burden. Even after a fragility fracture, osteoporosis remains widely underdiagnosed and undertreated. Common fracture risk assessment tools, such as FRAX and Garvan, confer risk over the long term but do not provide short-term risk estimates necessary to identify very high-risk patients likely to fracture in the next 1–2 years. Furthermore, these tools utilize cross-sectional data representing a subset of all available clinical risk factors for risk prediction. Thus, these methods are generalized across patient populations and may not fully utilize patient histories commonly found in electronic health records (EHRs) that contain temporal information for thousands of unique features. The Optum® de-identified EHR dataset (2007–2018) provides an opportunity to use historical medical data to generate short-term, personalized fracture risk predictions for individual patients. We used the Optum® dataset to develop Crystal Bone, a method that applies machine learning techniques commonly used in natural language processing to the temporal nature of patient histories in order to predict fracture risk over a 1- to 2-year timeframe. Specifically, we repurposed deep-learning models typically applied to language-based prediction tasks in which the goal is to learn the meanings of words and sentences to classify them. Crystal Bone uses context-based embedding techniques to learn an equivalent “semantic” meaning of various medical events. Similar to how language models predict the next word in a given sentence or the topic of an overall document, Crystal Bone can predict that a patient’s future trajectory may contain a fracture or that the “signature” of the patient’s overall journey is similar to that of a typical fracture patient. We applied Crystal Bone to two datasets, one enriched for fracture patients and one representative of a typical hospital system. In both datasets, when predicting likelihood of fracture in the next 1–2 years, Crystal Bone had an area under the receiver operating characteristic (AUROC) score ranging from 72% to 83% on a test (hold-out) dataset. These results suggest performance similar to that of FRAX and Garvan, which have 10-year fracture risk prediction AUROC scores of 64.4% +/- 3.7%. Our results suggest that it is possible to use each patient’s unique medical history as it changes over time to predict patients at risk for fracture in 1–2 years. Furthermore, it is theoretically possible to integrate a model like Crystal Bone directly into an EHR system, enabling “hands-off” fracture risk prediction, which could lead to improved identification of patients at very high risk for fracture.

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Tumor Biology
ENDOCRINE NEOPLASIA CASE REPORTS II
Primary Amenorrhea, Growth Arrest and Metabolic Syndrome Due to an Unclassified Hepatocellular Adenoma.
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MON-901
Primary Amenorrhea, Growth Arrest and Metabolic Syndrome Due to an Unclassified Hepatocellular Adenoma.

Background: Hepatocellular adenoma is a rare benign neoplasm, seldom ascribed as the cause of endocrine and metabolic derangement. We herein report a case of primary amenorrhea, growth arrest and metabolic syndrome due to huge hepatocellular adenoma. En bloc resection of the tumor normalized all the disturbances.

Clinical Case: A 16-year-old girl, who is one of the quintuplets, complained of primary amenorrhea and growth arrest for the past 2 years. Her height (150cm) and weight (40kg) was at the 3rd percentile, whereas waist circumference (75cm) was at the 90th percentile for chronological age. She was hypertensive (145/115mmHg) on admission. Plasma cholesterol (TC 6.3mmol/L, LDL-c 3.76mmol/L), triglyceride (2.66mmol/L) and uric acid (532μmol/L) were elevated. Evaluation of GH/IGF-1 axis showed normal GH (0.90–2.53 μg/L) with extremely low IGF-1 concentration (35.29–39.74 ng/mL), and the latter was unresponsive to hGH stimulation. Computer tomography identified a huge liver mass (18.2cm×13.7cm×21cm). The patient underwent an uneventful open right hepatic lobectomy and cholecystectomy, and the tumor was en bloc resected. Immunohistochemistry indicated an unclassified hepatocellular adenoma, which was confirmed by whole exome sequencing. Her menarche started 6 months later followed by regular cycles without hormone replacement. IGF-1 concentration (471 ng/mL), blood pressure (102/62mmHg), lipid profile (TC 4.2mmol/L, LDL-c 2.51mmol/L, TG 1.44mmol/L) were all normalized 10 months after surgery, and the girl had a reduction in waist circumference by 5cm, and a small gain in height by 2cm.

Conclusion: We provide evidence that liver-derived IGF-1 has a direct effect on skeletal and pubertal development, blood pressure, visceral adiposity and dyslipidemia. Though rare, we propose the need to look into cases with hepatocellular adenoma, for the existence of IGF-1 deficiency and its impact on endocrine and metabolic derangement.

Tumor Biology
TUMOR BIOLOGY: GENERAL, TUMORIGENESIS, PROGRESSION, AND METASTASIS

Rapid Decompensation from Complications of Severe Hypercortisolism in an Unusual Presentation of an Ectopic ACTH-Secreting Neuroendocrine Tumor
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SAT-118
Background: Ectopic Cushing’s syndrome from an ACTH-secreting neuroendocrine tumor (NET) is a rare condition whose onset and disease progression is often more aggressive than other forms of Cushing’s syndrome due to complications from severe hypercortisolism.

Clinical Case: A 75-year old woman presented with proximal muscle weakness, severe hypokalemia,
Cushingoid features, and biopsy-proven Candida esophagitis. Initial testing was consistent with ACTH-dependent Cushing syndrome: elevated 24 hour urinary cortisol excretion (1,310.54 mcg/24h; n < 50 mcg/24h), abnormal 1 mg dexamethasone suppression test (68.3 ug/dL), and elevated ACTH level (200 pg/mL; n: 7.2–63.3 pg/mL). MRI was negative for a pituitary lesion but abdominal CT revealed an 8.8 cm liver mass with biopsy consistent with a well-differentiated neuroendocrine tumor, WHO Grade 2. Subsequent 68Ga-DOTATATE-PET/CT noted DOTATATE uptake in the liver lesion, a 0.9 cm right pulmonary nodule, and the pancreatic tail without CT correlate. Initially, the patient was prescribed mifepristone and spironolactone for hypokalemia. Given her NET of unknown primary, metastatic disease, and immunocompromised state due to hypercortisolism, the patient was not a candidate for surgical resection of her NET but was instead referred for bilateral adrenalectomy. However, she rapidly decompensated from complications of her hypercortisolism prior to surgery. Her weakness progressed to immobility, and she developed acute psychosis manifested as agitation and mutism. The patient was immediately admitted to the hospital where she developed new-onset atrial flutter and myelosuppression requiring multiple transfusions. She underwent urgent bilateral adrenalectomy, but despite surgery, her post-operative course was complicated by hypoxemic respiratory failure and shock. The patient shortly thereafter expired from pulseless electrical activity arrest.

**Conclusion:** This atypical case of an ectopic ACTH-secreting NET highlights the life-threatening complications associated with severe hypercortisolism, including: opportunistic infection, severe metabolic abnormalities, psychosis, myopathy, and critical illness that can incite myelosuppression and unstable arrhythmias. These patients can quickly deteriorate and are at high risk for mortality. Early diagnosis and swift reversal of their hypercortisolism with bilateral adrenalectomy are oftentimes necessary to prevent these potentially fatal complications.

**Thyroid**

**BENIGN THYROID DISEASE AND HEALTH DISPARITIES IN THYROID I**

**Quality of Life Following Treatment for Graves’ Disease: A Comparison of Radioactive Iodine Ablation and Surgery**

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**SAT-427**

**Introduction:** Quality of Life (QoL) is reduced in patients with Graves’ disease, however the impact of treatment modality is unclear, with conflicting evidence from recent studies (1–3). We hypothesized that surgery would have a greater impact than radioiodine on QoL in Graves’ disease, especially with regard to the physical-symptom subdomain.

**Pediatric Endocrinology**

**PEDIATRIC SEXUAL DIFFERENTIATION, PUBERTY, AND BONE BIOLOGY**

**Effect of Pubertal Induction with Gonadotropins and GnRH Therapy in Male Hypogonadotropic Hypogonadism: Meta-Analysis**

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**SUN-092**

**Background:** The use of gonadotropins is a recent strategy for inducing puberty in adolescent males with hypogonadotropic hypogonadism (HH). Testosterone use has been discouraged in patients who desire to preserve fertility. Human chorionic gonadotropin (hCG) has been recommended for inducing puberty in HH; however, several clinicians administer hCG in combination with other gonadotropins. The benefits of using combination gonadotropin therapies (hCG+) over hCG monotherapy in prepubertal adolescent males with HH has not been clearly established. We performed a meta-analysis to assess the outcomes of hCG compared to hCG+ in terms of virilizing effects and testicular growth in peripubertal boys with HH.

**Methods:** We evaluated for heterogeneity among studies. We calculated pooled means for the post-treatment mean testicular volume (MTV), testosterone (T) level, and penile length for the hCG monotherapy and hCG+ treatment groups. We performed a meta-regression analysis to examine the contribution of various factors to post-treatment outcomes including baseline T level, age, treatment duration, and study quality.

**Results:** The meta-analysis included seven studies. All participants were prepubertal (age range: 13.3–25.9 years), with weighted mean treatment durations of 10.95 months for hCG monotherapy and 28.2 months for hCG. There was significant heterogeneity in baseline age (Q = 121.71; df = 1; P < 0.001) and T levels (Q = 436.74; df = 1; P < 0.001) between the two treatment groups. The hCG+ group had a larger post-treatment MTV, but it was not significantly different between the two groups (6.60 mL [95% CI, 3.18–10.02] for hCG monotherapy vs. 10.02 mL [95% CI, 8.30–11.75] for hCG+; P = 0.079). Post-treatment T levels differed significantly between the two groups (101.89 ng/dL [95% CI, 50.7–153.08] for hCG monotherapy vs. 424.10 ng/dL [95% CI, 304.59–543.62] for hCG+; P < 0.0001). A meta-regression analysis of post-treatment T levels showed that baseline age, baseline T level, and study grade did not contribute significantly to the difference between treatment groups. Treatment duration explained 3.04% of the difference between the two groups (P < 0.0001). After adjusting for treatment duration, the post-treatment T level remained significantly higher in the hCG+ group compared to the hCG monotherapy group. The hCG+ was also associated with better outcomes for post-treatment penile length, although these findings relied on data from only three studies.

**Conclusion:** Our study indicates that hCG+ therapies provide potential benefits over hCG monotherapy for pubertal induction in males with HH, regarding T levels and penile growth, with no difference in testicular growth between treatments. Prospective pediatric studies are needed to assess the benefits of these therapies in patients with HH and, ultimately, to establish guidelines for gonadotropin therapy in the adolescent population.