

TÜRKİYE ENDOKRİNOLOJİ VE METABOLİZMA DERNEĞİ BÜLTENİ



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Sayı 51 • Temmuz – Ağustos – Eylül - 2015

“
2015'in
Genç Araştırmacısı ”



Yrd. Doç. Dr. Uğur Ünlütürk

Konuşma özeti

Tiroidolojide elastografi kullanımı

Tiroid ultrasonunun endokrinologlar tarafından klinik pratikte uygulanması önerisi hem Avrupa hem de Amerikan menseili bilimsel örgütler tarafından 2000'li yıllarda tavsiye edilmeye başlanmıştır. Bu önerilerden çok daha önce, 1995 yılında Ankara Tıp Fakültesi Endokrinoloji Bilim Dalı bünyesinde tiroid ultrason uygulamaları başlamıştır.

Görüntüleme yöntemlerinde yaşanan hızlı teknolojik gelişmeler ve bu yöntemlere kolay ulaşılabilirlik beraberinde klinik tanıda sağladığı büyük yararlar yanı sıra, klinisyenleri giderek artan sıklıkta endokrin bezlerin insidental saptanan lezyonları ile baş etmek zorunda bırakmaktadır. Tiroid nodülleri bunlar içinde en sık görülenidir. Tiroid nodüllerinin değerlendirilmesinde en önemli klinik nokta bu nodüllerin malign olup olmadığı ortaya konulmasıdır. Bu amaçla var olan invaziv olmayan yöntemlerden en hassası, nodülün ultrasonografik özelliklerinin değerlendirilmesidir. Ancak malign lezyonları ayırt etmede ultrasonografi yardımcı olsa da tanı için yeterli güce sahip değildir. Halen en etkin yöntem olarak ince igne aspirasyon biopsi ve sitolojik inceleme (İİABS) kullanılmaktadır.

Hızla artan oranda tiroid insidentelomalarının saptanması, İİABS işlemlerinin artmasına, buna mukabil olarak da artan

oranda morbidite ve maliyete neden olmaktadır. Bu anlamda halen İİABS ihtiyacını azaltarak insidentelomalar kaynaklı morbidite, mortalite ve maliyet azaltıcı invaziv olmayan tanısal yöntem/teknolojiye ihtiyaç vardır.

Öte yandan teknolojide her ilerleme sağlandığında tiroid malign benign lezyonları ayırma konusunda bilim insanların merakı da alevlemiştir. Bu alevli ilginin getirdiği ilk çalışmaların sonuçları, yetersiz örneklem ve uygunsuz çalışma dizaynları nedeni ile tiroid ultrason özellikleri için yüksek duyarlılık ve özgürlük verirken, takiben çıkan geniş ölçekli çalışmalar bu sonuçları bütünüyle desteklememiştir.

Sert tiroid nodüllerinin malign olma ihtimali çok daha yüksektir. Sert lezyonları invaziv olmayan yolla tahmin eden ultrason elastografinin (ES) malign tiroid nodüllerini saptama gücü de bir çok çalışmada incelenmiştir. İlk çalışmalar ve takiben yayınlanan ilk metaanaliz verileri bu tekniğin malign nodülleri saptamada gücünün göreceli olarak oldukça yüksek olduğunu gösteriyordu. Ancak bu çalışmaların ortak özelliği, sınırlı vaka grupları ya da seçim yanılığı (yalnızca cerrahiye verilen vakalar) gibi majör sınırlayıcı faktörlere sahip olmalarıdır. Takiben yapılan geniş ölçekli prospektif çalışmaları içeren metaanalizler ultrason ES gücünü yaklaşık %80-85 sensitivite %75-80 spesifisite olarak vermektedir. Oldukça homojen yapıda hazırlanan yeni bir metaanalyze göre en yumuşak görünümlü olan nodüller (elastografi skoru 4 üzerinden 1) baz alındığında tekniğin negatif prediktif değerin %99'a çıktıgı raporlanmıştır. Bu sonuca göre ES skoru 1 olan nodüllere biyopsi yapılmadığı takdirde hastaların %14'ünde İİABS uygulamasına gerek kalmamaktadır. Bu veri özellikle ES uygulamasının İİABS'a bağlı morbidite ve maliyeti azaltabilme potansiyelini göstermesi açısından önemlidir. Bu uygulamanın klinik pratiğe girmesi için büyük ölçekli ve çok merkezli çalışma sonuçlarına ihtiyaç vardır. Bu alanda bir başka konu da indetermine sitoloji sonuçları elde edilen tiroid nodüllerinde ES uygulamasıdır. Bu konuda halen geniş ölçekli prospektif çalışmalara ihtiyaç devam etmektedir.¹⁻⁷



Kaynaklar

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Kısa Özgeçmiş

Hacettepe Üniversitesi Tıp Fakültesi'nden 2002 yılında mezun oldu. Mezuniyeti sonrası aynı üniversitede İç Hastalıkları ihtisasına başladı. İç Hastalıkları ihtisası sırasında 2006 yılında "Prof Dr Şeref Zileli başarılı asistan ödülü"nü aldı. İç Hastalıkları baş asistanlığı görevini yürüttü. 2008-2012 yılları arasında Ankara Üniveristesı Tıp Fakültesinde Endokrinoloji ve Metabolizma Hastalıkları üst ihtisasını tamamladı.

Sonrasında bir yıl süreyle A.B.D.'de Harvard Üniversitesi School of Public Health'te doktora sonrası çalışmalar yaptı. Türkiye Endokrinoloji Metabolizma Derneği 2015 yılı genç araştırmacı ödülü sahibi olan Dr. Ünlütürk Kırklareli Devlet Hastanesinde mecburi hizmetini tamamlaması sonrasında Hacettepe Tıp Fakültesi Endokrinoloji Bilim Dalına Yardımcı Doçent olarak atanmıştır.

Söyleşi

Yrd. Doç. Dr. Uğur Ünlütürk

2015 Genç Araştıracı ödülü için tebrik ederiz.

● Bu ödülün sizin için anlamı nedir?

- Tıp Fakültesine adım atmamın 20., ulusal endokrinoloji kongresine ilk kez katılmamın da 10. yılında bu ödülü almak benim için büyük bir mutluluk. Özellikle alma şansını yakaladığım nitelikli uzmanlık eğitimleri sonrasında akademik heyecanımın en yoğun olduğu bir dönemde araya giren mecburi hizmet görevi ile ciddi bir motivasyon kaybı yaşamıştım. Bu ödülü akademik çalışmalarım için tekrar kuvvetli bir itici güç oluşturduğunu düşünüyorum.

● (Genç Araştıracılar için) Bu ödülü almak için yaptığıınız çalışmalarınızda yaşadığınız zorluklar nelerdir? Bunları nasıl aştinız?

- İhtisaslarım boyunca yaptığım çalışmalar esnasında birçok zorlukla farkında olmadan mücadele ederken, şuanki sınırlı tecrübe düzeyimle geriye dönüp baktığımda 2 temel konu aklıma geliyor. İlk olarak söyleyebileceğim, hiçbir bilgi ve tecrübe olmadan başladığım akademik faaliyetlerde en önemli desteği bize yol gösteren öğretim üyeleri ve tecrübesi olan arkadaşlarımız verdi. Bu ustaların eğitimine geçilmeden (ya da mentor-mentee ilişkisi) önce, batıda da örnekleri olan, klinik araştırma eğitim programları (clinical research training programme) yandan çekirdek eğitim programının bir parçası haline getirilebilseydi hem zamanımızı hem de enerjimizi çok daha etkin kullanmamız sağlanabilirdi diye düşünüyorum. Bu araştırmacı eğitimleri genç beyinlerin hipotezlerini nasıl test etmeleri gereği sorusunu yanıtlayarak, farklı düşünme becerisi de kazandırmaktadır. Ayrıca okunan makalelerin de eleştirel gözle irdelemesi için gerekliliği alt yapı eğitimini vermektedir. En azından derneğimiz çatısında böyle bir eğitim faaliyeti başlatılabilir mi sorusu da aklıma geliyor.

- İkinci temel sorun ise yurt dışı tecrübe kazanma için gerekli mali destek konusudur. Artık onde gelen üniversitelerimiz bünyesine dahil etmek istediği akademisyenlerde yurt dışı deneyim şartı aramaktadır. Hem araştırmacıların kişisel gelişimi hem de çağdaşlaşmak için var olan en iyi örnekleri görerek vizyonunu geliştirmesi için çok önemli bir aşamadır. Ancak yan dal asistanları mecburi hizmet yükümlülüğü nedeni ile üniversite ile bağlarını kesmek zorundadırlar ve bu nedenle yurt dışı eğitim-araştırma bursu kazanma şansları çok azalmaktadır. Sonuç olarak değişen Türkiye koşullarında akademik kariyerin devamlılığı için uzmanlık derneklerinin verdikleri destek çok önemli hale gelmiştir. Bizim derneğimiz de yillardır bu imkanı genç endokrinologlara sağlamakta ve derneğimiz olarak verilen destek bu anlamda çok kıymetlidir. Derneğimizin sahip olduğu imkanlar göz önüne alındığında, bursiyerin yurt dışı asgari harcama miktarlarının karşılanması bu yönde hevesi olan genç endokrinologları teşvik edecektir. Getirişi maliyetinden çok daha fazla olacak ve Türkiye Endokrinoloji bilimini daha da ileriye gitmesinin önünü açacağına inandığım bu uygulama için dernek yönetimindeki ve gelecekteki yönetimimize gelecek Hocalarımıza bu vesile ile bir kez daha meslektaşlarım adına çağrıda bulunmak istiyorum.

● Endokrinoloji alanında yeni çalışmaya başlayan sizden genç meslektaşlarımıza önerileriz nelerdir?

- *Carpe diem* ☺. Geçirecekleri bu çok keyifli dönemde, gelecek için endişelenmek yerine yaşanılan anın değeri bilinmeli. Nitelikli bir eğitim aldıklarının farkında olmalıdır. Diğer taraftan da etki yaratılan, kliniğe yön verecek çalışmaların yapılabilmesi için taze beyinlere ihtiyaç olduğu gerektiğini bilerek kendilerine sorular sormalarını, hipotezler üretmelerini ve bunları test etmelerini öneririm.

3. ENDOKRİN ACİLLER KURSU

20 Şubat 2016

Swissotel Büyük Efes • İZMİR

PANEL 1

Acilde Elokt. Bozuklukları

09:30	Açılış Prof. Dr. Sait Gönen Prof. Dr. Dilek Yavuz
Oturum başkanları:	Prof. Dr. Sait Gönen, Prof. Dr. Eda Ertörer
09:30 – 09:50	Hipo ve Hipernatremi Doç. Dr. Barış Akıncı
09:50 – 10:20	Hiperkalsemi Prof. Dr. Dilek Yavuz
10:20 – 10:40	Hipokalsemi Prof. Dr. İbrahim Şahin

PANEL 2

Acilde Adrenal ve Tiroid

Oturum başkanı:	Prof. Dr. İbrahim Şahin
Oturum başkanı:	Prof. Dr. Önder Ersöz
10:45 – 11:00	Adrenal Yetmezlik Prof. Dr. Zeliha Hekimsoy
11:00 – 11:20	Hipotiroidi Ne Zaman Acıldır? Prof. Dr. Eda Ertörer
11:20 – 11:45	Tiroksik Kriz Doç. Dr. Tevfik Demir

PANEL 3

Acilde Glisemi Yönetimi

Oturum başkanı:	Prof. Dr. Eda Ertörer
Oturum başkanı:	Prof. Dr. Zeliha Hekimsoy
12:00 – 12:20	ADA-EASD Tedavi Algoritması Prof. Dr. Fırat Bayraktar
12:20 – 12:45	Diyabetik Ketoasidoz Prof. Dr. Ramazan Sarı
12:45 – 13:00	Hiperglisemik Hiperosmolar Nonketotik Durum Doç. Dr. Mehmet Erdoğan
13:00 – 13:25	Hipoglisemi Prof. Dr. Halil Önder Ersöz
13:30	Kapanış / Sertifika



Türkiye Endokrinoloji ve
Metabolizma Derneği



Türk İç Hastalıkları
Uzmanlık Derneği



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Bilimsel Kongreler, Ulusal ve Uluslararası Sempozyumlar

03 Ekim 2015

Endokrinologlar için Tiroid Kanseri, İleri Klinik ve Sonografik Tanı ve Takip Kursu
Mövenpick Otel - Zürih Salonu, Ankara
www.temd.org.tr

8-11 Ekim 2015

40th Symposium on Hormones and Cell Regulation European Society of Endocrinology
Mont Ste Odile, France
<http://hormones-cell-regulation.eu/>

15 - 18 Ekim 2015

EndoBridge 2015
Cornelia Diamond Hotel, Antalya
<http://endobridge.org/2015/>

18-23 Ekim 2015

15th International Thyroid Congress
Lake Buena Vista, Florida
<http://www.thyroid.org/itc2015/>

31 Ekim 2015

11. Hipofiz Sempozyumu
Sheraton Hotel & Convention Center, Ankara
www.hipofiz2015.org

14-15 Kasım 2015

4. Lipid Metabolizması ve Bozuklukları Eğitim Kursu
Erzurum
İletişim: Prof. Dr. Habib Bilen
drbilen@atauni.edu.tr

19-22 Kasım 2015

17th ESE Postgraduate Training Course on Endocrinology, Diabetes and Metabolism
Tirana, Albania,
<http://www.esepostgraduate2015.com/>

05-07 Aralık 2015

IOF Regionals 3rd Middle East and Africa Osteoporosis Meeting
Abu Dhabi, United Arab Emirates
<http://www.osteofound.org/abudhabi-2015>

10-12 Aralık 2015

4th ENEA Workshop: Acromegaly
Marseilles, France
www.atout-org.com/enea-workshop2015/

12 Aralık 2015

Endokrin Aciller Kursu
Hilton Otel, Adana
www.temd.org.tr

19 Aralık 2015

Tiroid Hastalıkları Kursu
Dedeman Otel, Konya
www.temd.org.tr

09.01.2016

Osteoporoz ve Metabolik Kemik Hastalıkları Kursu
Hilton, Kozyatağı, İstanbul
www.temd.org.tr

20.02.2016

3. Endokrin Aciller Kursu
Swissotel Büyük Efes, İzmir
www.temd.org.tr

11-15 Mayıs 2016

38. Türkiye Endokrinoloji ve Metabolizma Hastalıkları Kongresi ve
2. Ulusal Lipid Sempozyumu
Cornelia Diamond Otel, Belek, Antalya
www.temd.org.tr

20-23 Ekim 2016

EndoBridge 2016
Cornelia Diamond Hotel, Belek, Antalya
www.endobridge.org



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20-23 October 2016
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www.endobridge.org

Üyelerimizden Literatür Seçmeleri

EVALUATION OF AFFECTIVE TEMPERAMENT AND ANXIETY-DEPRESSION LEVELS OF PATIENTS WITH POLYCYSTIC OVARY SYNDROME.

Asik M¹, Altinbas K², Eroglu M³, Karaahmet E², Erbag G⁴, Ertekin H², Sen H⁴

J Affect Disord. 2015 Oct 1;185:214-8. doi: 10.1016/j.jad.2015.06.043. Epub 2015 Jul 26.

Background: Women with polycystic ovary syndrome (PCOS) are reported to experience depressive episodes at a higher rate than healthy controls (HC). Affective temperament features are psychiatric markers that may help to predict and identify vulnerability to depression in women with PCOS. Our aim was to evaluate the affective temperaments of women with PCOS and to investigate the association with depression and anxiety levels and laboratory variables in comparison with HC.

Methods: The study included 71 women with PCOS and 50 HC. Hormonal evaluations were performed for women with PCOS. Physical examination, clinical history, Hospital Anxiety and Depression Scale (HADS) and TEMPS-A were performed for all subjects. Differences between groups were evaluated using Student's t-tests and Mann-Whitney U tests. Correlations and logistic regression tests were performed.

Results: All temperament subtype scores, except hyperthymic, and HADS anxiety, depression, and total scores were significantly higher in patients with PCOS compared to HC. A statistically significant positive correlation was found between BMI and irritable temperament, and insulin and HADS depression scores in patients with PCOS. Additionally, hirsutism score and menstrual irregularity were correlated with HADS depression, anxiety and total scores in PCOS patients. In logistic regression analysis, depression was not affected by PCOS, hirsutism score or menstrual irregularity. However, HADS anxiety score was associated with hirsutism score.

Conclusions: Our study is the first to evaluate the affective temperament features of women with PCOS. Consequently, establishing affective temperament properties for women with PCOS may help clinicians predict those patients with PCOS who are at risk for depressive and anxiety disorders.

MEAN PLATELET VOLUME COULD BE A POSSIBLE BIOMARKER FOR PAPILLARY THYROID CARCINOMAS.

Baldane S¹, Ipekci SH, Sozen M, Kebapcilar L.

Asian Pac J Cancer Prev. 2015;16(7):2671-4.

Thyroid cancer is the most prevalent endocrine cancer and is evident in nearly 5% of thyroid nodules. The correlation between mean platelet volume (MPV) and many other cancer types has been investigated previously. However, the correlation between papillary thyroid carcinoma (PTC) and MPV has not yet been studied in detail. The aim of this study was to examine whether MPV would be a useful inflammatory marker to differentiate PTC patients from cases of benign goiter and healthy controls. Preoperative MPV levels in patients with PTC were found to be

significantly higher when compared with benign goiter patients and healthy controls ((respectively, 8.05 femtoliter (fl), 7.57 fl, 7.36 fl, p=0.001). After surgical treatment of PTC patients, a significant decrease in MPV levels was seen (8.05 fl versus 7.60 fl, p=0.005). ROC analysis suggested 7.81 as the cut-off value for MPV (AUC=0.729, sensitivity 60%, specificity 80%). In conclusion, maybe changes in MPV levels can be used as an easily available biomarker for monitoring the risk of PTC in patients with thyroid nodules, enabling early diagnosis of PTC.

LOCALIZATION OF THE AROMATASE ENZYME EXPRESSION IN THE HUMAN PITUITARY GLAND AND ITS EFFECT ON GROWTH HORMONE, PROLACTIN, AND THYROID STIMULATING HORMONE AXIS.

Caglar AS¹, Kapucu A, Dar KA, Ozkaya HM, Caglar E, Ince H, Kadioglu P. *Endocrine. 2015 Aug;49(3):761-8. doi: 10.1007/s12020-015-0537-6. Epub 2015 Feb 20.*

The aim of this study is to evaluate aromatase expression in prolactin (PRL), thyroid stimulating hormone (TSH), and growth hormone (GH) secreting cells. Nontumoral human pituitary specimens were obtained from autopsy samples. Aromatase co-expression was determined by double immunohistochemical staining and assessed using H scores. H scores for GH-aromatase co-expression (GH-aromatase), TSH-aromatase co-expression (TSH-aromatase), and PRL-aromatase co-expression (PRL-aromatase) were 83.1 ± 13.1 , 95.6 ± 16.1 , and 83.7 ± 14.5 , respectively. TSH producing cells exhibited the highest H score for co-expression of aromatase ($p < 0.001$). There was no gender difference in terms of H scores for aromatase expression and double immunohistochemical staining results ($p > 0.05$ for all). There was a negative correlation between the H scores for aromatase and PRL-aromatase, GH-aromatase and TSH-aromatase, respectively ($r = -0.592$, $p < 0.001$; $r = -0.593$, $p < 0.001$; $r = -0.650$, $p < 0.001$, respectively). Also, H scores for aromatase co-expression of each hormone were negatively correlated with the H scores for the corresponding hormone ($r = -0.503$, $p < 0.001$ for PRL-aromatase and PRL; $r = -0.470$, $p < 0.001$ for GH-aromatase, and GH; $r = -0.641$, $p < 0.001$ for TSH-aromatase and TSH). H scores for mean aromatase, GH-aromatase, TSH-aromatase were invariant of age ($p > 0.05$ for all). Age was negatively correlated with PRL-aromatase H score ($r = -0.373$, $p = 0.008$). Our study demonstrated significant aromatase co-expression in PRL, GH, and TSH secreting cells of the human anterior pituitary gland. The mutual paracrine regulation between aromatase and three adenohypophyseal hormones indicates that aromatase may have a regulatory role on the synthesis and secretion of these hormones.

CAN A GLUCAGON STIMULATION TEST CHARACTERIZED BY LOWER GH CUT-OFF VALUE BE USED FOR THE DIAGNOSIS OF GROWTH HORMONE DEFICIENCY IN ADULTS?

Diri H¹, Karaca Z¹, Simsek Y¹, Tanrıverdi F¹, Unluhizarci K¹, Selcuklu A², Kelestimur F³.

Pituitary. 2015 Dec;18(6):884-92. doi: 10.1007/s11102-015-0666-1.

Objective: The aim of this study was to assess diagnostic values of insulin tolerance test (ITT), glucagon stimulation test (GST), and insulin like growth factor-I (IGF-I) level, to find optimal GH cut-off values for GST, and to evaluate efficiencies of patient age, gender, body-mass index (BMI), and additional pituitary hormone deficiencies (PHDs) in the diagnosis of growth hormone deficiency (GHD).

Study Design: This retrospective study involved 216 patients with a pituitary disease and 26 healthy controls. Age, gender, BMI, medical histories, and hormonal data including baseline and stimulated hormone values were evaluated. Three cut-off values for peak GH responses to stimulation tests were evaluated: (a) 3.00 µg/L on ITT, (b) 3.00 µg/L on GST, and (c) 1.07 µg/L on GST.

Results: According to the ITT, GST with 3.00 µg/L cut-off, and GST with 1.07 µg/L cut-off, GHD was present in 86.1, 74.5, and 54.2% patients, respectively. Patient age, BMI, and number of PHDs, but not gender, were found to be correlated with IGF-I and peak GH concentrations. All patients with an IGF-I concentration ≤95 ng/ml or ≥3 PHD had GHD. None of the patients with adequate GH response to the GST with 1.07 µg/L cut-off, but blunted responses to ITT and GST with 3.00 µg/L cut-off, had ≥3 PHDs. 12 out of 26 (46.2%) healthy subjects failed the GST with 3.00 µg/L cut-off, but not with 1.07 µg/L cut-off.

Conclusions: Patient age, IGF-I, BMI, and number of PHDs are efficient factors associated with the diagnosis of GHD. A 4 h GST with a diagnostic GH threshold of 1.07 µg/L seems to be a good diagnostic method for GHD.

PREVALENCE OF GESTATIONAL DIABETES MELLITUS AND ASSOCIATED RISK FACTORS IN TURKISH WOMEN: THE TRABZON GDM STUDY.

Erem C¹, Kuzu UB², Deger O³, Can G⁴.

Arch Med Sci. 2015 Aug 12;11(4):724-35. doi: 10.5114/aoms.2015.53291. Epub 2015 Aug 11.

Introduction: The aim of this study was to investigate the prevalence of gestational diabetes mellitus (GDM) in Turkish pregnant women in the Trabzon Region and further to identify population-specific risk factors for GDM.

Material and methods: In this prospective cross-sectional survey, universal screening for GDM was performed in 815 pregnant women. Screening was done with a 50-g oral glucose challenge test (GCT) with a 140 mg/dl cut-off point, then a diagnostic 100 g oral glucose tolerance test (OGTT) was performed according to Carpenter and Coustan (CC) criteria.

Results: The GCT was positive in 182 (22.3%) cases. The OGTT was performed on the 182 screen-positive pregnant women. Thirty-five were diagnosed with GDM on the basis of their results for a prevalence of 4.3% (35/815). Of the pregnancies with negative GCT but having high risk factors for GDM (n = 31), 4 were diagnosed with GDM (0.5%). Prevalence of GDM was found to be 4.8% (n = 39) for all pregnant women. Gestational diabetes mellitus was positively associated with advanced maternal age ($p < 0.001$), prepregnancy body mass index ($p < 0.001$), cessation of cigarette smoking ($p < 0.001$), excessive weight gain during pregnancy ($p = 0.003$), previous history of GDM ($p < 0.001$), history of selected medical conditions ($p = 0.018$), family history of diabetes (FHD) ($p < 0.001$), and existence of at least one high risk factor for GDM ($p < 0.001$). In multiple logistic regression analysis, independent predictors for GDM were maternal age, cessation of cigarette smoking, increasing prepregnancy body mass index, weight gain of more than 8 kg during pregnancy, GDM history in previous pregnancies and a history of diabetes in first-degree relatives of pregnant women.

Conclusions: The prevalence of GDM in Trabzon province was found as moderate. Commonly recognized risk factors including older age, prepregnancy obesity, FHD and past history of GDM, are valid for our urban Turkish population. Also, excessive weight gain in pregnancy and cigarette cessation were observed to be nontraditional risk factors of GDM. It was concluded that all pregnant women should be screened for GDM if prevalence was not low.

DISCONTINUATION OF SOMATOSTATIN ANALOGS WHILE ACROMEGALY IS IN LONG-TERM REMISSION.

Hatipoglu E¹, Bozcan S, Kadioglu P.

Pituitary. 2015 Aug;18(4):554-60. doi: 10.1007/s11102-014-0608-3.

Purpose: We aimed to evaluate the disease activity of medically controlled patients with acromegaly after withdrawal of somatostatin receptor ligands (SRL).

Methods: Sixteen patients who were on a stable dose of SRL for more than 2 years and had at least 1 year of remission were included in the study. Five patients were on 10 mg, four were on 20 mg and three were on 30 mg of octreotide; whereas for lanreotide, one was on 60 mg, two were on 90 mg, and one was on 120 mg. All patients had received SRL with 28-day intervals. Basal GH, IGF1, glucose-suppressed GH levels were measured with 3-month intervals for a total of 12 months after withdrawal. Sella MRI evaluation was obtained at 6-month intervals. If the nadir GH level after glucose suppression was >1 ng/ml or IGF1 was above the normal limits during the follow-up period, SRL was restarted.

Results: Three months after stopping SRL, 10 (63%) had biochemical disease recurrence. After 12 months of follow-up, in total 13 (81%) of the patients recurred. The final basal GH levels before withdrawal, basal GH at month-3, and glucose suppressed GH levels were significantly lower in patients with sustained remission ($p = 0.003$, $p < 0.001$, and $p = 0.001$). Basal GH and glucose suppressed GH levels at month-3 were correlated with the basal GH levels at month-0 ($r = 0.6$, $p = 0.008$ and $r = 0.5$, $p = 0.03$).

Conclusion: The final GH levels prior to discontinuation of SRL should be taken into consideration in patients with acromegaly in long-term remission. Moreover, the first visit 3 months after withdrawal is critically important for determining the future status of remission.

PHYSICAL AND CARDIOVASCULAR PERFORMANCE IN CASES WITH ACROMEGALY AFTER REGULAR SHORT-TERM EXERCISE.

Hatipoglu E¹, Topsakal N², Erkut Atilgan O², Camliguney AF², Ikitimur B³, Ugurlu S⁴, Niyazoglu M¹, Cotuk HB², Kadioglu P¹.

Clin Endocrinol (Oxf). 2015 Jul;83(1):91-7. doi: 10.1111/cen.12708. Epub 2015 Feb 6.

Objective: Impaired physical performance is a disturbing complication of acromegaly. We aimed to evaluate the role of regular exercise in amelioration of the impaired physical performance in acromegaly.

Methods: Patients with acromegaly were divided into two groups according to their participation in a prescheduled programme of exercise. Participants in the study group were exercised 3 days a week for 3 consecutive months. Exercise tolerance was evaluated by maximal oxygen consumption (VO₂ max) and time (T) taken to complete the Bruce protocol, muscle flexibility by the sit and reach test (SRT) and muscle strength by the hand grip strength test (HGST). Concomitantly, anthropometric assessment was performed using body mass index (BMI), waist-to-hip ratio (WHR), skinfold measurements from 8 points, percentage body fat (PBF), fat mass (FM) and lean body mass (LBM).

Results: After 3 months of exercise, VO₂ max and T were higher in cases that exercised than in cases that did not ($P = 0.004$ and $P = 0.001$). Over 3 months, within the exercise group, VO₂ max and T of the Bruce protocol increased ($P = 0.003$ and $P = 0.004$) and heart rate during warming decreased ($P = 0.04$). SRT increased within the exercise group after 3 months ($P = 0.004$). HGSRT did not change significantly (right $P = 0.06$ and left $P = 0.2$). The sum of skinfolds, BMI, WHR and LBM remained stable over the study period ($P = 0.1$, $P = 0.08$, $P = 0.3$ and $P = 0.09$). PBF decreased slightly and FM decreased significantly over 3 months ($P = 0.05$ and $P = 0.03$).

Conclusion: Even short-term exercise may improve impaired physical performance, muscle activity and disturbed body fat composition in acromegaly.

PEPTIC ULCER DISEASE IN ENDOGENOUS HYPERCORTISOLISM: MYTH OR REALITY?

Hatipoglu E¹, Caglar AS¹, Caglar E², Ugurlu S³, Tuncer M², Kadioglu P⁴.

Endocrine. 2015 Nov;50(2):489-95. doi: 10.1007/s12020-015-0608-8. Epub 2015 Apr 21.

Many clinicians believe hypercortisolism is ulcerogenic. However, data from clinical studies show that prophylaxis for peptic ulcer disease is no longer recommended in patients receiving corticosteroid treatment. This has not yet been verified in endogenous hypercortisolism by controlled clinical studies. The purpose of the current study was to evaluate the relationship between endogenous Cushing's syndrome (CS) and peptic ulcer disease and Helicobacter pylori infection. The study group contained 20 cases with CS resulting from ACTH-dependent endogenous hypercortisolism. The control groups consisted of 14 age- and gender-matched cases receiving exogenous corticosteroid therapy and 100 cases of dyspepsia with non-cushingoid features. Upper gastrointestinal endoscopy was performed on all cases. Biopsies were taken from five different points: two samples from the antrum, two samples from the corpus, and one sample from the fundus. A histological diagnosis of Helicobacter pylori infection was also obtained from evaluation of biopsy specimens. The frequency of stomach and duodenal ulcers did not vary between the groups ($p = 0.5$ and $p = 0.7$). Antral gastritis was less frequent and pangastritis was more common in cases with CS compared to the healthy controls ($p = 0.001$ and $p < 0.001$). The incidence of Candida esophagitis was more frequent in cases with CS compared to cases with corticosteroid treatment and healthy controls ($p = 0.03$). Histopathological findings and frequency of Helicobacter pylori based on pathology results did not vary between the three groups. It is possible that neither exogenous nor endogenous corticosteroid excess directly causes peptic ulcer or Helicobacter pylori infection. Prophylactic use of proton pump inhibitors is not compulsory for hypercortisolism of any type.

INCREASED ARTERIAL STIFFNESS AND ITS RELATIONSHIP WITH INFLAMMATION, INSULIN, AND INSULIN RESISTANCE IN CELIAC DISEASE.

Korkmaz H¹, Sozen M, Kebapcilar L.

Eur J Gastroenterol Hepatol. 2015 Oct;27(10):1193-9. doi: 10.1097/MEG.0000000000000437.

Objective: Celiac disease (CD) is a lifelong, chronic, immune-mediated, inflammatory small bowel disorder, precipitated by exposure to dietary gluten and related proteins in genetically predisposed individuals. Recent studies have shed new light on the importance of inflammation in the pathogenesis of arterial stiffness. The aim of this study was to evaluate arterial stiffness using pulse wave velocity (PWV) in adult CD patients without cardiovascular risk factors in comparison with a control group.

Patients and methods: A total of 58 patients with CD without cardiovascular risk factors and age-matched and sex-matched healthy controls were enrolled in the study. All patients completed a standard questionnaire form, and various laboratory parameters were assessed. Vascular measurements, including PWV, were carried out using a Mobil-O-Graph 24-h pulse wave analysis monitor, an automatic oscillometric device.

Results: Although cardiovascular risk factors, such as low-density lipoprotein cholesterol and triglyceride, were significantly lower ($P < 0.05$) in celiac patients than in controls, the erythrocyte sedimentation rate, C-reactive protein, insulin, homeostasis model assessment of insulin resistance, homocysteine, and 24 h, day, and night PWV values were higher in patients with CD than in controls ($P < 0.05$). A multiple linear regression analysis showed that PWV was correlated positively with age and the duration of CD.

Conclusion: This study found increased arterial stiffness, homocysteine, erythrocyte sedimentation rate, C-reactive protein, insulin, and homeostasis model assessment of insulin resistance in patients with CD and provides evidence for the potential contribution of these parameters and inflammation toward arterial stiffening, independent of conventional cardiovascular risk factors.

EVALUATION OF PARA- AND PERIRENAL FAT THICKNESS AND ITS ASSOCIATION WITH METABOLIC DISORDERS IN POLYCYSTIC OVARY SYNDROME.

Sahin SB, Durakoglugil T, Ayaz T, Sahin OZ, Durakoglugil E, Sumer F, Aktas E, Alyildiz N.

Endocr Pract. 2015 Aug;21(8):878-86. doi: 10.4158/EP14435.OR. Epub 2015 Jun 29.

Objective: The aim of this study was to compare para- and perirenal fat (PFT) and subcutaneous abdominal fat (SFT) measurements between patients with polycystic ovary syndrome (PCOS) and control subjects and to assess the possible relation with metabolic disorders.

Methods: This study included 68 patients with PCOS and 40 age- and body mass index (BMI)-matched healthy controls. We evaluated anthropometric, hormonal, and metabolic parameters, and abdominal ultrasonography was performed to measure PFT and SFT.

Results: The mean PFT values were 6.1 ± 2.9 mm in patients with PCOS and 4.3 ± 2.3 mm in healthy controls ($P = .002$). SFT values were also higher in the patient group (9.6 ± 5 mm) compared to healthy subjects (3.5 ± 0.5 mm) ($P = .017$). A significant positive correlation was found between PFT and BMI ($r = 0.368$), waist circumference (WC) ($r = 0.441$), Ferriman-Gallwey (FG) score ($r = 0.313$), blood pressure (systolic, SBP, $r = 0.213$; diastolic, DBP, $r = 0.215$), plasma glucose ($r = 0.195$), homeostasis model assessment-insulin resistance (HOMA-IR, $r = 0.273$), SFT ($r = 0.555$). Conversely, negative correlations were found between PFT and estradiol ($r = -0.218$) and sex hormone-binding globulin (SHBG, $r = -0.304$). Nonobese PCOS patients (6.1 ± 3.07 mm) had higher PFT values than nonobese controls (3.47 ± 1.5 mm); however, SFT measurements did not differ ($P = .086$). In multiple linear regression analysis, SFT ($P = .006$) was a significant and independent predictor for PFT, along with WC ($P = .023$). In a stepwise model, SFT was the predictor of PFT ($P = .001$).

Conclusion: PFT values were higher particularly in nonobese PCOS patients compared to nonobese control subjects. There was a significant interaction between PCOS and obesity on PFT.

Abbreviations: BMI = body mass index CT = computed tomography DBP = diastolic blood pressure FPG = fasting plasma glucose HDL-cholesterol = high-density lipoprotein cholesterol HOMA-IR = homeostasis model assessment-insulin resistance hsCRP = high-sensitivity C-reactive protein LDL-cholesterol = low-density lipoprotein cholesterol LH = luteinizing hormone NCAH = nonclassic congenital adrenal hyperplasia 17-OHP = 17-hydroxyprogesterone PCOS = polycystic ovary syndrome PFT = para- and perirenal fat SAT = subcutaneous abdominal adipose tissue SBP = systolic blood pressure SFT = abdominal subcutaneous fat thickness TG = triglyceride US = ultrasound VAT = visceral abdominal adipose tissue WC = waist circumference.

FREQUENCY OF METABOLIC SYNDROME IN PATIENTS WITH KNUCKLE PADS.

Saylam Kurtipek G¹, Kutlu O², Duran C³, Kurku H⁴, Ataseven A¹, Tunçez Akyurek F⁵.

J Dermatol. 2015 Dec;42(12):1165-8. doi: 10.1111/1346-8138.13012. Epub 2015 Jun 29.

Knuckle pads are hyperkeratotic, benign skin lesions that we commonly observe in obese patients. There is no study that investigates the association between metabolic syndrome (MetS) and knuckle pads. We aimed to investigate the frequency of MetS in patients with knuckle pads. Forty-seven patients with knuckle pads and 46 age- and sex-matched controls were enrolled. The presence of MetS was evaluated according to National Cholesterol Education Program-Adult Treatment Panel III criteria. In the patient group, waist circumference ($P < 0.01$), body mass index (BMI; $P < 0.01$), and systolic ($P < 0.01$) and diastolic blood pressure ($P < 0.01$) were higher than controls, and most of the patients had a history of hypertension ($P < 0.01$). The presence of MetS was found in 66% of the patients with knuckle pads and in 52.2% of the controls ($P = 0.25$). In the patient group, compared with controls, more patients had blood pressure above reference values or were on antihypertensive therapy (70.2% and 43.5%, $P = 0.017$, respectively), and had greater waist circumference value (93.6% and 76.1%, $P = 0.038$, respectively). The presence of the other three criteria were similar in both groups. Although we found similar MetS frequency in both groups, patients with knuckle pads should be examined for the presence of MetS components, especially abdominal obesity and hypertension.

ENDOTHELIAL DYSFUNCTION, INSULIN RESISTANCE AND INFLAMMATION IN CONGENITAL HYPOGONADISM, AND THE EFFECT OF TESTOSTERONE REPLACEMENT.

Sonmez A¹, Haymana C, Aydogdu A, Tapan S, Basaran Y, Meric C, Baskoy K, Dinc M, Yazici M, Taslipinar A, Barcin C, Yilmaz MI, Bolu E, Azal O. *Endocr J. 2015;62(7):605-13. doi: 10.1507/endocrj.E15-0125. Epub 2015 May 28.*

Patients with hypogonadism have poor cardiovascular and metabolic outcomes, and the effect of testosterone replacement therapy (TRT) is not clear. We investigated the presence of inflammation, insulin resistance and endothelial dysfunction in an unconfounded population of congenital hypogonadotropic hypogonadism (CHH) and the effect of TRT on these subjects. A total of 60 patients with CHH (mean age 21.82 ± 2.22 years) and 70 healthy control subjects (mean age 21.32 ± 1.13 years) were enrolled. The demographic parameters, Asymmetric dimethylarginine (ADMA), TNF-like weak inducer of apoptosis (TWEAK), high sensitive C reactive protein (hs-CRP) and homeostatic model assessment of insulin resistance (HOMA-IR) levels were measured before and after TRT. The patients had higher Waist Circumferences (WC) ($p=0.009$), Diastolic Blood Pressures ($p=0.02$), Triglycerides ($p=0.03$), ADMA, insulin and HOMA-IR levels ($p<0.001$ for all) and lower TWEAK levels ($p<0.001$), compared to the healthy controls. After 5.56 ± 2.04 months of TRT, the patients had significantly elevated systolic blood pressures ($p=0.01$), body mass indexes and WC ($p<0.001$ and $p=0.001$ respectively) and decreased total and HDL

cholesterol levels ($p=0.032$ and $p<0.001$ respectively). ADMA levels significantly increased ($p=0.003$), while the alterations in TWEAK, hsCRP and HOMA-IR were not significant. The results of the present study show that endothelial dysfunction, inflammation and insulin resistance are prevalent even in the very young subjects with CHH, who have no metabolic or cardiac problems at present. This increased cardiometabolic risk however, do not improve but even get worse after six months of TRT. Long term follow-up studies are warranted to investigate the unfavorable cardiometabolic effects of TRT.

THE ROLE OF PLASMA TRIGLYCERIDE/HIGH-DENSITY LIPOPROTEIN CHOLESTEROL RATIO TO PREDICT CARDIOVASCULAR OUTCOMES IN CHRONIC KIDNEY DISEASE.

Sonmez A¹, Yilmaz MI², Saglam M³, Unal HU⁴, Gok M⁵, Cetinkaya H⁶, Karaman M⁷, Haymana C⁸, Eyleten T⁹, Oguz Y¹⁰, Vural A¹¹, Rizzo M¹², Toth PP¹³. *Lipids Health Dis. 2015 Apr 16;14:29. doi: 10.1186/s12944-015-0031-4.*

Background: Cardiovascular disease (CVD) risk is substantially increased in subjects with chronic kidney disease (CKD). The Triglycerides (TG) to High-Density Lipoprotein Cholesterol (HDL-C) ratio is an indirect measure of insulin resistance and an independent predictor of cardiovascular risk. No study to date has been performed to evaluate whether the TG/HDL-C ratio predicts CVD risk in patients with CKD.

Methods: A total of 197 patients (age 53 ± 12 years) with CKD Stages 1 to 5, were enrolled in this longitudinal, observational, retrospective study. TG/HDL-C ratio, HOMA-IR indexes, serum asymmetric dimethyl arginine (ADMA), high sensitivity C-reactive protein (CRP), parathyroid hormone (PTH), calcium, phosphorous, estimated glomerular filtration rate (eGFR), and albumin levels were measured. Flow mediated vasodilatation (FMD) of the brachial artery was assessed by using high-resolution ultrasonography.

Results: A total of 11 cardiovascular (CV) deaths and 43 nonfatal CV events were registered in a mean follow-up period of 30 (range 9 to 35) months. Subjects with TG/HDL-C ratios above the median values (>3.29) had significantly higher plasma ADMA, PTH, and phosphorous levels ($p=0.04$, $p=0.02$, $p=0.01$ respectively) and lower eGFR and FMD values ($p=0.03$, $p<0.001$ respectively). The TG/HDL-C ratio was an independent determinant of FMD ($\beta=-0.25$ $p=0.02$) along with TG, HDL-C, hsCRP, serum albumin, phosphate levels, systolic blood pressure, PTH, eGFR and the presence of diabetes mellitus. The TG/HDL-C ratio was also a significant independent determinant of cardiovascular outcomes [HR: 1.36 (1.11-1.67) ($p=0.003$)] along with plasma ADMA levels [HR: 1.31 (1.13-1.52) ($p<0.001$)] and a history of diabetes mellitus [HR: 4.82 (2.80-8.37) ($p<0.001$)].

Conclusion: This study demonstrates that the elevated TG/HDL-C ratio predicts poor CVD outcome in subjects with CKD. Being a simple, inexpensive, and reproducible marker of CVD risk, the TG/HDL-C ratio may emerge as a novel and reliable indicator among the many well-established markers of CVD risk in CKD.

LOW- AND HIGH-DENSITY LIPOPROTEIN SUBCLASSES IN SUBJECTS WITH NONALCOHOLIC FATTY LIVER DISEASE.

Sonmez A¹, Nikolic D², Dogru T³, Ercin CN³, Genc H³, Cesur M⁴, Tapan S⁵, Karslioğlu Y⁶, Montaldo G², Banach M⁷, Toth PP⁸, Bagci S³, Rizzo M⁹. *J Clin Lipidol.* 2015 Jul-Aug;9(4):576-82. doi: 10.1016/j.jacl.2015.03.010. Epub 2015 Apr 4.

Background: Nonalcoholic fatty liver disease (NAFLD) is associated with increased cardiometabolic risk. Although dyslipidemia represents a key factor in this disease, its impact on serum levels of distinct lipoprotein subfractions is largely unknown.

Objective: To assess the full low-density lipoprotein (LDL) and high-density lipoprotein (HDL) profiles in patients with NAFLD.

Methods: Seven LDL and 10 HDL subfractions were assessed by gel electrophoresis (Lipoprint, Quantimetrix Corporation, USA) in men with biopsy proven NAFLD (simple steatosis [n = 17, age, 34 ± 7 years] and nonalcoholic steatohepatitis [NASH; n = 24, age, 32 ± 6 years]). Exclusion criteria included robust alcohol consumption, infection with hepatitis B or C virus, body mass index ≥ 40 kg/m², diabetes mellitus, and hypertension.

Results: Compared with simple steatosis, NASH patients had similar body mass index, homeostasis model assessment of insulin resistance index and plasma lipids, with increased levels of both aspartate aminotransferase and alanine transaminase. NASH subjects had lower levels of larger LDL1 (10 ± 4 vs 13 ± 4%, P = .010) and increased smaller LDL3 and LDL4 particles (9 ± 5 vs 5 ± 5%, P = .017 and 3 ± 3 vs 1 ± 2%, P = .012, respectively). No changes were found in the HDL subclass profile. By multiple regression analysis, we found that NASH was associated only with increased levels of LDL3 (P = .0470).

Conclusions: The increased levels of small, dense LDL3 and LDL4 in NASH may help to at least partly explain the increased risk for atherosclerosis and cardiovascular diseases in these patients.

ENTERAL NUTRITION AND GLUCAGON-LIKE PEPTIDE-1 IN INTENSIVE CARE UNIT PATIENTS

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Abstract

Glucagon-like peptide-1 is a peptide with antihyperglycemic activity secreted from distal parts of the intestine in response to enteral feeding. It augments insulin secretion via increasing glucose sensitivity of pancreatic beta cells without the risk of hypoglycemia. Slowing of gastric emptying and suppression of appetite are the other mechanisms of action which potentiate its antihyperglycemic activity. It may also exert neuroprotective, cardioprotective, nephroprotective, and immunomodulatory effects via acting through GLP-1 receptors located on many vital organs. Dipeptidyl peptidase 4 (DPP4) inhibitors that inhibit its enzymatic destruction, thus prolonging its plasma half-life or GLP-1 analogues that are resistant to enzymatic destruction, have been introduced as alternative therapeutic options for type 2 diabetes mellitus (DM) recently. Inability of critically ill ICU patients to secrete sufficient amounts of GLP-1 has given the inspiration for studying GLP-1 based therapies on this group of patients for glucose regulation and for its other potential benefits.

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