

TÜRKİYE ENDOKRİNOLOJİ VE METABOLİZMA DERNEĞİ BÜLTENİ



Üç ayda bir online yayımlanır

Sayı 75 • Temmuz – Ağustos – Eylül • 2021



CANLI YAYIN

TOPLANTILARIMIZ...



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ADA 2021 KONGRESİ ÖNE ÇIKANLAR 1

- Diyabete Bağlı Gelişen Kronik Komplikasyonlar
- Kardiyovasküler Sonlanım Çalışmaları
- Obezite Tedavisindeki Gelişmeler
- Gestasyonel Diyabet ve Tedavisi

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ADA 2021 KONGRESİ ÖNE ÇIKANLAR 2

- Tip 1 Diyabet Tedavisindeki Gelişmeler
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BAYRAMLARIMIZ KUTLU OLSUN



Sevdiklerimizle birlikte
Nice Mutlu Bayramlara



30
AĞUSTOS
ZAFER BAYRAMI
Kutlu Olsun

"Türk milleti istiklalsiz yaşamamıştır, yaşayamaz ve yaşamayacaktır."
Mustafa Kemal Atatürk



KONGRE, KURSLAR VE SEMPOZYUMLAR



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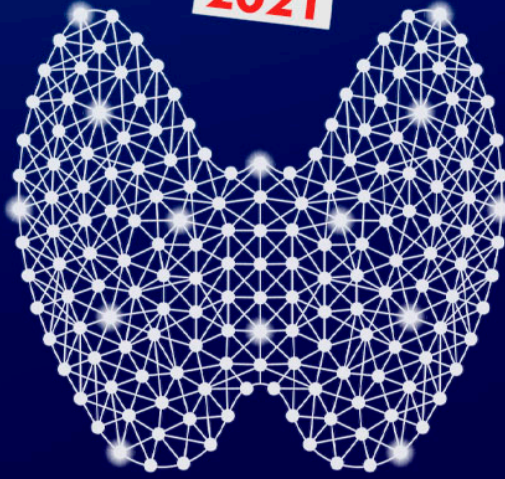
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- 21 - 24 Ekim 2021
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- 5 - 6 Kasım 2021
16. Hipofiz Sempozyumu
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<https://tiroidkongresi2021.org/>
- 6-11 Aralık 2021
IDF Virtual Congress 2021
<https://idf2021.org/>
- 18-22 Mayıs 2022
43. Türkiye Endokrinoloji ve Metabolizma Hastalıkları Kongresi
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<https://temd.org.tr/haberler/225-turkiye-endokrinoloji-ve-metabolizma-hastaliklari-kongresi>
- 21 - 24 Mayıs 2022
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Milano, İtalya
<https://www.es-hormones.org/events-deadlines/european-congress-of-endocrinology/ece-2022/>
- 3 - 7 Haziran 2022
82nd ADA Scientific Sessions
New Orleans, LA
<https://professional.diabetes.org/scientific-sessions>
- 11 - 14 Haziran 2022
ENDO 2022, Annual Meeting of the Endocrine Society
Atlanta, GA
<https://www.endocrine.org/endo2022>
- 7-10 Eylül 2022
Lyon ENEA 2022 Congress - 20th Congress of the European Neuroendocrine Association
Lyon, Cité Internationale – Centre de Congrès, France
<https://eneassoc.org/>
- 10-13 Eylül 2022
44th Annual Meeting of the European Thyroid Association (ETA)
Brussels, Belgium
www.eurothyroid.com
- 19-23 Eylül 2022
58th Annual Meeting - European Association for the Study of the Diabetes
Stockholm, Sweden
<https://www.easd.org/annual-meeting/easd-2022.html>

ÜYELERİMİZDEN LİTERATÜR SEÇMELERİ

THE COMPATIBILITY OF THE TREATMENT MODALITIES TO THE RECOMMENDATIONS OF THE KIDNEY DISEASE OUTCOMES QUALITY INITIATIVE GUIDELINE IN CHRONIC KIDNEY DISEASE PATIENTS WITH DIABETES

Zelal Adibelli¹, Cevdet Duran²

Iran J Public Health. 2021 Jun;50(6):1206-1212. PMID: 34540741 PMCID: PMC8410973 DOI: 10.18502/ijph.v50i6.6419

Background: Diabetes mellitus (DM) and chronic kidney disease (CKD) are global growing health problems. Since DM is the major cause for CKD etiology, its development can be prevented with simple measures, like achievements of glycemic, lipid and blood pressure targets. This study aimed to evaluate whether the treatment goals for CKD patients with DM are achieved under the Kidney Disease Outcomes Quality Initiative (KDOQI) guideline.

Methods: Overall, 160 CKD patients with DM were enrolled in the study performed in Usak, Turkey from Jan 2016 to Jan 2018. Compatibility with treatment goals defined in KDOQI 2012 guideline for HbA1c levels, hypertension and dyslipidemia were evaluated retrospectively.

Results: Of 160 CKD patients [15 (9.4%) in stage 3a, 53 (33.1%) stage 3b, 51 (31.9%) stage 4 and 41 (25.6%) stage 5], 23 patients in stage 5 were on hemodialysis. Total compliance rate to hyperglycemia treatment was 94 of 160 patients (58.8%). Compatibility rates between different stages of CKD were similar. Hypertension was detected only in 134 patients. Sixty-six (49.3%) patients were compatible with the treatment goals, and as the CKD stages progressed, the rate of patients achieving hypertension treatment goals was declined ($P=0.001$). One-hundred and thirty-seven patients were not on hemodialysis and fifty-four (39.9%) of 137 patients achieved dyslipidemia goal. There was no difference between different stages of CKD.

Conclusion: Under KDOQI 2012 guideline, treatment goal for hyperglycemia was better achieved than the treatment goals for hypertension and dyslipidemia. In CKD patients with DM the physicians should be also focused on the treatment of hypertension and dyslipidemia.

SWEET DREAMS: THERAPEUTIC INSIGHTS, TARGETING IMAGING AND PHYSIOLOGIC EVIDENCE LINKING SLEEP, MELATONIN AND DIABETIC NEPHROPATHY

Baris Afsar¹, Rengin Elsurer Afsar¹, Alan A Sag², Asiye Kanbay³, Hakan Korkmaz⁴, José Cipolla-Neto⁵, Adrian Covic⁶, Alberto Ortiz⁷, Mehmet Kanbay⁸
Clin Kidney J. 2020 Feb 6;13(4):522-530.eCollection 2020 Aug. PMID: 32905249 PMCID: PMC7467577 DOI: 10.1093/ckj/sfz198

Melatonin is the main biochronologic molecular mediator of circadian rhythm and sleep. It is also a powerful antioxidant and has roles in other physiologic pathways. Melatonin deficiency is associated with metabolic derangements including glucose

and cholesterol dysregulation, hypertension, disordered sleep and even cancer, likely due to altered immunity. Diabetic nephropathy (DN) is a key microvascular complication of both type 1 and 2 diabetes. DN is the end result of a complex combination of metabolic, haemodynamic, oxidative and inflammatory factors. Interestingly, these same factors have been linked to melatonin deficiency. This report will collate in a clinician-oriented fashion the mechanistic link between melatonin deficiency and factors contributing to DN.

EFFECTS OF TREATMENT ADHERENCE ON QUALITY OF LIFE IN HYPOPARATHYROID PATIENTS

Inan Anaforoglu¹, Seda Sancak², Emin Murat Akbas³, Guzide Gonca Oruk⁴, Masum Canat⁵, Kadriye Aydın Tezcan⁶, Ziyneet Alphan Uc⁷, Suheyla Gorar⁸, Gulhan Cavlak Duman⁹, Guzin Fidan Yaylali¹⁰, Merve Yılmaz¹¹, Betül Ekiz Bilir¹², Humeyra Bozoglan¹³, Gulhan Akbaba¹⁴, Mazhar Muslum Tuna¹⁵, Seckin Akcay¹⁵, Dilek Tuzun¹⁶, Gulay Simsek Bagir¹⁷, Filiz Eksi Haydardedeoglu¹⁷, Gulsah Elbuken¹⁸, Goknur Yorulmaz¹⁹, Ozlem Celik²⁰, Murat Topbas²¹

Exp Clin Endocrinol Diabetes. 2021 Mar 10. Online ahead of print. PMID: 33694151 DOI: 10.1055/a-1400-2668

Objectives: This study aimed to evaluate the current situation of hypoparathyroid patients and to investigate the relationship between treatment adherence and quality of life.

Study design: Prospective, multicentre study.

Methods: Adult patients presenting with the diagnosis of hypoparathyroidism to 20 different endocrinology clinics were included. They were receiving conventional therapies for hypoparathyroidism, using calcium, active vitamin D, and magnesium. We collected data on demographic features, disease- and treatment-related information, and results of routine laboratory tests, treatment adherence, and presence of complications. Beck Depression Inventory, Beck Anxiety Inventory, and Short Form-36 quality of life assessments were administered.

Results: Among the 300 patients studied, 60.7% were adherent to their treatment, and 34.1% had complications. Anxiety and depression scores were significantly higher in non-adherent versus treatment-adherent patients ($p<0.001$ and $p=0.001$, respectively). Most of the domains of quality-of-life scores were also significantly lower in non-adherent patients. Both anxiety and depression scores showed significant, negative correlations with serum calcium and magnesium concentrations ($r=-0.336$, $p<0.001$ and $r=-0.258$, $p<0.001$, respectively).

Conclusions: Nearly 40% of the patients were non-adherent to conventional treatment for hypoparathyroidism, and such patients had higher anxiety and depression scores and poorer quality of life scores. Conventional treatment might not be sufficient to meet the needs of patients with hypoparathyroidism. In addition to seeking new therapeutic options, factors influencing quality of life should also be investigated and strategies to improve treatment adherence should be developed.

LONG-TERM EXPOSURE TO OUTDOOR AND HOUSEHOLD AIR POLLUTION AND BLOOD PRESSURE IN THE PROSPECTIVE URBAN AND RURAL EPIDEMIOLOGICAL (PURE) STUDY

Raphael E Arku¹, Michael Brauer², Suad H Ahmed³, Khalid F AlHabib⁴, Álvaro Avezum⁵, Jian Bo⁶, Tarzia Choudhury⁷, Antonio MI Dans⁸, Rajeev Gupta⁹, Romaina Iqbal¹⁰, Noorhassim Ismail¹¹, Roya Kelishadi¹², Rasha Khatib¹³, Teo Koon¹⁴, Rajesh Kumar¹⁵, Fernando Lanas¹⁶, Scott A Lear¹⁷, Li Wei⁶, Patricio Lopez-Jaramillo¹⁸, Viswanathan Mohan¹⁹, Paul Poirier²⁰, Thandi Puoane²¹, Sumathy Rangarajan¹⁴, Annika Rosengren²², Biju Soman²³, Ozge Telci Caklili²⁴, Shunyun Yang²⁵, Karen Yeates²⁶, Lu Yin⁶, Khalid Yusoff²⁷, Tomasz Zatoński²⁸, Salim Yusuf¹⁴, Perry Hystad²⁹

Environ Pollut. 2020 Jul;262:114197. Epub 2020 Feb 24. PMID: 32146361 PMCID: PMC7767575 DOI: 10.1016/j.envpol.2020.114197

Exposure to air pollution has been linked to elevated blood pressure (BP) and hypertension, but most research has focused on short-term (hours, days, or months) exposures at relatively low concentrations. We examined the associations between long-term (3-year average) concentrations of outdoor PM_{2.5} and household air pollution (HAP) from cooking with solid fuels with BP and hypertension in the Prospective Urban and Rural Epidemiology (PURE) study. Outdoor PM_{2.5} exposures were estimated at year of enrollment for 137,809 adults aged 35-70 years from 640 urban and rural communities in 21 countries using satellite and ground-based methods. Primary use of solid fuel for cooking was used as an indicator of HAP exposure, with analyses restricted to rural participants (n = 43,313) in 27 study centers in 10 countries. BP was measured following a standardized procedure and associations with air pollution examined with mixed-effect regression models, after adjustment for a comprehensive set of potential confounding factors. Baseline outdoor PM_{2.5} exposure ranged from 3 to 97 $\mu\text{g}/\text{m}^3$ across study communities and was associated with an increased odds ratio (OR) of 1.04 (95% CI: 1.01, 1.07) for hypertension, per 10 $\mu\text{g}/\text{m}^3$ increase in concentration. This association demonstrated non-linearity and was strongest for the fourth (PM_{2.5} >62 $\mu\text{g}/\text{m}^3$) compared to the first (PM_{2.5} <14 $\mu\text{g}/\text{m}^3$) quartiles (OR = 1.36, 95% CI: 1.10, 1.69). Similar non-linear patterns were observed for systolic BP (β = 2.15 mmHg, 95% CI: -0.59, 4.89) and diastolic BP (β = 1.35, 95% CI: -0.20, 2.89), while there was no overall increase in ORs across the full exposure distribution. Individuals who used solid fuels for cooking had lower BP measures compared to clean fuel users (e.g. 34% of solid fuels users compared to 42% of clean fuel users had hypertension), and even in fully adjusted models had slightly decreased odds of hypertension (OR = 0.93; 95% CI: 0.88, 0.99) and reductions in systolic (-0.51 mmHg; 95% CI: -0.99, -0.03) and diastolic (-0.46 mmHg; 95% CI: -0.75, -0.18) BP. In this large international multi-center study, chronic exposures to outdoor PM_{2.5} was associated with increased BP and hypertension while there were small inverse associations with HAP.

IMPACT OF A HIGH VISCERAL ADIPOSITY INDEX ON FEMALE SEXUAL DYSFUNCTION IN SEXUALLY ACTIVE WOMEN? RESULTS OF A CROSS-SECTIONAL STUDY

Ramazan Asci¹, Mustafa Suat Bolat², Cihad Dünder³, Ayşe Zehra Özdemir⁴, Ayşegül Atmaca⁵

Int J Clin Pract. 2021 Oct;75(10):e14611. doi: 10.1111/ijcp.14611. Epub 2021 Jul 20. PMID: 34235836 DOI: 10.1111/ijcp.14611

Aims: To our knowledge, this is the first study investigating the impact of high visceral adiposity index (VAI) on female sexual dysfunction (FSD). We aimed to show the impact of increased levels of VAI on FSD compared with body mass index (BMI) and waist circumference (WC) particularly in those with metabolic syndrome (MeTS).

Methods: We included 158 participants in two groups: Group 1 (n = 68 with normal sexual function) and Group 2 (n = 90 with sexual dysfunction). Demographic, clinic data, presence of MeTS and comorbidities were recorded. The BMI, WC and the VAI were calculated. Sexual function was assessed using the female sexual function index.

Results: The mean age and all the anthropometric variables were similar between the groups (P > .05). MeTS was associated with lower arousal and lubrication scores than those without MeTS (P = .023). The higher VAI was associated with lower desire, lubrication and orgasm scores (P < .05). Each integer increase of the VAI weakly predicted decrease of desire (P = .015), arousal (P = .015), lubrication (P = .005) and satisfaction (P = .046). The WC and BMI were not a good predictor for FSD in women (OR=1.019, P = .318).

Conclusion: The VAI was linked with lower scores in some female sexual function subdomains, but the correlation coefficient was low, indicating a weak association. Further studies with a higher number of participants are needed to conclude that the VAI may increase the risk of FSD, particularly in patients with MeTS.

NO ASSOCIATION OF ANTI-OSTEOPOROSIS DRUGS WITH COVID-19-RELATED OUTCOMES IN WOMEN: A NATIONWIDE COHORT STUDY

A Atmaca¹, I Demirci², C Haymana², I Tasci³, I Sahin⁴, E Cakal⁵, N Ata⁶, S Dagdelen⁷, S Salman⁸, R Emral⁹, M Sahin⁹, O Celik¹⁰, T Demir¹¹, D Ertugrul¹², U Unluturk⁷, M Caglayan¹³, I Satman^{14,15}, A Sonmez¹⁶

Osteoporos Int. 2021 Aug 17;1-10. Online ahead of print. PMID: 34402949 PMCID: PMC8369875 DOI: 10.1007/s00198-021-06067-2

This study was performed to evaluate whether the use of drugs in the treatment of osteoporosis in women is associated with COVID-19 outcomes. The results showed that the risk of hospitalization, intensive care unit admission, and mortality was not altered in individuals taking anti-osteoporosis drugs, suggesting no safety issues during a COVID-19 infection.

Introduction: Whether patients with COVID-19 receiving anti-osteoporosis drugs have lower risk of worse outcomes has not been reported yet. The aim of this study was to evaluate the association of anti-osteoporosis drug use with COVID-19 outcomes in women.

Methods: Data obtained from a nationwide, multicenter, retrospective cohort of patients diagnosed with COVID-19 from March 11th to May 30th, 2020 was retrieved from the Turkish Ministry of Health Database. Women 50 years or older with confirmed COVID-19 who were receiving anti-osteoporosis drugs were compared with a 1:1 propensity score-matched COVID-19 positive women who were not receiving these drugs. The primary outcomes were hospitalization, ICU (intensive care unit) admission, and mortality.

Results: A total of 1997 women on anti-osteoporosis drugs and 1997 control patients were analyzed. In the treatment group, 1787 (89.5%) women were receiving bisphosphonates, 197 (9.9%) denosumab, and 17 (0.9%) teriparatide for the last 12 months. Hospitalization and mortality rates were similar between the treatment and control groups. ICU admission rate was lower in the treatment group (23.0% vs 27.0%, $p = 0.013$). However, multivariate analysis showed that anti-osteoporosis drug use was not an independent associate of any outcome. Hospitalization, ICU admission, and mortality rates were similar among bisphosphonate, denosumab, or teriparatide users.

Conclusion: Results of this nationwide study showed that preexisting use of anti-osteoporosis drugs in women did not alter the COVID-19-related risk of hospitalization, ICU admission, and mortality. These results do not suggest discontinuation of these drugs during a COVID-19 infection.

MODIFYING EFFECTS OF GLUCOSE AND INSULIN/INSULIN-LIKE GROWTH FACTORS ON COLON CANCER CELLS

Şeyda Berk^{1,2}, Joseph A M J L Janssen², Peter M van Koetsveld², Fadime Dogan², Naci Değerli¹, Servet Özcan^{3,4}, Fahrettin Kelestimur^{3,5}, Leo J Hofland²
Front Oncol. 2021 Jul 5;11:645732. eCollection 2021. PMID: 34290976 PMCID: PMC8287530 DOI: 10.3389/fonc.2021.645732

There are only a few experimental studies which have investigated effects of glucose alone, and glucose in combination with insulin/insulin-like growth factors (IGF) on the growth of colon cancer. In the present study, we studied *in vitro* in human colorectal cancer cells originating from four Dukes' stages of colorectal cancer the effects of glucose, insulin and IGFs on proliferation, migration, cell cycle progression and gene expression of the IGF system. Growth of colon cancer cells originating from a Dukes' stage A was glucose-dependent, whereas growth of cancer cells from Dukes' stage B, C and D was glucose-independent. Stimulatory effects of insulin and IGFs on cell growth were observed only in colon cancer cells originating from Dukes' stage C and D. IGF-II stimulated migration in Dukes' stage B cells only. The growth stimulatory effects in Dukes' stage C and D colorectal cancer cells were accompanied by G2/M arrest and associated with an increased IGF-IR/IGF-II receptor ratio. In conclusion, our *in vitro* data suggest that the stimulating effects of glucose, IGFs and insulin on proliferation differ between colorectal cancer cells from early and late Dukes' stages. Stimulatory effects of glucose on proliferation appear predominantly present in stage Dukes' stage A colorectal cancer cells, while in contrast growth factor-mediated stimulation of cell proliferation is more pronounced in Dukes' late stage (metastasized) colorectal cancer cells.

Moreover, our study suggests that a stringent glucose control may be important to control tumor growth in early stages of colorectal cancer, while inhibition of the endocrine actions of the IGFs and insulin become more important in the late (metastasized) stages of colorectal cancer to restrain growth of colon cancer cells.

TWO IMPORTANT ISSUES IN SUBACUTE THYROIDITIS MANAGEMENT: DELAYED DIAGNOSIS AND INAPPROPRIATE USE OF ANTIBIOTICS

Hayri Bostan¹, Muhammed Erkam Sencar¹, Murat Calapkulu¹, Sema Hepsen¹, Hakan Duger¹, İlknur Ozturk Unsal¹, Mustafa Ozbek¹, Erman Cakal¹
Eur Thyroid J. 2021 Jul;10(4):323-329. Epub 2021 Mar 18. PMID: 34395304 PMCID: PMC8314756 (available on 2022-01-01) DOI: 10.1159/000513745

Background: Subacute thyroiditis (SAT) is a rare inflammatory disease of the thyroid gland. It has been noticed that patients with a diagnosis of SAT visit more other clinics and receive antibiotics unnecessarily. Therefore, the aim of this study was to reveal the degree of delay in the diagnosis of SAT, prediagnosis antibiotic use rates, and the awareness of clinics for the diagnosis of SAT.

Methods: A total of 121 patients with SAT were enrolled in the study. A retrospective analysis was made of the history of patient symptoms during the diagnosis, which physicians they visited, antibiotic use, laboratory test results, and ultrasonographic findings.

Results: The median age of the patients was 41 years. Neck pain radiating to the jaw/ear was seen in most patients (71.1%). The median time from symptom onset to a diagnosis of SAT was 23 days (range, 6-70 days). Antibiotics were erroneously prescribed to 71 patients (58.7%) before the diagnosis. The median time to diagnosis was 28 days in patients using antibiotics and 20 days in the group not using antibiotics ($p < 0.001$). Two or more physicians had been visited before SAT diagnosis by 89 (73.6%) patients, and more antibiotics were prescribed to these patients than the group who visited fewer physicians ($p < 0.05$). The frequency of prescribing antibiotics by physicians was 73.7% by emergency physicians, 53.1% by family doctors, 51.1% by ENT specialists, and 35.4% by internal medicine specialists.

Conclusion: The diagnosis of SAT is often delayed, and misdiagnosis leads to erroneous antibiotic overuse. Physicians should increase their awareness of the diagnosis of SAT in patients with neck pain.

ULTRASONOGRAPHIC EVALUATION OF SHOULDER TENDONS IN PATIENTS WITH HASHIMOTO'S DISEASE

Dilek Eker Buyuksireci¹, Duygu Tecer², Basak Bolayir³, Merve Ecem Erdogan Yon⁴, Mujde Akturk⁵, Zafer Gunendi⁶, Feride Gogus⁶
Int J Rheum Dis. 2020 Nov;23(11):1497-1504. Epub 2020 Sep 3. PMID: 32885607 DOI: 10.1111/1756-185X.13956

Objectives: To investigate the thickness of the shoulder tendons and the measurement of acromiohumeral distance (AHD) in patients with Hashimoto's disease (HD).

Material and methods: Twenty-eight patients with subclinical hypothyroid HD, 40 patients with euthyroid HD, and 51 healthy subjects were included. The thicknesses of biceps brachii, subscapularis, supraspinatus, infraspinatus tendons at both shoulders were evaluated with ultrasonography. Serum levels of thyroid stimulated hormone (TSH), free triiodothyronine, free thyroxine (FT4), anti-thyroid peroxidase (TPO) and anti-thyroglobulin (anti-TG) antibodies levels were measured.

Results: Height, weight, body mass index (BMI), free T3 and free T4 levels were similar between the three groups ($P = .839$, $P = .205$, $P = .374$, $P = .430$ and $P = .497$, respectively). Biceps brachii, supraspinatus and infraspinatus tendon thicknesses in dominant arm and biceps brachii, subscapularis and infraspinatus tendon thicknesses in non-dominant arm were significantly increased in euthyroid HD compared to healthy controls ($P = .003$, $P = .030$, $P < .001$; $P = .035$, $P = .042$, $P < .001$, respectively). Biceps brachii tendon thickness in dominant arm and subscapularis and supraspinatus tendon thicknesses in non-dominant arms were significantly increased in subclinical hypothyroid HD compared to healthy controls ($P = .025$; $P = .046$, $P = .017$, respectively). However there was no such difference between euthyroid HD and subclinical hypothyroid HD groups ($P < .05$). There was low correlation between biceps brachii tendon thickness and free T4 level in non-dominant shoulder in patients with HD ($r = .272$ $P = .030$). For the rest of the tendons, there was no correlation between TSH, anti-TPO, anti-TG levels and tendon thicknesses in patients with HD.

Conclusions: This study suggests that thyroid autoimmunity in HD may lead to an increase in thickness of shoulder tendons.

LONG-TERM OUTCOMES OF TAMOXIFEN CITRATE THERAPY AND HISTO- AND IMMUNOPATHOLOGICAL PROPERTIES IN RIEDEL THYROIDITIS

Aseña Gökçay Canpolat¹, Murat Cinel¹, Serpil Dizbay Sak², Işıl Tayşaldıran³, Hakan Korkmaz⁴, Özgür Demir¹, Reyhan Ersoy⁵, Selçuk Dağdelen⁶, Dilek Berker⁷, Klara Dalva⁸, Adile Begüm Bahçeciöglü Mutlu¹, Murat Faik Erdoğan¹

Eur Thyroid J. 2021 Jun;10(3):248-256. Epub 2020 Dec 8. PMID: 34178711 PMID: PMC8216025 (available on 2021-12-01) DOI: 10.1159/000512017

Background: Riedel thyroiditis (RT) is a rare form of thyroiditis; thus, data about the disease course and treatment options are limited. Therefore, we aimed to assess the clinical, serological, radiological, and histopathological features, as well as short- and long-term follow-up of RT patients under glucocorticoid (GC) and tamoxifen citrate (TMX). Parameters related to IgG4-related diseases (IgG4-RD) were also investigated.

Methods: Eight patients with RT diagnosed between 2000 and 2019 were enrolled. Data were collected in a retrospective and prospective manner. The diagnosis was confirmed with histopathological features in all patients. Results of the treatment with GCs on short- to mid-term, followed by TMX in the long term, were evaluated.

Results: The mean age at diagnosis was 40.5 ± 6.8 years; female predominance was observed (F/M:7/1). Parameters related to IgG4-RD, like increase in IgG4 serum levels, total

plasmablast counts, and IgG4+ plasmablasts, were negative in most of our patients in both active and inactive states of the disease. Likewise, an increased ratio of IgG4/IgG-positive plasma cells $>40\%$ could only be observed in 2 cases. GCs followed by TMX were given to the patients with an over-all median follow-up time of 67 (8-216) months. All the patients considerably improved clinically and had a reduction in the size of the mass lesion on GCs, followed by TMX therapy. None of the patients had a recurrence under TMX therapy for a median period of 18.5 (7-96) months.

Conclusion: Even though RT is suggested to be a member of IgG4-RD, serologic or histological evidence of IgG4 elevation or positivity is only useful for diagnosis and follow-up of RT. The diagnosis should be based on clinical and radiological evidence and confirmed by histopathology. GCs are effective for initial treatment, and TMX is a successful and safe therapeutic option for long-term maintenance therapy.

USE OF INSULIN DEGLUDEC/INSULIN ASPART IN THE MANAGEMENT OF DIABETES MELLITUS: EXPERT PANEL RECOMMENDATIONS ON APPROPRIATE PRACTICE PATTERNS

Tevfik Demir¹, Serap Turan², Kursad Unluhizarci³, Oya Topaloglu⁴, Tufan Tukek⁵, Dilek Gogas Yavuz⁶

Front Endocrinol (Lausanne). 2021 Mar 12;12:616514.2021.616514. eCollection 2021. PMID: 33776914 PMID: PMC7996092 DOI: 10.3389/fendo.2021.616514

Insulin degludec/insulin aspart (IDegAsp) is a fixed-ratio co-formulation of insulin degludec (IDeg), which provides long-lasting basal insulin coverage, and insulin aspart (IAsp), which targets post-prandial glucose. This expert panel aimed to provide a practical and implementable guidance document to assist clinicians in prescribing IDegAsp in the diabetes management with respect to different patient populations including children and adults with type 1 diabetes (T1D) or type 2 diabetes (T2D) as well as pregnant, elderly and hospitalized patients and varying practice patterns (insulin-naïve, insulin-treated, switching from basal, basal bolus and premix regimens). The experts recommended that IDegAsp can be used in insulin-naïve T2D patients with poor glycemic control (HbA1c $>8.5\%$) despite optimal oral antidiabetic drugs (OADs) as well as in insulin-treated T2D patients by switching from basal insulin, basal-bolus therapy or premixed insulins in relation to lower risk of nocturnal hypoglycemia, fewer injections and lower intraday glycemic variability, respectively. The experts considered the use of IDegAsp in children with T2D as a basal bolus alternative rather than as an alternative to basal insulin after metformin failure, use of IDegAsp in adult T1D patients as a simplified basal bolus regimen with lesser nocturnal hypoglycemia, fewer injections and better fasting plasma glucose control and in children with T1D as an alternative insulin regimen with fewer injection to increase treatment adherence. The proposed expert opinion provides practical information on use of IDegAsp in different patient populations and practice patterns to assist clinicians, which seems to compensate the need for easily implementable guidance on this novel insulin regimen.

CLINICOPATHOLOGICAL VARIABLES THAT CORRELATE WITH SESTAMIBI POSITIVITY IN UNIGLANDULAR PARATHYROID DISEASE: A RETROSPECTIVE ANALYSIS OF 378 PARATHYROID ADENOMAS

Elif Tutku Durmuş¹, Ayşegül Atmaca², Mehmet Kefeli³, Özgür Mete^{4,5}, Fevziye Canbaz Tosun⁶, Deniz Bayçelebi³, Cafer Polat⁷, Ramis Çolak²
Ann Nucl Med. 2021 Sep 28. Online ahead of print. PMID: 34580842 DOI: 10.1007/s12149-021-01681-w

Purpose: Technetium-99 m sestamibi parathyroid scintigraphy (MIBI scan) has been used to localize abnormal glands in patients with primary hyperparathyroidism to guide parathyroidectomy. This series aimed to identify the biochemical and histopathological correlates of MIBI scan findings in patients with parathyroid adenoma.

Methods: A total of 378 patients with histologically and biochemically proven parathyroid adenoma were included. The results of MIBI scan, histopathological (gland volume and weight, oxyphil cell ratio), biochemical (blood and 24 h urine calcium, creatinine, glomerular filtration rate, parathormone, alkaline phosphate, and vitamin D3) variables were recorded. A positive uptake on the MIBI scan referred to a localized adenoma. Among histological variables, a cutoff of 30% was applied to define parathyroid adenomas with low ($\leq 30\%$) and high ($> 30\%$) oxyphil cell content. Statistical analyses were performed to assess the relationship among variables.

Results: MIBI scan localized the adenoma in 306 patients. Parathyroid gland volume and weight, and oxyphil ratio were significantly higher in the MIBI scan-positive group. Among the biochemical variables, only PTH was found to be significantly increased in the MIBI scan-positive group. Binary logistic regression models identified statistically significant cutoffs for the gland volume (1700 mm³), gland weight (1.3 g) and PTH levels (170 pg/mL) that can be used to predict the MIBI scan positivity.

Conclusion: In addition to PTH levels, this series underscored the impact of cellular composition along with the parathyroid gland volume and weight, both of which correlate with sestamibi positivity in patients with benign uniglandular parathyroid disease.

LOWER COVID-19 MORTALITY IN PATIENTS WITH TYPE 2 DIABETES MELLITUS TAKING DIPEPTIDYL PEPTIDASE-4 INHIBITORS: RESULTS FROM A TURKISH NATIONWIDE STUDY

Rifat Emral¹, Cem Haymana², Ibrahim Demirci², Ilker Tasci³, Mustafa Sahin⁴, Erman Cakal⁵, Naim Ata⁶, Ugur Unluturk⁷, Tefvik Demir⁸, Derun Ertugrul⁹, Ibrahim Sahin¹⁰, Aysegül Atmaca¹¹, Osman Celik¹², Murat Caglayan¹³, Kazim Yalcin Arga^{14,15}, Selcuk Dagdelen⁷, Serpil Salman¹⁶, Ilhan Satman^{15,17}, Alper Sonmez¹⁸

Diabetes Ther. 2021 Aug 16;1-14. Online ahead of print. PMID: 34398433 PMCID: PMC8365288 DOI: 10.1007/s13300-021-01133-8

Introduction: To investigate the effect of preexisting treatment with dipeptidyl peptidase-4 inhibitors (DPP-4is) on COVID-19-related hospitalization and mortality in patients with type 2 diabetes mellitus (T2DM).

Methods: A multicenter, retrospective cohort study was conducted using patient data extracted from the Turkish National Electronic Database. All patients who tested positive for COVID-19 (PCR test) between 11 March through to 30 May 2020 were screened for eligibility (n = 149,671). Following exclusion of patients based on pre-determined inclusion criteria, patients with T2DM using a DPP-4i or glucose-lowering medications other than a DPP-4i were compared for mortality and hospitalization. The propensity score method was used to match age, gender, micro- and macrovascular complications, and medications in the two groups. Independent associates of mortality were analyzed using multivariable analysis on the whole T2DM population.

Results: A total of 33,478 patients with T2DM who tested positive for COVID-19 who met the inclusion criteria were included in the analysis. Median (interquartile range) age was 54 (22) years and 42.4% were male. Of these, 9100 patients using DPP-4is (n = 4550) or other glucose-lowering drugs (n = 4550) were matched in two groups. After matching, analysis revealed a lower mortality in the DPP-4i group (9.5 vs. 11.8%; p < 0.001). In the multivariable model, the use of DPP-4is (odds ratio [OR] 0.57, 95% confidence interval [CI] 0.35-0.91; p = 0.02) was associated with lower mortality in the whole sample, while age, male gender, computed tomography finding of COVID-19, obesity, low glomerular filtration rate, and an insulin-based regimen also predicted increased risk of death. There was no association between the preexisting treatment with DPP-4is and COVID-19-related hospitalization in the matched analysis or multivariate model. The rate of admission to the intensive care unit and/or mechanical ventilation favored the DPP-4i group (21.7 vs. 25.2%; p = 0.001), although this association became saturated in the multivariate analysis (OR 0.65, 95% CI 0.39-1.08; p = 0.099).

Conclusions: The results of this study demonstrate an association between DPP-4i use and reduced mortality in people with T2DM who tested PCR positive for COVID-19.

DNA REPAIR PROTEINS MAY DIFFERENTIATE PAPILLARY THYROID CANCER FROM CHRONIC LYMPHOCYTIC THYROIDITIS AND NODULAR COLLOIDAL GOITER

Bahri Evren¹, Sami Yılmaz², Neşe Karadağ³, Ayşe Çıkım Sertkaya⁴, Ömercan Topaloğlu⁵, Faruk Kılınç⁶
Sci Rep. 2021 May 11;11(1):9932. PMID: 33976347 PMCID: PMC8113225 DOI: 10.1038/s41598-021-89403-0

Malignant thyroid lesions are the most common malignancy of the endocrine glands with increasing rates in the last two decades. Papillary thyroid cancer is the most common thyroid malignancy. In our study, we aimed to quantitatively evaluate the levels of DNA repair proteins MSH2, MLH1, MGMT, which are representative blocks of patients diagnosed with papillary carcinoma, chronic thyroiditis, or colloidal goiter. Total or subtotal thyroidectomy material of 90 patients diagnosed with papillary carcinoma, nodular colloidal goiter, or chronic thyroiditis between 2009 and 2012 were retrospectively evaluated. Tissue samples obtained from paraffin blocks were stained with MGMT, MSH2, MLH1 proteins and their

immunohistochemistry was evaluated. Prepared sections were examined qualitatively by an impartial pathologist and a clinician, taking into account the staining method under the trinocular light microscope. Although there was no statistically significant difference in MGMT, MSH2, MLH1, follicular cell positivity, staining intensity, and immunoreactivity values, papillary carcinoma cases showed a higher rate of follicular cell positivity, and this difference was more pronounced between papillary carcinoma and colloid goiter. In the MSH2 follicular cell positivity evaluation, the difference between chronic thyroiditis and colloid goiter was significant ($p = 0.023$). The difference between chronic thyroiditis and colloid goiter was significant in the MSH2 staining intensity evaluation ($p = 0.001$). The difference between chronic thyroiditis and colloid goiter was significant in MLH1 immunoreactivity evaluation ($p = 0.012$). Papillary carcinoma cases were demonstrated by nuclear staining only for MSH2 and MLH1 proteins as opposed to hyperplastic nodules. The higher levels of expression of DNA repair genes in malignant tumors compared to benign tumors are attributed to the functional activation of DNA repair genes. Further studies are needed for DNA repair proteins to be a potential test in the development and progression of thyroid cancer.

GUT MICROBIOTA IN PATIENTS WITH NEWLY DIAGNOSED ACROMEGALY: A PILOT CROSS-SECTIONAL STUDY

Aysa Hacioglu¹, Ayca Gundogdu²³, Ufuk Nalbantoglu³⁴, Zuleyha Karaca¹, Muhammed Emre Urhan¹, Serdar Sahin⁵, Hatice Sebile Dokmetas⁶, Pinar Kadioglu⁵, Fahrettin Kelestimur⁷, Pituitary Microbiom Study Group (PITMIT-SG)
Pituitary. 2021 Aug;24(4):600-610. Epub 2021 Mar 15. PMID: 33721175 DOI: 10.1007/s11102-021-01137-4

Purpose: Microbiota has crucial biological importance for human well-being. Bidirectional interaction exists between microbiota and the host, and there have been no studies investigating this interaction in patients with acromegaly. We aimed to analyze the composition of microbiota in patients with newly diagnosed acromegaly.

Method: Stool samples were obtained from the patients with newly diagnosed acromegaly in the Endocrinology Clinic of Erciyes University Medical School. The composition of microbiota was analyzed, and the results were compared to healthy volunteers matched to the patients in terms of age, gender and body mass index.

Results: Seven patients (three male, four female) with a mean age of 48 ± 17.6 years were included in the study. The stool analysis revealed a significantly lower bacterial diversity in the patients with acromegaly. Bacteroidetes phylum was predominating in the patient group, and Firmicutes/Bacteroidetes ratio was altered significantly. Bifidobacterium, Collinsella, Bacteroides, Butyrivibrio, Clostridium, Oscillospira, and Dialister were predominating in the control group.

Conclusion: The gut microbiota is significantly altered in patients with newly diagnosed acromegaly. Further prospective studies are needed to elucidate the causative relationship between acromegaly, colorectal pathologies, and microbial alterations.

CLINICAL OUTCOMES OF NON-DIABETIC COVID-19 PATIENTS WITH DIFFERENT BLOOD GLUCOSE LEVELS: A NATIONWIDE TURKISH STUDY (TURCOGLYCEMIA)

Cem Haymana¹, Ibrahim Demirci², Ilker Tasci³, Erman Cakal⁴, Serpil Salman⁵, Derun Ertugrul⁶, Naim Ata⁷, Ugur Unluturk⁸, Selcuk Dagdelen⁸, Aysegül Atmaca⁹, Mustafa Sahin¹⁰, Osman Celik¹¹, Tefvik Demir¹², Rifat Emral¹⁰, Ibrahim Sahin¹³, Murat Caglayan¹⁴, Ilhan Satman^{15,16}, Alper Sonmez¹⁷
Endocrine. 2021 Aug;73(2):261-269. Epub 2021 Jun 22. PMID: 34156609 PMID: 8218282 DOI: 10.1007/s12020-021-02789-9

Purpose: New coronavirus disease 2019 (COVID-19) has a worse prognosis in patients with diabetes. However, there are insufficient data about the effect of hyperglycemia on COVID-19 prognosis in non-diabetic patients. This study aimed to investigate the relationship between random blood glucose levels measured at the time of diagnosis and prognosis of COVID-19 disease in non-diabetic patients.

Methods: A nationwide retrospective cohort of non-diabetic patients with confirmed COVID-19 infection from 11 March to 30 May 2020 in the Turkish Ministry of Health database was investigated. The patients were stratified into three groups according to blood glucose levels which were <100 mg/dL in group-1, in the range of 100-139 mg/dl in group-2, and the range of 140-199 mg/dl in group-3. Clinical characteristics and outcomes were compared among the groups. The primary outcome was mortality.

Results: A total of 12,817 non-diabetic patients (median age [IQR]: 44 [25] years, females: 50.9%) were included. Patients in group-2 (5%) and group-3 (14%) had higher mortality rates than patients in group-1 (2.1%). The rates of hospitalization, hospital stays longer than 8 days, intensive care unit (ICU) admission, ICU stay more than 6 days, and mechanical ventilation were also significantly higher in group-3 patients. Likewise, glucose levels in the range of 140-199 mg/dL were an independent associate of mortality and composite of ICU admission and/or mechanical ventilation.

Conclusion: Hyperglycemia at the time of COVID-19 diagnosis is associated with poor prognosis in non-diabetic patients. Clinicians should be more careful in the treatment of non-diabetic COVID-19 patients with hyperglycemia.

KLOTHO GENE G395A AND C1818T POLYMORPHISMS IN ACROMEGALY: ASSOCIATION WITH CLINICAL PRESENTATION AND COMORBIDITIES

Nafiye Helvacı¹, Serkan Kabacam², Selcuk Dagdelen¹, Incilay Lay³, Erdem Karabulut⁴, Melike Mut⁵, Mehmet Alikasifoglu², Tomris Erbas¹
Clin Endocrinol (Oxf). 2021 Apr;94(4):598-605. Epub 2020 Dec 9. PMID: 33296101 DOI: 10.1111/cen.14380

Background: Klotho is a new identified anti-ageing gene with tumour suppressor activities. Current data suggest that there is a tight relationship between Klotho protein and growth hormone (GH)/insulin-like growth factor-1 (IGF-1) axis.

Purpose: This study aimed to investigate the possible association of Klotho gene polymorphisms with acromegaly and to assess whether these polymorphisms contribute

to clinical characteristics, comorbidities and biochemical variables in these patients.

Methods: The study included 52 patients with acromegaly and 52 unrelated healthy subjects. The Klotho G395A and C1818T polymorphisms were assessed by Sanger sequencing. Serum levels of sKlotho were determined by ELISA method.

Results: Subjects carrying GA genotype of Klotho G395A polymorphism had 3.27 times higher risk of developing acromegaly [odds ratio (OR), 3.27; 95% confidence interval (CI): 1.37-7.81; $p = .023$]. The A allele of G395A was significantly associated with acromegaly risk (OR, 2.27; 95% CI: 1.1-4.72; $p = .022$). No association was observed between the studied polymorphisms and disease characteristics including age at acromegaly diagnosis, size of adenoma, baseline GH and IGF-1 concentrations, and final outcome. G395A polymorphism was associated with the presence of malignancy (OR, 2.24, 95% CI: 1.63-3.08; $p = .019$) and colorectal polyps (OR, 1.99; 95% CI: 1.02-3.88; $p = .047$) in patients with acromegaly. Serum sKlotho levels were significantly higher and correlated with GH and IGF-1 levels among acromegaly patients. There was no association between the studied polymorphisms and sKlotho levels.

Conclusions: Klotho G395A polymorphism is associated with acromegaly susceptibility and increased risk of malignancy and colorectal polyps in these patients.

THE ASSESSMENT OF VENTRICULAR ARRHYTHMIA INDICATORS BASED ON ELECTROCARDIOGRAPHY IN PATIENTS WITH DIFFERENTIATED THYROID CANCER FOLLOWED UP WITH LEVOTHYROXINE SUPPRESSION

Sema Hepsen¹, Davut Sakiz¹, Hilal Erken Pamukcu², Ismail Emre Arslan¹, Hakan Duger¹, Pinar Akhanli¹, Muhammed Erkam Sencar¹, Ilknur Ozturk Unsal¹, Bekir Ucan¹, Muhammed Kizilgul¹, Erman Cakal¹

Angiology. 2021 Aug;72(7):657-663. PMID: 33557584 DOI: 10.1177/0003319721993343 Epub 2021 Feb 9.

Levothyroxine suppression therapy (LST) can cause some unfavorable effects on the cardiovascular system in patients with differentiated thyroid cancer (DTC). The aim of this study was to evaluate ventricular arrhythmia predictors based on electrocardiography (ECG) in patients with DTC with LST. The ECG parameters including QT, corrected QT (QTc), Tp-e intervals, Tp-e/QT, and Tp-e/QTc ratios of 265 patients with DTC who met the inclusion criteria were compared with 100 controls. No difference was observed in the number of patients with DTC and controls with prolonged and borderline QTc interval ($P = .273$). Tp-e interval, Tp-e/QT, and Tp-e/QTc ratios were significantly higher in patients ($P = .002$, $P = .02$, $P = .003$; respectively). Linear regression analysis suggested that male gender was a predictor of higher Tp-e interval, Tp-e/QT, and Tp-e/QTc ratios ($\beta = 4.322$, $R^2 = 0.024$, $P = .042$; $\beta = 0.016$, $R^2 = 0.048$, $P = .005$; $\beta = 0.015$, $R^2 = 0.044$, $P = .006$, respectively). A higher serum fT4 level was found to be associated with a higher Tp-e/QT ratio ($\beta = 0.018$, $R^2 = 0.089$, $P = .007$). Ventricular arrhythmia indicators were found to be higher in patients with DTC with LST. Defining ventricular arrhythmia predictors

through ECG, an easily accessible cardiac diagnostic tool, can be potentially useful in raising awareness of the possible cardiac harm of LST.

THE EVALUATION OF LOW- AND HIGH-DOSE STEROID TREATMENTS IN SUBACUTE THYROIDITIS: A RETROSPECTIVE OBSERVATIONAL STUDY

Sema Hepsen¹, Pinar Akhanli², Muhammed Erkam Sencar², Hakan Duger², Davut Sakiz², Muhammed Kizilgul², Ilknur Ozturk Unsal², Bekir Ucan², Mustafa Ozbek², Erman Cakal²

Endocr Pract. 2021 Jun;27(6):594-600. Epub 2020 Dec 13. PMID: 34024631 DOI: 10.1016/j.eprac.2020.11.009

Objective: The optimal steroid regimen in the treatment of subacute thyroiditis (SAT) is controversial. This study aims to compare low- and high-dose steroid regimens in the treatment of SAT.

Methods: A single-center, retrospective observational cohort study with up to 1 year of follow-up was conducted. A total of 44 patients in the 16-mg methylprednisolone (MPS) group and 47 patients in the 48-mg MPS group were enrolled. Clinical and laboratory findings from the time of diagnosis to 1-year of the follow-up were assessed. Treatment response, recurrence, and hypothyroidism (HPT) rates were evaluated.

Results: Clinical symptoms, sedimentation rates, C-reactive protein, and thyroid hormone levels of the patients were similar in the 2 groups. Recovery was achieved in all patients at the end of the treatments; however, treatment duration needed to be extended for 6 (13.6%) and 1 (2.1%) of the patients in the 16-mg and 48-mg MPS groups, respectively. The 48-mg MPS group had a higher SAT recurrence rate than the 16-mg MPS group ($P = .04$). Logistic regression analysis suggested that a lower thyroid-stimulating hormone level at the end of the treatment was a predictor of recurrence ($\beta = -0.544$, $P = .014$, 95% CI: 0.376-0.895). While the transient HPT rate was 10 (21.3%) and 10 (22.7%) in the 48-mg and 16-mg MPS groups, respectively, a permanent HPT developed in 5 (10.6%) of patients in the 48-mg MPS and 3 (6.8%) in the 16-mg MPS group. The permanent and transient HPT rates were determined to be similar in the low- and high-dose groups ($P > .05$).

Conclusion: Low-dose steroid therapy may be sufficient to achieve a complete recovery and better outcomes in SAT.

THREE CASES OF SUBACUTE THYROIDITIS FOLLOWING SARS-COV-2 VACCINE: POSTVACCINATION ASIA SYNDROME

Burçin Gönül İremli¹, Süleyman Nahit Şendur¹, Uğur Ünlütürk¹

J Clin Endocrinol Metab. 2021 Aug 18;106(9):2600-2605. doi: 10.1210/clinem/dgab373. PMID: 34043800 PMCID: PMC8194612 DOI: 10.1210/clinem/dgab373

Context: Autoimmune/inflammatory syndrome induced by adjuvants (ASIA syndrome) can be seen as a postvaccination phenomenon that occurs after exposure to adjuvants in vaccines that increase the immune responses. There are very limited data regarding ASIA syndrome following severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) vaccines.

Objectives: This work aims to report cases of subacute thyroiditis related to the SARS-CoV-2 vaccine.

Methods: We describe the clinical, laboratory, and imaging features of 3 cases of subacute thyroiditis after inactivated SARS-CoV-2 vaccine (CoronaVac®). Three female healthcare workers have applied to our clinic with anterior neck pain and fatigue 4 to 7 days after SARS-CoV-2 vaccination. Two of them were in the breastfeeding period. They were negative for thyroid antibodies, and there was no previous history of thyroid disease, upper respiratory tract infection, or COVID-19. Laboratory test results and imaging findings were consistent with subacute thyroiditis.

Results: SARS-CoV-2 vaccination can lead to subacute thyroiditis as a phenomenon of ASIA syndrome. Subacute thyroiditis may develop within a few days after the SARS-CoV-2 vaccination. Being in the postpartum period may be a facilitating factor for the development of ASIA syndrome after the SARS-CoV-2 vaccination.

Conclusions: This is the first report of subacute thyroiditis as a phenomenon of ASIA syndrome after inactivated COVID-19 vaccination. Clinicians should be aware that subacute thyroiditis may develop as a manifestation of ASIA syndrome after the inactive SARS-CoV-2 vaccine.

INVESTIGATION OF THE HYPOTHALAMO-PITUITARY-ADRENAL (HPA) AXIS: A CONTEMPORARY SYNTHESIS

Zuleyha Karaca¹, Ashley Grossman^{2,3}, Fahrettin Kelestimur⁴

Rev Endocr Metab Disord. 2021 Jun;22(2):179-204. Epub 2021 Mar 26. PMID: 33770352 DOI: 10.1007/s11154-020-09611-3

The hypothalamo-pituitary-adrenal (HPA) axis is one of the main components of the stress system. Maintenance of normal physiological events, which include stress responses to internal or external stimuli in the body, depends on appropriate HPA axis function. In the case of severe cortisol deficiency, especially when there is a triggering factor, the patient may develop a life-threatening adrenal crisis which may result in death unless early diagnosis and adequate treatment are carried out. The maintenance of normal physiology and survival depend upon a sufficient level of cortisol in the circulation. Life-long glucocorticoid replacement therapy, in most cases meeting but not exceeding the need of the patient, is essential for normal life expectancy and maintenance of the quality of life. To enable this, the initial step should be the correct diagnosis of adrenal insufficiency (AI) which requires careful evaluation of the HPA axis, a highly dynamic endocrine system. The diagnosis of AI in patients with frank manifestations is not challenging. These patients do not need dynamic tests, and basal cortisol is usually enough to give a correct diagnosis. However, most cases of secondary adrenal insufficiency (SAI) take place in a gray zone when clinical manifestations are mild. In this situation, more complicated methods that can simulate the response of the HPA axis to a major stress are required. Numerous studies in the assessment of HPA axis have been published in the world literature. In this review, the tests used in the diagnosis of secondary AI or in the investigation of suspected HPA axis insufficiency are discussed in detail, and in the light of this, various recommendations are made.

LOW SERUM URIC ACID PREDICTS RISK OF A COMPOSITE DISEASE ENDPOINT

Fatma Özpamuk-Karadeniz¹, Yusuf Karadeniz², Adnan Kaya³, Servet Altay⁴, Günay Can⁵, Altan Onat⁶

Medicina (Kaunas). 2021 Apr 8;57(4):361. PMID: 33917823 PMCID: PMC8068308 DOI: 10.3390/medicina57040361

Background and objectives: Mortality may increase in hypouricemia as well as in hyperuricemia. We assessed the predictive value of low serum uric acid (SUA) levels on the risk of overall mortality or a composite endpoint of death and nonfatal events.

Materials and Methods: In 1013 community-based middle-aged adults, free of uncontrolled diabetes and coronary heart disease at baseline, the association of sex-specific SUA tertiles with defined outcomes was evaluated prospectively by logistic regression, stratified to gender and presence of type-2 diabetes, using recent criteria.

Results: Totally, 43 deaths and additional incident nonfatal events in 157 cases were recorded at a median 3.4 years' follow-up. Multivariable linear regression disclosed SUA to be significantly associated among non-diabetic individuals positively with creatinine, triglycerides, and body mass index in women further with fasted glucose. In multivariable-adjusted logistic regression analysis, sex-specific dichotomized baseline uric acid (<5.1 and <4.1 mg/dL vs. higher values) significantly predicted the non-fatal events in the whole sample (relative risk (RR) 1.51 [95% confidence interval (CI) 1.02; 2.26]), as well as in men, while composite endpoint in the whole sample tended to rise (RR 1.38). Compared with the intermediate one, the top and bottom SUA tertiles combined tended to confer mortality risk (RR 2.40 [95% CI 0.89; 6.51]). Adverse outcomes in diabetic women were predicted by tertiles 2 and 3.

Conclusions: Inverse association of SUA with adverse outcomes, especially in men, is consistent with the involvement of uric acid mass in autoimmune activation. The positive association of uric acid with adverse outcomes in diabetic women is likely mediated by concomitant high-density lipoprotein dysfunction.

IMPACT OF LOCKDOWN COVID-19 ON METABOLIC CONTROL IN TYPE 2 DIABETES MELLITUS AND HEALTHY PEOPLE

Savas Karatas¹, Tijen Yesim², Selvihan Beysel³

Prim Care Diabetes. 2021 Jun;15(3):424-427. Epub 2021 Jan 9. PMID: 33441263 PMCID: PMC7834877 DOI: 10.1016/j.pcd.2021.01.003

Aims: The impact of prolonged COVID-19 lockdown on metabolic control in type 2 diabetes patients and healthy individuals has not exactly been known. We aimed to evaluate the change in body weight and metabolic control in type 2 diabetic and non-diabetic healthy subjects during the prolonged lockdown period.

Methods: Diabetic (n = 85), and age-and sex-matched non-diabetic subjects (n = 55) were included in this prospective study. Body mass index and metabolic parameters were compared between before and 6th months of lockdown.

Changes in values were evaluated using the difference before and after lockdown.

Results: Age (54.81 ± 10.53 vs. 52.61 ± 4.88 years), gender (female, 68.2% vs. 56.4%) and, BMI (33.44 ± 6.48 vs. 31.63 ± 3.57 kg/m²) were similar between groups ($p > 0.05$). Before and after lockdown, BMI increased both in non-diabetic (0.54 ± 0.95 kg) and diabetic groups (1.91 ± 5.48 kg) ($p > 0.05$). Increase in HbA1c was more in diabetic than in non-diabetic groups (0.71 ± 1.35 vs. $0.02 \pm 0.19\%$, $p = 0.002$). Glucose, LDL-C, and TG increased in diabetic (39.69 ± 74.69 , 7.60 ± 34.33 , and 58.21 ± 133.54 mg/dl, $p < 0.05$) whereas non significantly decreased in non-diabetic group (-0.51 ± 4.40 , -3.52 ± 14.53 , and -6.47 ± 41.77 mg/dl, respectively). After adjusting BMI, increase in blood glucose ($p = 0.021$), HbA1c ($p = 0.018$), and TG ($p = 0.041$) levels were more in diabetic than non-diabetic group. Duration of diabetes was an independent predictor of the change in HbA1c (OR: 1.2, 95% CI = 1.1-1.8, $p = 0.032$).

Conclusions: Body weight gain was observed in type 2 diabetic patients and healthy subjects. This is the first study to show that prolonged lockdown COVID-19 pandemic worsened glucose regulation and increased TG level in diabetes mellitus independent of weight gain.

THE METABOLIC EQUIVALENT BMI IN PATIENTS WITH FAMILIAL PARTIAL LIPODYSTROPHY (FPLD) COMPARED WITH THOSE WITH SEVERE OBESITY

Eden Koo¹², Maria C Foss-Freitas¹, Rasimcan Meral¹, Muhammet Ozer¹, Abdelwahab J Eldin¹, Baris Akinci¹³, Nicole Miller¹, Amy E Rothberg¹, Elif A Oral¹
Obesity (Silver Spring). 2021 Feb;29(2):274-278. PMID: 33491315 DOI: 10.1002/oby.23049

Objective: This study aimed to investigate the shortcoming of BMI as a measurement of adiposity in patients with familial partial lipodystrophy (FPLD).

Methods: Two different matching procedures were used to compare 55 FPLD versus control patients with severe obesity (N = 548 patients) to study the relationship between body weight, fat distribution, and metabolic diseases, such as diabetes mellitus, hypertriglyceridemia, and nonalcoholic steatohepatitis. In MATCH1, the patients with FPLD were matched to controls with obesity (OCs) by truncal mass, and in MATCH2, the patients with FPLD were matched to OCs with respect to glucose control.

Results: With MATCH1, the FPLD group had worse glycemic control (hemoglobin A1c $8.2\% \pm 1.6\%$ vs. $5.9\% \pm 0.9\%$), higher triglycerides ($884 \pm 1,190$ mg/dL vs. 139 ± 79 mg/dL), and lower leptin (20.5 ± 15.8 ng/mL vs. 41.9 ± 29.4 ng/mL, $P < 0.001$ for all comparisons). In MATCH2, metabolic comorbidity-matched FPLD patients had significantly lower BMI compared with OCs (29.5 ± 5.7 kg/m² vs. 38.6 ± 5.2 kg/m², $P < 0.001$).

Conclusions: Patients with FPLD with similar truncal mass have worse metabolic profiles than non-FPLD OCs. The differential BMI between the FPLD and OCs, when matched for their metabolic comorbidities, approximates 8.6 BMI units.

COULD THERE BE A ROLE OF SERUM ZONULIN INCREASE IN THE DEVELOPMENT OF HYPERCALCEMIA IN PRIMARY HYPERPARATHYROIDISM

Hakan Korkmaz¹, Fevziye Burcu Sirin², Bora Torus³

Endocrine. 2021 Apr;72(1):234-238. Epub 2020 Sep 28. PMID: 32989570 DOI: 10.1007/s12020-020-02504-0

Purpose: To evaluate the serum level of zonulin, which is an intestinal permeability (IP) biomarker, in primary hyperparathyroidism (PHPT) and to investigate the relationship between zonulin, calcium, and parathormone (PTH) levels.

Methods: The study included 34 healthy control (HC) and 39 patients with PHPT. Serum calcium, phosphorus, magnesium, creatinine, albumin, and 24 h urine calcium levels were measured in all groups. Serum levels of zonulin were measured quantitatively by enzyme-linked immunosorbent assay (ELISA). Urinary ultrasonography (to assess the presence of nephrolithiasis) and dual energy X-ray absorptiometry (to assess the presence of osteoporosis) were used to evaluate complications related to PTH.

Results: Serum zonulin levels were significantly higher in the PHPT group than the HC group ($p < 0.001$). Zonulin levels were significantly positively correlated with plasma PTH and serum calcium levels ($r = 0.600$, $p < 0.001$ and $r = 0.610$, $p < 0.001$; respectively). There was no correlation between serum zonulin levels and adenoma volume.

Conclusion: Serum zonulin level increases in patients with PHPT. Serum zonulin levels show a moderate/strong positive correlation with serum calcium and plasma PTH levels. This suggests that IP increase may play a role in the development of hypercalcemia in patients with PHPT.

ENDOTHELIAL DYSFUNCTION IN PATIENTS WITH ACROMEGALY AND IT'S ASSOCIATION WITH ENDOCAN

Seref Kul¹, Ozge Telci Caklili², Yasemin Tutuncu³, Fatma Betul Ozcan¹, Feyza Aksu¹, Omer Faruk Baycan¹, Adem Atici¹, Ummuhan Zeynep Bilgili⁴, Mumtaz Takir⁵, Mustafa Caliskan¹

Growth Horm IGF Res. 2021 Feb;56:101362. Epub 2020 Nov 2. PMID: 33221710 DOI: 10.1016/j.ghir.2020.101362

Objective: This study aims to assess endocan levels in patients with acromegaly who have active disease or disease in remission and to investigate a relation between endocan levels and endothelial dysfunction in these patients.

Design: The study is a case-control study. Study was conducted at Istanbul Medeniyet University Goztepe Training and Research Hospital between 2013 and 2019. Patients who were older than 18 years with acromegaly diagnosis were recruited if they agreed to participate. Patients with uncontrolled diabetes (DM), hypertension (HT), hyperlipidemia, decompensated heart failure, immune or infectious diseases, moderate-severe valve disease and stage 3 or more advanced chronic kidney disease were excluded. There were 30 healthy control subjects who agreed to participate to the study. Patients with acromegaly were divided into two groups as: disease active patients

and patients in remission. Serum endocan levels were measured with enzyme linked immunosorbent assay (ELISA) method endothelial function was assessed with flow mediated dilatation (FMD).

Results: There were 85 patients included to the study. Twenty-three patients had active disease, 31 were in remission and 31 were healthy controls. FMD was higher in controls compared to patients in active disease and patients in remission ($p < 0.001$). There was no difference between patients with active disease for FMD and patients in remission ($p = 0.088$). There was statistically significant correlation between FMD and endocan and insulin like growth hormone-1 (IGF-1) levels of patients with acromegaly. As FMD increased endocan and IGF-1 decreased. A moderate negative relation between FMD and endocan was identified ($p < 0.001$, $r: -0.409$) as well as FMD and IGF-1 levels ($p: 0.011$, $r: -0.377$). Along with endocan and IGF-1, DM, HT, sex, body mass index, age and uric acid were associated with changes in FMD.

Conclusions: Endocan levels and endothelial function measured with FMD have an inverse relationship. Endocan may prove to be a marker for endothelial dysfunction in acromegaly.

AGING VERSUS YOUTH: ENDOCRINE ASPECTS OF VULNERABILITY FOR COVID-19

Seda Hanife Oguz¹, Meltem Koca², Bulent Okan Yildiz³

Rev Endocr Metab Disord. 2021 Apr 16;1-20. Online ahead of print. PMID: 33860905
PMCID: PMC8050510 DOI: 10.1007/s11154-021-09656-y

Coronavirus Disease 2019 (COVID-19) is characterized with a wide range of clinical presentations from asymptomatic to severe disease. In patients with severe disease, the main causes of mortality have been acute respiratory distress syndrome, cytokine storm and thrombotic events. Although all factors that may be associated with disease severity are not yet clear, older age remains a leading risk factor. While age-related immune changes may be at the bottom of severe course of COVID-19, age-related hormonal changes have considerable importance due to their interactions with these immune alterations, and also with endothelial dysfunction and comorbid cardiometabolic disorders. This review aims to provide the current scientific evidence on the pathogenetic mechanisms underlying the pathway to severe COVID-19, from a collaborative perspective of age-related immune and hormonal changes together, in accordance with the clinical knowledge acquired thus far.

AN UPDATE ON CONTRACEPTION IN POLYCYSTIC OVARY SYNDROME

Seda Hanife Oguz¹, Bulent Okan Yildiz¹

Endocrinol Metab (Seoul). 2021 Apr;36(2):296-311. Epub 2021 Apr 15. PMID: 33853290
PMCID: PMC8090477 DOI: 10.3803/EnM.2021.958

Polycystic ovary syndrome (PCOS) is a common endocrine disorder in reproductive-aged women, characterized by hyperandrogenism, oligo/anovulation, and polycystic ovarian

morphology. Combined oral contraceptives (COCs), along with lifestyle modifications, represent the first-line medical treatment for the long-term management of PCOS. Containing low doses of estrogen and different types of progestin, COCs restore menstrual cyclicity, improve hyperandrogenism, and provide additional benefits such as reducing the risk of endometrial cancer. However, potential cardiometabolic risk associated with these agents has been a concern. COCs increase the risk of venous thromboembolism (VTE), related both to the dose of estrogen and the type of progestin involved. Arterial thrombotic events related to COC use occur much less frequently, and usually not a concern for young patients. All patients diagnosed with PCOS should be carefully evaluated for cardiometabolic risk factors at baseline, before initiating a COC. Age, smoking, obesity, glucose intolerance or diabetes, hypertension, dyslipidemia, thrombophilia, and family history of VTE should be recorded. Patients should be re-assessed at consecutive visits, more closely if any baseline cardiometabolic risk factor is present. Individual risk assessment is the key in order to avoid unfavorable outcomes related to COC use in women with PCOS.

SPHENOID SINUS MUCOSAL THICKENING IN PATIENTS WITH NON-FUNCTIONING PITUITARY ADENOMA

Bayram Şahin¹, Ömercan Topaloğlu²

Int J Clin Pract. 2021 Oct;75(10):e14604. Epub 2021 Jul 14. PMID: 34228864 DOI: 10.1111/ijcp.14604

Aim: The aim of this study was to evaluate magnetic resonance imaging findings of sphenoid sinus (SS), pituitary gland and related structures in patients with non-functioning pituitary adenoma (NFPA) and compare to a control group.

Methods: This study was conducted in a tertiary referral hospital between January 2018 and July 2020. Sixty-five patients diagnosed with NFPA and age- and gender-matched controls (n = 40) were included.

Results: The average age in the NFPA group was 37.46 ± 11.2 years and in the control group was 41.97 ± 14.88 years, and they did not differ significantly ($P = .103$). SS mucosal thickness greater than 1 mm was determined in a higher proportion of NFPA (67.7%) than in the control group (12.5%) ($P < .001$). A mucosal thickness greater than 3 mm was only present in the NFPA group (43.1%). The distance between optic nerves was significantly longer in the NFPA group compared with control ($P < .001$). There was a strong positive correlation between adenoma volume and distance between the two optic nerves ($r = .728$, $P < .001$). Also, there was a moderate positive correlation between adenoma volume and petrous intercarotid distance (ICD) ($r = .561$, $P < .001$) and a low positive correlation between adenoma volume and cavernous ICD ($r = .408$, $P < .001$).

Conclusions: The present study showed an association between NFPA and both SS mucosal thickening and increased distance between optic nerves. Also, our study demonstrated that there was a strong positive correlation between adenoma volume and distance between the two optic nerves.

CLINICAL CHARACTERISTICS AND OUTCOMES OF COVID-19 PATIENTS WITH OVERWEIGHT AND OBESITY: TURKISH NATIONWIDE COHORT STUDY (TURCOBESITY)

Ibrahim Sahin¹, Cem Haymana², Tevfik Demir³, Ibrahim Demirci², Ilker Tasci⁴, Aysegul Atmaca⁵, Erman Cakal⁶, Naim Ata⁷, Rifat Emral⁸, Ugur Unluturk⁹, Derun Ertugrul¹⁰, Serpil Salman¹¹, Mustafa Sahin¹¹, Selcuk Dagdelen⁴, Osman Celik¹², Murat Caglayan¹³, Ilhan Satman^{14,15}, Alper Sonmez¹⁶

Exp Clin Endocrinol Diabetes. 2021 Aug 12. Online ahead of print. PMID: 34384122 DOI: 10.1055/a-1552-4449

Purpose: While obesity is related to more severe outcomes of coronavirus disease 2019 (COVID-19), factors leading to poor prognosis still remain unclear. The present study evaluated the outcomes of COVID-19 patients who were overweight or obese and variables associated with severe disease in a large group of consecutive cases.

Methods: A nationwide retrospective cohort study was performed using the Turkish National Healthcare Database. Demographic characteristics, laboratory tests, comorbidities, and medications of patients registered between March 11 and May 30, 2020, were recorded.

Results: A total of 14, 625 patients (median age:42, IQR:26 years; female 57.4%) with normal weight (34.7%), overweight (35.6%), and obesity (29.7%) were included. Hospitalization, ICU admission, intubation/mechanical ventilation, pulmonary involvement, and mortality were significantly higher in patients who were overweight or obese. In adjusted analyses, both overweight (OR, 95% CI: 1.82, 1.04-3.21; p=0.037) and obesity (OR, 95% CI: 2.69, 1.02-1.05; p<0.001) were associated with a higher intubation/mechanical ventilation rate but only obesity was associated with increased mortality (OR, 95% CI: 2.56, 1.40-4.67; p=0.002). Old age, male gender, chronic kidney disease, and high C reactive protein levels were independently associated with COVID-19 mortality in overweight or obese patients.

Conclusions: COVID-19 patients who were overweight or obese were more likely to have adverse outcomes but only obesity was a predictor of mortality. Such patients should receive urgent medical attention and active management, especially the elderly, men, and people with chronic kidney disease.

EFFECTS OF BARIATRIC SURGERY ON HEART RHYTHM DISORDERS: A SYSTEMATIC REVIEW AND META-ANALYSIS

Elijah E Sanches¹, Besir Topal², Frank W de Jongh³, Eylem Cagiltay⁴, Alper Celik⁵, Magnus Sundbom⁶, Rui Ribeiro⁷, Chetan Parmar⁸, Surendra Ugale⁹, Kamal Mahawar¹⁰, Marc P Buijsse¹¹, Lukas R Dekker¹², Dharmanand Ramnarain¹³, Sjaak Pouwels¹⁴

Obes Surg. 2021 May;31(5):2278-2290. Epub 2021 Mar 13. PMID: 33712936 DOI: 10.1007/s11695-021-05314-z

The aim of this systematic review is to provide an overview of the literature on the effects of bariatric surgery on obesity-associated electrocardiogram (ECG) abnormalities

and cardiac arrhythmias. Fourteen studies were included with a methodological quality ranging from poor to good. Majority of the studies showed a significant decrease of QT interval and related measures after bariatric surgery. Seven studies were included in the meta-analysis on effects of bariatric surgery on QTc interval and a significant decrease in QTc interval of - 33.6 ms, 95%CI [- 49.8 to - 17.4] was seen. Bariatric surgery results in significant decrease in QTc interval and P-wave dispersion, i.e., a normalization of initial pathology. The effects on atrial fibrillation are conflicting and not yet fully understood.

THE VALUE OF ROUTINE MEASUREMENT OF SERUM CALCITONIN ON INSUFFICIENT, INDETERMINATE, AND SUSPICIOUS THYROID NODULE CYTOLOGY

Muhammed Erkam Sencar¹, Sema Hepsen¹, Murat Çalapkulu¹, Hayri Bostan¹, Davut Sakiz¹, Ilknur Ozturk Unsal¹, Hakan Duger¹, Muhammed Kizilgul¹, Bekir Ucan¹, Tugba Taskin Turkmenoglu², Mustafa Ozbek¹, Erman Cakal¹

Bosn J Basic Med Sci. 2021 May 21. Online ahead of print. PMID: 34247569 DOI: 10.17305/bjbm.2021.5756

Routine calcitonin measurement in patients with nodular thyroid disease is rather controversial. The aim of this study was to evaluate the contribution of serum calcitonin measurement in the diagnostic evaluation of thyroid nodules with insufficient, indeterminate, or suspicious cytology. Out of 1668 patients who underwent thyroidectomy with the diagnosis of nodular thyroid disease and were screened, 873 patients with insufficient, indeterminate, or suspicious fine needle aspiration biopsy results were included in the study. From the total number of patients in this study, 10 (1.1%) were diagnosed as medullary thyroid cancer (MTC) using histopathology. The calcitonin level was detected to be above the assay-specific cut-off in 23 (2.6%) patients ranging between 6.5 - 4450 pg/mL. While hypercalcitoninemia was detected in all 10 MTC patients, a false positive elevation of serum calcitonin was detected in 13 patients (1.5%). Of the MTC group, 7 patients had cytology results that were suspicious for malignancy (Bethesda V), one patient's cytology showed atypia of undetermined significance (Bethesda III) and two patient's cytology results were suspicious for follicular neoplasm (Bethesda IV). Among the cases with non-diagnostic cytology (Bethesda I), none of the patients were diagnosed with MTC. In conclusion, routine serum calcitonin measurement can be performed in selected cases rather than in all nodular thyroid patients. While it is reasonable to perform routine calcitonin measurement in patients with Bethesda IV and Bethesda V, this measurement was not useful in Bethesda I patients. In Bethesda III patients, patient-based decisions can be made according to their calcitonin measurement.

ENEMY BEYOND THE WALL: CLINICOPATHOLOGICAL FEATURES OF INTRATHYROIDAL PAPILLARY THYROID CARCINOMA (T1-T3A) THAT METASTASIZE TO LYMPH NODES WITHOUT EXTRATHYROIDAL EXTENSION

Abbas Ali Tam¹, Nurcan Ince¹, Husniye Baser¹, Ayşegül Aksoy Altinboga², Mehmet Kilic³, Oya Topaloglu¹, Didem Ozdemir¹, Afra Alkan⁴, Reyhan Ersoy¹, Bekir Cakir¹

Cancer Invest. 2021 May;39(5):401-408. Epub 2021 Mar 12. PMID: 33650923 DOI: 10.1080/07357907.2021.1897833

The aim of this study was to determine the clinicopathological features of papillary thyroid carcinomas (PTC) without extrathyroidal extension (ETE) and with lymph node metastasis (LNM). PTC > 1 cm increased the risk of LNM by 2.161 times compared to papillary thyroid microcarcinoma. The risk increased by 3.774 times in males and 1.553 times in the presence of multifocality. Presence of vascular invasion (VI) increased the risk of LNM by 3.093 times in patients without capsular invasion (CI). Clinicians should be careful about possible LNM in patients with large primary tumor diameter, multifocal tumors, CI and VI.

OUTCOMES OF PATIENTS WITH MACROPROLACTINOMA DESIRING PREGNANCY: FOLLOW-UP TO 23 YEARS FROM A SINGLE CENTER

Seher Tanrikulu^{1,2}, Sema Yarman¹

Horm Metab Res. 2021 Jun;53(6):371-376. Epub 2021 Apr 26. PMID: 33902136 DOI: 10.1055/a-1468-4608

Macroprolactinomas are rarely seen in women, and pregnancy is a risk factor for tumor growth. More studies are needed to determine appropriate management for macroprolactinoma and pregnancy. The aim of our study is to evaluate effects of treatment with dopamine agonists on macroadenoma before and during pregnancy, safety of dopamine agonists on fetus, post-pregnancy prognosis and long-term results. This is a single center retrospective study. Thirty-four pregnancies occurred in 21 patients under medical therapy. Prolactin levels, treatment results, tumor diameter changes, maternal-fetal outcomes, and disease activity were evaluated. The median tumor size at the time of diagnosis was 15 mm (10-28). Residual adenoma diameter was smaller in those receiving medical therapy longer than one year till the conception (p=0.047). Treatment was discontinued in 28 pregnancies after pregnancy confirmation, and 6 patients were exposed to bromocriptine throughout pregnancy. There was no symptomatic tumor growth during gestation. Among 27 live births, none of the fetuses developed neonatal malformation except for a case of Down syndrome. While early remission rate after pregnancy was 9.5%, this rate reached 33.3% at last follow-up visit. Lowered PRL levels at postpartum period (p=0.040), smaller tumor size at last follow-up visit (p=0.030), and total disappearance of tumor (p=0.026) were the contributor factors for remission. Use of dopamine agonist over one year may reduce the risk of symptomatic tumor growth during pregnancy in patients without invasive or large macroprolactinoma before pregnancy. Exposure to dopamine agonists seems generally safe for the fetus.

ASSOCIATION OF LEPTIN LEVELS AND DISEASE ACTIVITY IN PATIENTS WITH EARLY RHEUMATOID ARTHRITIS

Ali Taylan¹, Baris Akinci², Burak Toprak³, Merih Birlik⁴, Fatma Demet Arslan³, Hasan Ekerbicer⁵, Baris Gundogdu⁶, Ayfer Colak³, Bahar Engin⁷
Arch Med Res. 2021 Jul;52(5):544-553. Epub 2021 Feb 23. PMID: 33632629 DOI: 10.1016/j.arcmed.2021.02.002

Abstract

Objective: Previous studies have reported a link between metabolic parameters and disease activity in rheumatoid arthritis (RA), although the evidence is limited in early RA. We aimed to investigate the relationship between disease activity and adipocytokine levels in subjects with early RA.

Methods: Forty-seven patients with early RA (symptom duration ≤12 months) were enrolled. Disease activity was determined by DAS28-CRP. Patients were treated with DMARDs according to the EULAR recommendations. Subjects were tested before and five months after treatment.

Results: Early RA patients with high disease activity (DAS28-CRP > 4.9) had greater BMI (31.2 ± 6.8 kg/m² vs. 26.7 ± 4.1 kg/m²; p = 0.006) and higher leptin levels (14.62 ± 15.60 ng/mL vs. 7.82 ± 8.00 ng/mL; p = 0.048). Levels of other adipocytokines were not significantly different. Leptin levels were similar in subjects with mild/moderate disease activity and controls. DAS28-CRP was correlated with leptin (r = 0.303, p = 0.039). Leptin levels decreased significantly after treatment (from 10.86 ± 12.34 ng/mL to 9.22 ± 9.29 ng/mL; p = 0.047) along with insulin levels (from 13.68 ± 21.90 mU/L to 7.09 ± 4.72 mU/L; p = 0.010) and HOMA-IR (from 4.39 ± 9.53 to 1.70 ± 1.38; p = 0.012). HDL cholesterol levels increased (from 41 ± 10 mg/dL to 48 ± 10 mg/dL; p < 0.001).

Conclusion: Leptin levels were associated with disease activity in patients with early RA and these levels decreased after treatment with DMARDs. Further research is needed to elicit leptin's role to regulate disease activity in early RA.

THE FRONTAL QRS-T ANGLE IN PATIENTS WITH INCIDENTALLY DISCOVERED NONFUNCTIONAL ADRENAL ADENOMAS

O Topaloğlu¹, M Çimci

Eur Rev Med Pharmacol Sci. 2021 Apr;25(7):3028-3037. PMID: 33877666 DOI: 10.26355/eurrev_202104_25556

Objective: Few studies have used electrocardiography (ECG) to examine nonfunctional adrenal adenomas (NFAAs). No study has investigated the QRS-T angle in NFAA patients. We analyzed the frontal QRS-T angle of patients with incidentally discovered NFAAs.

Patients and methods: Adult patients with incidentally discovered NFAAs were included. Patients with chronic diseases other than hypertension or obesity were excluded. The overnight dexamethasone suppression test was performed. Levels of plasma renin and aldosterone, as well as metanephrine fractions in 24-h urine were measured. We performed abdominal magnetic resonance imaging and computed tomography to

exclude hormonal hypersecretion and nonadenomas. The frontal QRS-T angle was calculated and verified based on surface ECG. Patients were grouped in terms of QRS-T angle as normal and abnormal, and the abnormal patients were divided into positive and negative subgroups.

Results: Of all patients (n=58), six (10.34%) had abnormal QRS-T angles. Hypertension increased the risk of an abnormal QRS-T angle six-fold (odds ratio 6.000; 95% confidence interval 0.982-36.652, p=0.034). The frequency of hypertension was similar between the normal, abnormally positive, and abnormally negative groups (p=0.086). The mean SV1+RV5 value was lower in the abnormal QRS-T angle group (p=0.012). Age, gender, obesity, antihypertensive medication use, prediabetes status, adenoma size or side, hyperlipidemia, and adrenal hormone levels were all not associated with the QRS-T angle.

Conclusions: Our study is the first to analyze the association between an abnormal QRS-T angle and NFAA. An abnormal QRS-T angle was found in a significant proportion of patients and was associated with hypertension but seemingly, not with left ventricular hypertrophy. We recommend ECG and blood pressure measurement at the time of diagnosis of an NFAA and on follow-up.

EVALUATION OF ADHERENCE TO LEVOTHYROXINE AND OUT-OF-RANGE THYROID-STIMULATING HORMONE LEVELS IN PREGNANT WOMEN WITH PRIMARY HYPOTHYROIDISM

Ömercan Topaloğlu¹, Arzu Yavuz², Ahsen Banu Tiryaki Aylıkçı³
Int J Clin Pract. 2021 Aug;75(8):e14312. *Epub* 2021 May 17. PMID: 33999516 DOI: 10.1111/ijcp.14312

Purpose: Adherence to levothyroxine (LT4) and attaining thyroid-stimulating hormone (TSH) goal in pregnancy has not been well-defined yet. We aimed to investigate adherence to LT4, success to reach TSH goal, and association between them in pregnant women with primary hypothyroidism.

Materials and methods: Eight-item Morisky Medication Adherence Scale (MMAS-8) was applied in third trimester in pregnant women with primary hypothyroidism (Hashimoto's thyroiditis, surgical hypothyroidism or iodine deficiency) whom LT4 was given for at least 3 months. Those with chronic illness or thyroid cancer were excluded. We grouped the patients according to MMAS-8 score (<6, low adherence vs ≥6, medium/high adherence), and TSH measurement in third trimester (in-range vs out-of-range).

Results: Of total (n = 85), 57.64% (n = 49) had medium/high adherence to LT4, and 41.17% (n = 35) out-of-range TSH, but no association was found among them (P = .937). LT4 initiation in pregestational period, surgical hypothyroidism, high LT4 dose in second/third trimester and alternate-day dosing were associated with medium/high adherence. Age, number of visits, and less time between ingestion of LT4 and breakfast were associated with medium/high adherence. LT4 dose in second trimester and dose increment at the beginning of pregnancy were positively associated with in-range TSH.

Conclusion: Non-adherence and treatment failure are

frequent in LT4-treated pregnant women. Adherence seems not to be associated with treatment success. Regular follow-up may improve adherence. Our study is the first to analyse both treatment success and adherence to LT4 in pregnancy.

PITUITARY SOCIETY DELPHI SURVEY: AN INTERNATIONAL PERSPECTIVE ON ENDOCRINE MANAGEMENT OF PATIENTS UNDERGOING TRANSSPHE-NOIDAL SURGERY FOR PITUITARY ADENOMAS

Nicholas A Tritos #¹, Pouneh K Fazeli #², Ann McCormack³, Susana M Mallea-Gil⁴, Maria M Pineyro⁵, Mirjam Christ-Crain⁶, Stefano Frara⁷, Artak Labadzhyan⁸, Adriana G Ioachimescu⁹, Ilan Shimon¹⁰, Yutaka Takahashi¹¹, Mark Gurnell¹², Maria Fleseriu¹³, "Pituitary Society Delphi Collaborative Group"

Pituitary. 2021 Jul 20;1-10. Online ahead of print. PMID: 34283370 PMCID: PMC8294287 DOI: 10.1007/s11102-021-01170-3

Purpose: In adults and children, transsphenoidal surgery (TSS) represents the cornerstone of management for most large or functioning sellar lesions with the exception of prolactinomas. Endocrine evaluation and management are an essential part of perioperative care. However, the details of endocrine assessment and care are not universally agreed upon.

Methods: To build consensus on the endocrine evaluation and management of adults undergoing TSS, a Delphi process was used. Thirty-five statements were developed by the Pituitary Society's Education Committee. Fifty-five pituitary endocrinologists, all members of the Pituitary Society, were invited to participate in two Delphi rounds and rate their extent of agreement with statements pertaining to perioperative endocrine evaluation and management, using a Likert-type scale. Anonymized data on the proportion of panelists' agreeing with each item were summarized. A list of items that achieved consensus, based on predefined criteria, was tabulated.

Results: Strong consensus (≥ 80% of panelists rating their agreement as 6-7 on a scale from 1 to 7) was achieved for 68.6% (24/35) items. If less strict agreement criteria were applied (ratings 5-7 on the Likert-type scale), consensus was achieved for 88% (31/35) items.

Conclusions: We achieved consensus on a large majority of items pertaining to perioperative endocrine evaluation and management using a Delphi process. This provides an international real-world clinical perspective from an expert group and facilitates a framework for future guideline development. Some of the items for which consensus was not reached, including the assessment of immediate postoperative remission in acromegaly or Cushing's disease, represent areas where further research is needed.

THE EFFECTS OF GLUCAGON-LIKE PEPTIDE 1 RECEPTOR AGONIST (EXENATIDE) ON MEMORY IMPAIRMENT, AND ANXIETY- AND DEPRESSION-LIKE BEHAVIOR INDUCED BY REM SLEEP DEPRIVATION

Inci Turan¹, Hale Sayan Ozacmak², V Haktan Ozacmak², Meryem Ergenc³, Taner Bayraktaroğlu⁴

Brain Res Bull. 2021 Sep;174:194-202. Epub 2021 Jun 17. PMID: 34146656 DOI: 10.1016/j.brainresbull.2021.06.011

Previous investigations have shown that REM sleep deprivation impairs the hippocampus-dependent memory, long-term potentiation and causing mood changes. The aim of the present study was to explore the effects of exenatide on memory performance, anxiety- and depression like behavior, oxidative stress markers, and synaptic protein levels in REM sleep deprived rats. A total of 40 male Wistar rats were randomly divided to control, exenatide-treated control, sleep deprivation (SD), wide platform (WP) and exenatide-treated SD groups. During experiments, exenatide treatment (0.5 µg/kg, subcutaneously) was applied daily in a single dose for 9 days. Modified multiple platform method was employed to generate REM sleep deprivation for 72 h. The Morris water maze test was used to assess memory performance. Anxiety- and depression-like behaviors were evaluated by open field test (OFT), elevated plus maze (EPM) forced swimming test (FST), respectively 72 h after REMSD. The levels of Ca²⁺/calmodulin-dependent protein kinase II (CaMKII) and postsynaptic density proteins 95 (PSD95) were measured in tissues of hippocampus and prefrontal cortex. The content of malondialdehyde (MDA) and reduced glutathione (GSH) were also measured. In the present study, an impairment in memory was observed in SD rats at the 24th hour of SD in compare to those of other groups. REMSD increased depression-like behavior in FST as well as the number of rearing and crossing square in OFT. Anxiety is the most common comorbid condition with depressive disorders. Contents of CaMKII and PSD95 decreased in hippocampus of SD rats. Exenatide treatment improved the impaired memory of SD rats and increased CaMKII content in hippocampus. There was no difference in MDA and GSH levels among groups. Exenatide treatment also diminished locomotor activity in OFT. In conclusion, treatment with exenatide, at least in part, prevented from these cognitive and behavioral changes possibly through normalizing CaMKII levels in the hippocampus.

THE PREVALENCE OF CANCER AND ITS RELATION TO ACTIVITY IN PATIENTS WITH ACROMEGALY: TWO CENTERS' EXPERIENCE

Bekir Ucan¹, Muhammed Kizilgul², Alper Cagri Karci³, Hakan Duger¹, Muhammed Erkam Sencar¹, Narin Nasiroglu Imga³, Taner Demirci¹, Dilek Berker³, Erman Cakal¹

Endocr Pract. 2021 Jan;27(1):51-55. Epub 2020 Nov 18. PMID: 33475501 DOI: 10.4158/EP-2020-0398

Objective: Acromegaly is characterized by increased serum concentrations of growth hormone (GH) and insulin-like growth factor 1 (IGF-1). Although animal studies have

demonstrated a relationship between these hormones and cancer risk, the results of human studies evaluating cancer prevalence in acromegaly are inconsistent. We aimed to investigate the prevalence of malignant neoplasms in patients with acromegaly.

Methods: Cancer risk was evaluated in a cohort of 280 patients (male/female: 120/160; mean age: 50.93 ± 12.07 years) with acromegaly. Patients were categorized into 2 groups according to the presence or absence of cancer. Standard incidence ratios were calculated as compared to the general population.

Results: From 280 patients, cancer was diagnosed in 19 (6.8%) patients; 9 (47%) of them had thyroid cancer, which was the most common cancer type. Standard incidence ratios of all cancers were 0.8 (95% CI, 0.5-1.1) and 1.0 (95% CI, 0.8-1.3) in men and women, respectively. Compared to patients without cancer, the current age was higher in patients with cancer (59 [49-65] to 51 [42-59], P = .027). In contrast, the age at diagnosis was similar in both groups. Not only was the time to diagnosis and disease duration similar in both groups but also the basal and current GH and IGF-1 levels. The prevalence of active disease was also similar between the groups (32% to 23%, P = .394).

Conclusion: Our findings were not consistent with the studies suggesting that patients with acromegaly encounter an increased cancer risk. Furthermore, there were similar basal and current GH and IGF-1 levels in patients with acromegaly, both with and without cancer.

ROLE OF INSULIN AND INSULIN RESISTANCE IN ANDROGEN EXCESS DISORDERS

Kursad Unluhizarci¹, Zuleyha Karaca², Fahrettin Kelestimur³

World J Diabetes. 2021 May 15;12(5):616-629. PMID: 33995849 PMCID: PMC8107978 DOI: 10.4239/wjdv12.i5.616

Insulin has complex effects on cell growth, metabolism and differentiation, and these effects are mediated by a cell-surface bound receptor and eventually a cascade of intracellular signaling events. Among the several metabolic and growth-promoting effects of insulin, insulin resistance is defined as an attenuated effect of insulin on glucose metabolism, primarily the limited export of blood glucose into skeletal muscle and adipose tissue. On the other hand, not all the signaling pathways and insulin-responsive tissues are equally affected, and some effects other than the metabolic actions of insulin are overexpressed. Ovaries and the adrenal glands are two examples of tissues remaining sensitive to insulin actions where insulin may contribute to increased androgen secretion. Polycystic ovary syndrome (PCOS) is the most common form of androgen excess disorder (AED), and its pathogenesis is closely associated with insulin resistance. Patients with idiopathic hirsutism also exhibit insulin resistance, albeit lower than patients with PCOS. Although it is not as evident as in PCOS, patients with congenital adrenal hyperplasia may have insulin resistance, which may be further exacerbated with glucocorticoid overtreatment and obesity. Among patients with severe insulin resistance syndromes, irrespective of the type of disease, hyperinsulinemia promotes ovarian androgen synthesis independently of gonadotropins.

It is highly debated in whom and how insulin resistance should be diagnosed and treated among patients with AEDs, including PCOS. It is not suitable to administer an insulin sensitizer relying on only some mathematical models used for estimating insulin resistance. Instead, the treatment decision should be based on the constellation of the signs, symptoms and presence of obesity; acanthosis nigricans; and some laboratory abnormalities such as impaired glucose tolerance and impaired fasting glucose.

PREVALENCE OF VERTEBRAL FRACTURES AND SERUM SCLEROSTIN LEVELS IN ACROMEGALY

Meliha Melin Uygur¹, Dilek Dereli Yazıcı², Onur Buğdaycı³, Dilek Gogas Yavuz²
Endocrine. 2021 Sep;73(3):667-673. Epub 2021 May 21. PMID: 34019235 DOI: 10.1007/s12020-021-02751-9

Objective: An increased prevalence of vertebral fractures (VFs) has been reported in previous studies. The aim of this study was to evaluate the association between bone mineral density (BMD), bone turnover markers, serum sclerostin levels, and vertebral fractures (VFs) in acromegaly patients. We also evaluated the effects of gonadal status, disease activity, treatment modality, age, sex, and body mass index (BMI) on skeletal endpoints.

Design: Case-control study.

Patients and measurements: Seventy acromegaly patients (M/F:36/34, mean age 45.5 ± 11.9 years) and 70 controls (M/F:31/39; mean age 45.66 ± 11.9 years) were included. VFs, BMD, calcium metabolism, markers of bone turnover, and sclerostin levels were evaluated. BMD was measured by dual-energy X-ray absorptiometry (Hologic QDR 4500). Conventional lateral radiography of the spine was performed and the Genant method was used for the assessment of fractures of T4-L5 vertebrae.

Results: The prevalence of vertebral fractures was higher in acromegalic patients as compared with the control group (72.9 vs. 20%; $p < 0.001$). Serum phosphate (P) levels (3.46 ± 0.59 mg/dl vs. 3.11 ± 0.44 mg/dl; $p < 0.001$) and b-cross laps (CTx) levels (0.47 µg/l, range 0.04-2.38 vs. 0.28 µg/l, range 0.11-0.80; $p < 0.001$) were significantly higher in acromegaly patients than control subjects. Serum sclerostin levels were similar between either acromegaly patients and control subjects or acromegaly patients with VF and without VF. In the means of treatment modality, VFs were more frequent in patients treated with adjuvant gamma knife radiosurgery (GKS) ($p = 0.07$). In the binary logistic regression analysis, the age of the acromegaly patients, the presence of hypogonadism, and GKS treatment were the factors significantly correlated with the occurrence of spinal fractures.

Conclusions: The prevalence of VFs in patients with acromegaly is higher than in control subjects. Since advanced age, the presence of hypogonadism and GKS treatment were the factors predicting VFs in acromegaly; radiological evaluations should be considered as an emerging tool especially in those patients. Although markers of bone turnover elevated in acromegaly, they were not useful for the prediction of fractures. Serum sclerostin levels showed no discrepancy between the two groups and further studies are required for assessment of sclerostin role in this form of secondary osteoporosis.

OXYSTEROL SPECIES GENERATED BY AUTO-OXIDATION IN SUBCLINICAL HYPOTHYROIDISM

Uğur Ünlütürk¹, Merve Savaş², Seda Hanife Oğuz³, Afshin Samadi⁴, Büşra Fırlatan², Deniz Yüce⁵, İncilay Lay⁴, Alper Gürlek³
Clin Biochem. 2021 Jul;93:73-79. Epub 2021 Apr 20. PMID: 33861988 DOI: 10.1016/j.clinbiochem.2021.04.007

Background: Auto-oxidized oxysterols are implicated in the pathogenesis of various chronic diseases. Their concentrations are indicators of oxidative stress in vivo and associated with atherosclerosis. Subclinical hypothyroidism is related with cardiac diseases and oxidative stress, but the exact mechanisms underlying these associations are not clear yet.

Objective: To investigate the auto-oxidized oxysterols, 7-ketocholesterol (7-KC) and cholestane-3β,5α,6β-triol (chol-triol), in patients with subclinical hypothyroidism, as well as to evaluate the impact of restoring euthyroidism on oxysterol concentrations.

Methods: In this prospective observational study, 64 patients with newly diagnosed autoimmune thyroiditis (41 with subclinical hypothyroidism and 23 euthyroidism), and 45 healthy controls were enrolled. Age, gender, and body mass index were matched among patient groups and healthy controls. Anthropometric measurements were obtained and fasting plasma 7-ketocholesterol and cholestane-3β,5α,6β-triol concentrations were measured by using liquid chromatography coupled with tandem mass spectrometry. Levothyroxine was then administered to all patients with subclinical-hypothyroidism. After three months, measurements of the oxysterols and serum cholesterols from the patients who have become euthyroid were repeated.

Results: Concentrations of 7-ketocholesterol and cholestane-3β,5α,6β-triol were significantly higher in patients with subclinical-hypothyroidism when compared to both euthyroid patients and healthy controls ($p < 0.001$ for both oxysterols). After restoration of euthyroidism, concentrations of 7-ketocholesterol and cholestane-3β,5α,6β-triol decreased significantly and reached similar concentrations observed in healthy controls ($p < 0.001$ for both oxysterols).

Conclusions: Auto-oxidized oxysterol species are higher in patients with mild thyroid dysfunction, and supported the rationale for treating subclinical-hypothyroidism.

Keywords: Atherosclerosis; Autoimmune thyroiditis; Oxidative stress; Oxysterol; Subclinical hypothyroidism; Tandem mass spectrometry.

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