans islet cells in all OTA-treated groups. Immunohistochemistry of pancreatic tissue revealed decreased insulin and increased glucagon expression. This study demonstrated that OTA may cause pancreatic damage in the Langerhans islet and predispose rats to DM.

Keywords: Ochatoxin A; glucagon; glucose; immunohistochemistry; insulin; pathology; rat plasma

MULTIDISCIPLINARY APPROACH FOR ACROMEGALY: A SINGLE TERTIARY CENTER'S EXPERIENCE.

Haliloglu O¹, Kuruoglu E², Ozkaya HM¹, Keskin FE¹, Gunaldi O², Oz B³, Gazioglu N², Kadioglu P¹, Tanriover N⁴.

World Neurosurg. 2016 Apr;88:270-6. doi: 10.1016/j.wneu.2015.12.092. Epub 2016 Jan 12.

BACKGROUND: Acromegaly is a multisystemic disease that requires a multidisciplinary approach. The aim of this study was to determine early and late remissions of patients who underwent surgery at our center and to evaluate relations between pathologic and radiologic properties of adenoma and medical and radiosurgical treatments with remissions.

METHODS: The medical records of 103 patients with acromegaly who underwent endoscopic endonasal transsphenoidal surgery in Cerrahpasa Medical Faculty, Istanbul University, between 2007 and 2014 were reviewed. Clinical, biochemical, radiologic, and pathologic properties were determined.

RESULTS: The total median follow-up time was 38 months [interquartile range: 24-53.5 months]. Thirty-two percent of the adenomas were microadenomas and 68% were macroadenomas. The early remission rate was 51.5% and late remission was 75.2%. The sellar floor invasion was significantly lower in patients with early and late remissions (P = 0.01 and P = 0.009, respectively). The initial growth hormone (GH; P < 0.001), first-day GH (P = 0.03), 3-month GH (P = 0.001), insulin-like growth factor-1 (P = 0.004), and 6-month insulin-like growth factor-1 (P = 0.02) levels were significantly greater in patients with sellar floor invasion. The late remission rates (P = 0.004) were greater and reoperation needs (P = 0.05) were lower in patients with Ki-67 <3% than in patients with ≥3%. Seventy (68.6%) patients needed medical therapy during follow-up.

CONCLUSIONS: Late remission was achieved using a multidisciplinary approach in 75.2% of 103 patients with acromegaly, and young age, male sex, high Ki-67 and mitosis indices, and cavernous sinus and sellar-floor invasion had negative effects on clinical and biochemical control of the disease.

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Keywords: Acromegaly; Early remission; Late remission; Proliferation indices

DAILY LIFE REFLECTIONS OF ACROMEGALY GUIDELINES.

Apaydin T¹, Ozkaya HM², Keskin FE², Haliloglu OA², Karababa K², Erdem S³, Kadioglu P^{4,5}.

J Endocrinol Invest. 2017 Mar;40(3):323-330. doi: 10.1007/s40618-016-0567-9. Epub 2016 Oct 20.

PURPOSE: To determine the differences in acromegaly diagnosis, treatment, and follow-up among Turkish endocrinologists, and to investigate how the published guidelines are applied in clinical practice.

METHODS: The questionnaire was formatted as an electronic survey, conducted between November and December 2015, and sent weekly for 6 weeks via e-mail to 528 endocrinologists in Turkey.

RESULTS: The questionnaire was answered by 37.4 % of endocrinologists. Insulin-like growth factor-1 and nadir growth hormone level after 75 g oral glucose tolerance test (nadir GH-OGTT) were the most commonly preferred methods for the initial diagnosis. A total of 49.5 % of the participants reported using preoperative medical therapy (MT) either routinely or on a case-to-case basis. Somatostatin analogs were the most commonly used drugs, both in pre- and postoperative MT. Disease activity following surgery was assessed in the 3rd postoperative month using IGF-1 levels. Similarly, IGF-1 monitoring was preferred in the follow-up period. Monitoring nadir GH-OGTT levels was the most commonly used method in the assessment of discordant test results. The dose titration was done at month 3 after the start of MT. Resistance to SRLs was considered after using the maximal dose for at least 6 months. Pegvisomant was generally used in second- and third-line therapy. Similarly, cabergoline was not preferred in monotherapy by the majority of participants. Radiotherapy was considered in patients with incomplete response to surgery and medical treatments.

CONCLUSIONS: Although there were subtle differences, clinical practice guidelines were usually followed among Turkish endocrinologists.

Keywords: Acromegaly; Daily life practice; Growth hormone; Insulin-like growth factor 1; Questionnaire

LOCALLY PRODUCED ESTROGEN THROUGH AROMATIZATION MIGHT ENHANCE TISSUE EXPRESSION OF PITUITARY TUMOR TRANSFORMING GENE AND FIBROBLAST GROWTH FACTOR 2 IN GROWTH HORMONE-SECRETING ADENOMAS.

Ozkaya HM¹, Comunoglu N², Keskin FE¹, Oz B², Haliloglu OA¹, Tanriover N³, Gazioglu N³, Kadioglu P⁴.

Endocrine. 2016 Jun;52(3):632-40. doi: 10.1007/s12020-015-0802-8. Epub 2015 Nov 17.

Aromatase, a key enzyme in local estrogen synthesis, is expressed in different pituitary tumors including growth hormone (GH)-secreting adenomas. We aimed to evaluate aromatase, estrogen receptor α (ER α), estrogen receptor β (ER β), pituitary tumor transforming gene (PTTG), and fibroblast growth factor 2 (FGF2) expressions in GH-secreting adenomas, and investigate their correlation with clinical, pathologic, and radiologic parameters. This cross-sectional study was conducted in a tertiary center in Turkey. Protein expressions were determined via immunohistochemical staining in ex vivo tumor samples of 62 patients with acromegaly and ten normal pituitary tissues. Concordantly increased aromatase, PTTG, and FGF2 expressions were detected in the tumor samples as compared with controls ($p < 0.001$ for all). None of the tumors expressed ER α while ER β was detected only in mixed somatotroph adenomas. Aromatase, ER β , PTTG expressions were not significantly different between patients with and without remission ($p > 0.05$ for all). FGF2 expression was significantly higher in patients without postoperative and late remission ($p = 0.002$ and $p = 0.012$, respectively), with sphenoid bone invasion, optic chiasm compression, and somatostatin analog resistance ($p = 0.005$, $p = 0.033$, and $p = 0.013$, respectively). Aromatase, PTTG and FGF2 expressions were positively correlated with each other ($r = 0.311$, $p = 0.008$ for aromatase, FGF2; $r = 0.380$, $p = 0.001$ for aromatase, PTTG; $r = 0.400$, $p = 0.001$ for FGF2, PTTG). PTTG-mediated FGF2 upregulation is associated with more aggressive tumor features in patients with acromegaly. Also, locally produced estrogen through aromatization might have a role in this phenomenon.

Keywords: Acromegaly; Aromatase; Estrogen; FGF2; PTTG protein

LATE-NIGHT SALIVARY CORTISOL IS UNALTERED IN PATIENTS WITH POLYCYSTIC OVARIAN SYNDROME (PCOS), IRRESPECTIVE OF DISEASE PHENOTYPE, AND IN OBESE WOMEN, IRRESPECTIVE OF THE PRESENCE OF PCOS.

Ozkaya HM, Keskin FE, Tuten A, Korkmaz E, Oktay HZ, Kadioglu P.

Endocr Pract. 2017 Sep;23(9):1045-1052. doi: 10.4158/EP171887.OR. Epub 2017 Jul 6.

OBJECTIVE: To determine cutoff values of late-night salivary cortisol (LNSC) using an electrochemiluminescent immunoassay and investigate whether the diagnostic performance of the assay is influenced by the presence of obesity or polycystic ovary syndrome (PCOS).

METHODS: A total of 124 subjects comprising 25 patients with Cushing syndrome (CS), 44 with PCOS (22 nonobese and 22 obese), 21 with constitutional obesity (CO), and 34 healthy subjects (HS) were included in the study. Two consecutive LNSC samples were collected from all participants.

RESULTS: The median LNSC levels of patients with CS were significantly higher than LNSC levels of HS, patients with CO, and obese and nonobese patients with PCOS, respectively ($P < .01$ for all). Healthy subjects, patients with CO, and obese and nonobese patients with PCOS did not differ in terms of median LNSC levels ($P > .05$ for all). The cutoff values and corresponding sensitivity and specificity were similar between the groups. The comparisons of the area under curve of the first LNSC (0.963; 95% confidence interval [CI], 0.910 to 0.989), second LNSC (0.954; 95% CI, 0.898 to 0.984), and the mean of two consecutive LNSC (mLNSC) values (0.962; 95% CI, 0.909 to 0.989) did not differ significantly ($P > .05$ for all). A cutoff value for mLNSC of 7.45 nmol/L yielded a sensitivity of 100% and specificity of 87.5% in HS.

CONCLUSION: In conclusion, LNSC is a reliable test with high diagnostic accuracy in both HS and patients with PCOS and obesity.

ABBREVIATIONS: ACTH = adrenocorticotrophic hormone AUC = area under the curve BMI = body mass index CO = constitutional obesity CS = Cushing syndrome E2 = estradiol ECLIA = electrochemiluminescent immunoassay FPG = fasting plasma glucose FSH = follicle-stimulating hormone HOMA-IR = homeostasis model assessment of insulin resistance HPA = hypothalamo-pituitary-adrenal HS = healthy subjects IQR = interquartile range LH = luteinizing hormone LNSC = late-night salivary cortisol LR = likelihood ratio mLNSC = mean of two consecutive LNSC samples PCOS = polycystic ovarian syndrome ROC = receiver operating characteristic UFC = urinary free cortisol WHR = waist-to-hip ratio.

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