

disturbances. These negative emotions were related to the whole spectrum of disease state, the associated treatments, pre-treatment, post-treatment care, and personal aspects of daily life. Uncertainties in medical outcomes were associated with the personal need for further information. Functional psychosocial impairments and socioeconomic disruptions have a strong ability to arouse the anxiety of outcome uncertainties further. Getting treatment and independence in routine daily activities were prioritized while acknowledging treatments may differ in modality and risk of complications. Physician-patient interactions were valued in alleviating concerns and fear. Four salient themes emerged suggesting emotional security, functional ability, self-care (including psychosocial and socioeconomic well-being), and quality of physician-patient relationships were what matters to these participants. **Conclusion:** This insight into the problems of patients with TD underlined the need for quality patient-centered thyroid care and may be enhanced, personalized, and improved through outcomes that mattered most to patients in clinical research/trials, routine clinical practice, and the health system.

Thyroid

THYROID AUTOIMMUNITY, COVID-19 & THYROID DISEASE

A Higher Cutoff for TSI Would Better Predict Recurrence in Patients With Graves' Disease?

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Introduction: GD is an autoimmune disease mediated by immunoglobulins (Igs) that activate TSH receptor (rTSH). Relapse after withdrawal of antithyroid drugs (ATD) can reach 60%. Measurement of TSH receptor antibodies (TRAb) and thyroid stimulating immunoglobulin (TSI) could be an indirect indicator of GD activity. TRAb assays measures thyroid-stimulating, thyroid-blocking and neutral Igs; TSI assays measures only stimulating Igs. Objective: Evaluate, prospectively, autoimmunity before and after ATD therapy for thyrotoxicosis through TSI measurement. **Methods:** Patients were evaluated at the first visit and at the time of ATD withdrawal. TSH, thyroid hormones, TPO antibody, thyroglobulin antibody, and TRAb were measured using electrochemiluminescent assays Roche Diagnostics; TSI was determined by chemiluminescent assay Siemens Diagnostics. According to manufacturers, TRAb < 1.75 IU/L and TSI < 0.55 IU/L were negative. **Results:** Sixty-seven patients mean age 45.7±2.45 years, 65 women, were evaluated: 50 at the first visit, 40 (80%) with GD, and 10 (20%) with toxic multinodular goiter (TMNG). TSI diagnostic sensitivity (Sen%) and specificity (Spe%) to diagnose GD were 90% and 100% respectively, similar to that of TRAb, of 89% and 100%. Thirty-six patients were evaluated for recurrence after suspension of ATD (19 of them also had the initial assessment): 21 (58.3%) did not present recurrence

in an mean period of 9.5±2.1 months (3-18); and 15 (41.7%) relapsed in 4.4±2.6 months (2-12). In 10/21 patients who did not relapse, and whose TRAb was negative, TSI was positive at low levels, which was responsible for the low Spe% of this test. Assessing possible other cutoff points for the TSI in the recurrence assessment, an adjustment to 1.4 (TSI <1.4 IU/L = negative) raised the Spe% to 86%. **Conclusions:** In this group, TSI and TRAb were equivalent for GD diagnosis. Many clinical factors have been suggested and TRAb measurement is known to be useful for predicting GD relapse because of the active pathogenic role of TRAb. For predicting recurrence, with the proposed cutoff point proposed by the kit manufacturer for TSI, a better sensitivity was obtained when compared with TRAb (93% versus 67%), despite very low specificity (38%); by raising the cutting point to 1.4 specificity could be increased to 86% without reduced sensitivity. A larger sample is needed to support a higher TSI cutoff point in the clinical routine for the assessment of GD recurrence after ATD.

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Abnormal Thyroid Function Is Associated With Lymphopenia in Bacterial Sepsis and COVID-19

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Background: Lymphopenia is a key feature of immune dysfunction in bacterial sepsis and COVID-19 patients and is associated with poor clinical outcomes, but the cause is largely unknown. These severely ill patients may also present with thyroid function abnormalities, so-called non-thyroidal illness syndrome (NTIS), and several studies have suggested that TSH, thyroxin (T4) and triiodothyronine (T3) play a crucial role in the homeostatic regulation and function of lymphocyte populations.

Aim: The purpose of this study was to test the hypothesis that abnormal thyroid function correlates with lymphopenia in severely ill patients with bacterial sepsis or COVID-19.

Methods: Retrospective analysis of absolute lymphocyte counts and circulating TSH, T4, FT4, T3, albumin and inflammatory biomarkers was performed in two independent cohorts of bacterial sepsis (n=224) and hospitalized COVID-19 patients (n=35).

Results: Only T3 correlated (rho=0.252, p-value: <0.001) with lymphocyte counts in the bacterial sepsis population and lower concentrations were found in severe lymphopenic compared to non-lymphopenic patients (p-value: <0.001; n=56 per group). Severe lymphopenic COVID-19 patients (n=17) showed significantly lower plasma concentrations of TSH, T4, FT4 and T3 (p-value: 0.026, <0.001, 0.001, <0.001, respectively) compared to patients without lymphopenia

(n=18), and demonstrated significantly increased values of the inflammatory parameters IL-6, C-reactive protein and ferritin (p-value: <0.001, 0.023, and 0.008, respectively). Remarkable, after one week follow-up, the majority of (12/15) COVID-19 patients showed quantitative recovery of their lymphocyte numbers, while TSH and thyroid hormones remained mainly disturbed.

Conclusions: Abnormal thyroid function correlates with low lymphocyte counts in severe sepsis and COVID-19 patients, but future studies need to establish whether a causal relationship is involved.

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Amiodarone-Induced Thyrotoxicosis, Risk Factors and Predictors of Outcome: A Retrospective Study

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Background Amiodarone induced thyrotoxicosis (AIT) is not uncommon and is often associated with significant morbidity and mortality. Factors that predict poor prognosis in AIT have not yet been sufficiently investigated. **Objective:** To examine the characteristics and short-term clinical outcomes of patients with AIT (up to six months from diagnosis). We evaluated the relationship between T3 and T4 levels at the time of presentation and complications associated with AIT. **Methods:** A retrospective epidemiological study on patients admitted to Carmel Medical Center between the years 2004-2018. We reviewed electronic medical records of patients who bear the diagnosis of thyrotoxicosis and consumed amiodarone. Demographic and clinical characteristics of patients that develop AIT were evaluated. We evaluated the association between T3 and T4 levels at the time of presentation a poor prognosis. Three primary outcomes were defined: 1. Mortality. 2. Development of AIT-related complications that required hospitalization. 3. The need for thyroidectomy. **Results:** 400 patients bear a diagnosis of thyrotoxicosis and consumed amiodarone. However, only 39 patients met the full definition of AIT. The composite outcome of mortality, AIT-related complications and thyroidectomy was achieved in the vast majority of patients (94.8%, 37 out of 39 participants). Three patients (7.6%) died, 35 (89.7%) were hospitalized with AIT-related complications and 8 (20.5%) required thyroidectomy. There was a statistically significant relationship between high T4 levels and the composite of two main endpoints: mortality and the need for thyroidectomy in the first half year of diagnosis (P=0.009). **Conclusions:** AIT is associated with significant morbidity and mortality. An elevated level of free T4 reflects the severity of AIT. In patients with significantly increased T4 values, an early surgical intervention should be considered.

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Anxiety and Fear During the Covid-19 Pandemic: A Web-Based Survey of Thyroid Cancer Survivors

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Background: The coronavirus (COVID-19) pandemic has led to rapid changes in our society and healthcare system. Cancer patients and survivors may be disproportionately affected by these changes, including decreased access to healthcare, increased infection risk, and economic challenges. We sought to determine the effects of the pandemic on thyroid cancer survivors' quality of life. **Methods:** An anonymous web-based survey was administered in collaboration with ThyCa: Thyroid Cancer Survivors' Association, consisting of questions about (1) demographics, (2) thyroid cancer clinical characteristics, (3) attitudes toward and impact of COVID-19, and (4) the Patient-Reported Outcomes Measurement Information System (PROMIS) 29-item profile. The survey was linked on the ThyCa homepage. PROMIS measures were scored using item response theory models with a T-score metric relative to U.S. reference data via the HealthMeasures Scoring Service (<https://www.healthmeasures.net>). T-scores were analyzed using Mann-Whitney U, Wilcoxon signed-rank, Kruskal-Wallis, and Spearman's rank correlation tests. **Results:** From 5/6/2020 - 10/8/2020, 505 participants accessed the survey, and all completed surveys by U.S.-based thyroid cancer survivors were analyzed (n=378, 75%). Mean age was 53 years, 89% were female, 90% were white, 74% had papillary thyroid cancer, 97% had surgery, and 70% received radioactive iodine. The vast majority agreed or strongly agreed (83%) that their lives were very different during COVID-19, as was the way they interacted with their doctors (79%). Less than half (43%) agreed or strongly agreed that they were satisfied with the amount of information from their doctor's office regarding COVID-19 changes. Compared to previously-published PROMIS data for this population, T-scores were significantly higher in the domain of anxiety/fear (57.8 vs. 56.5, p<0.01) and lower for ability to participate in social roles and activities (46.2 vs. 48.1, p<0.01). Younger age was weakly correlated with greater anxiety/fear (Spearman's rho=-0.38, p<0.01), and greater anxiety/fear was associated with pending treatment (p<0.01), lower cancer stage (p=0.01), and female sex (p=0.02). **Conclusions:** During the COVID-19 pandemic, thyroid cancer survivors reported increased anxiety/fear and decreased social participation. In our efforts to care for patients both physically and mentally as the pandemic continues, we must better understand their fears and concerns and improve communication about potential changes to their care.

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