were inconclusive. These findings should trigger suspicion for functional parathyroid lesions. Cystic components should be evaluated for PTH levels and if significantly elevated should be treated as a parathyroid adenoma.

Bone and Mineral Metabolism
PARATHYROID AND RARE BONE DISORDERS

Risk of Chronic Kidney Disease in Adult Patients With Chronic Hypoparathyroidism Treated With rhPTH(1–84) Compared With a Historical Control Cohort

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Patients (pts) with chronic hypoparathyroidism are at increased risk of renal complications. This study evaluated chronic kidney disease (CKD) outcomes over a period of up to 5 years in adult pts with chronic hypoparathyroidism treated with recombinant human parathyroid hormone (1–84), rhPTH(1–84), compared with a historical control cohort of pts who did not receive rhPTH(1–84). The cohort of pts with chronic hypoparathyroidism treated with rhPTH(1–84) was derived from the NCT00732615 (REPLACE), NCT01268098 (RELAY), NCT01297309 (RACE) and NCT01199614 (HEXT) clinical trials. The control cohort of adult pts who did not receive rhPTH(1–84) or rhPTH(1–34) was selected from the US Explorys electronic medical record database (Jan 2007−Aug 2019), using criteria similar to the enrollment criteria used in the trials. Index date was the day after treatment initiation for the rhPTH(1–84) cohort, and the day after the first calcitriol prescription for the control cohort. Pts with CKD at baseline (defined as estimated glomerular filtration rate [eGFR] <60 mL/min/1.73 m^2 at the closest eGFR measurement before the index date) were excluded. All included pts had ≥1 eGFR measurement within 6 months before the index date and ≥2 eGFR measurements ≥3 months apart during the 5 years on or after the index date. The CKD outcome was defined as first occurrence of eGFR <60 mL/min/1.73 m^2 confirmed by a second measurement ≥3 months after. Risk of CKD was assessed in a Kaplan-Meier analysis and a Cox proportional hazards model adjusted for demographic characteristics, baseline clinical conditions (including acute manifestations of hypoparathyroidism), and baseline laboratory measurements. The analysis included 118 pts in the rhPTH(1–84) cohort and 478 pts in the control cohort. Pts in the rhPTH(1–84) cohort, compared with pts in the control cohort, were younger (mean ± SD age, 45.3±11.4 vs 51.5±16.2 years; P<0.001), a higher proportion were White (97.5% vs 81.6%; P<0.001), and a lower proportion had acute manifestations of hypoparathyroidism before the index date (15.3% vs 73.2%; P<0.001). In a Kaplan-Meier analysis, rhPTH(1–84)-treated pts had a significantly reduced risk of developing CKD compared with pts in the control cohort, with 11.0% and 27.0% of pts in each cohort, respectively, developing CKD during follow-up (P<0.01). The adjusted hazard ratio of developing CKD associated with rhPTH(1–84) treatment vs no rhPTH(1–84) treatment was 0.47 (95% CI, 0.25−0.88; P<0.05). Pts with chronic hypoparathyroidism treated with rhPTH(1–84) in long-term clinical trials had a significantly reduced risk of developing CKD compared with pts in a control cohort who did not receive rhPTH(1–84). These results should be viewed in light of possible treatment differences in the studied cohorts (ie, predefined trial protocols vs real-word practice for the control cohort).

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Secondary Hyperparathyroidism Among Bariatric Patients: Unraveling the Prevalence of an Overlooked Foe.

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Introduction: Bariatric surgery (BS) is an effective therapeutic approach for obese patients. It is associated with important gastrointestinal anatomic changes, predisposing these subjects to altered nutrient absorption that impact phosphocalcium metabolism. This study aims to clarify the prevalence of secondary hyperparathyroidism (SHPT) and its predictors in patients submitted to BS. **Methods:** Retrospective unicentric study of 1431 obese patients who underwent metabolic surgery between January/2010 and June/2017 and who were followed for, at least, a year. In this group, 185 subjects were submitted to laparoscopic adjustable gastric banding (LAGB), 830 underwent Roux-en-Y gastric bypass (RYGB) and 416 sleeve gastrectomy (SG). Data comprising 4 years of follow-up were available for 333 patients. We compared the clinical and analytical characteristics of patients with and without secondary hyperparathyroidism (considering SHPT a PTH>69pg/mL), taking also into account the type of surgery. A multiple logistic regression was performed to study the predictors of SHPT after BS. **Results:** The overall prevalence of SHPT before surgery was 24.9%, 11.2% one year after surgery and 21.3% four years after surgery. At 12 months after surgery, LAGB had the highest prevalence of patients with SHPT (19.4%, N=36), RYGB had 12.8% (N=274) and SG 5.3% (N=131). At 48 months after surgery, RYGB had the highest prevalence of SHPT (27.0%, N=222), LAGB had 13.2% (N=53) and SG 6.9% (N=58). Multi-variate logistic analysis showed that increased body mass index and age, decreased levels of vitamin D and RYGB were independent predictors of SHPT one year after surgery. The only independent predictor of

SHPT four years after surgery was RYGB. **Conclusion:** The prevalence of SHPT is considerably higher before and four years after BS than 1 year after surgery. This fact raises some questions about the efficacy of the implemented follow-up plans of vitamin D supplementation on the long term, mainly among patients submitted to RYGB.

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Serum Calcium Levels in Adult Patients With Chronic Hypoparathyroidism Treated With rhPTH(1–84) Compared With a Historical Control Cohort

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Adult patients (pts) with chronic hypoparathyroidism (HypoPT) have wide fluctuations in albumin-corrected serum calcium (Ca) measurements.[1] This study assessed Ca levels over a 5-yr period in adult pts with chronic HypoPT treated with or without recombinant human parathyroid hormone (1–84), rhPTH(1–84). The rhPTH(1–84)-treated pt cohort was from NCT01297309 (RACE) and NCT01199614 (HEXT) clinical trials. A historical control pt cohort with chronic HypoPT who did not receive rhPTH(1–84) or rhPTH(1–34) came from the US Explorys electronic medical record database (Jan 2007−Aug 2019); selection criteria were similar to those used for the rhPTH(1–84)-treated cohort. The index date was the day after initiation of treatment for the rhPTH(1–84) cohort and the day after the first calcitriol prescription for the control cohort. Pts were required to have ≥1 pair of serum albumin and Ca values occurring on the same date during the 6 months before index and 5 yrs (±6 months) after index. For pts from RACE, baseline and study visit data after rhPTH(1–84) initiation were collected from the antecedent trials. Specified ranges for albumin-corrected serum Ca values were: <7.5 mg/dL (<1.875 mmol/L); ≥7.5−<8.0 mg/dL (≥1.875−<2.0 mmol/L); ≥8.0−<9.0 mg/dL (≥2.0−<2.25 mmol/L); ≥9.0−<10.2 mg/dL (≥2.25−<2.55 mmol/L); and ≥10.2 mg/dL (≥2.55 mmol/L). Changes in Ca levels were assessed using multivariable regression models. There were 71 pts in the rhPTH(1–84) cohort and 119 pts in the control. Before the index date, rhPTH(1–84)-treated pts, compared with the control, were younger (mean±SD, 47.8±10.8 vs 54.9±15.5 years; P<0.001) and a lower proportion had acute manifestations of HypoPT (22.5% vs 64.7%; P<0.001). Over a 5-yr period, in adjusted analyses rhPTH(1–84)-treated pts, compared with the control, had a similar mean proportion of <7.5 mg/dL Ca measurements per pt (13.1% vs 13.1%; P=0.41), a higher proportion of ≥7.5−<8.0 mg/dL Ca measurements per pt (18.8% vs 10.6%; P<0.001), a similar proportion of ≥8.0−<9.0 mg/dL Ca measurements per pt (50.7% vs 48.5%; P=0.68), a lower proportion of ≥9.0−<10.2 mg/dL Ca measurements per pt (15.6% vs 24.1%; P<0.001), and a lower proportion of ≥10.2 mg/dL Ca measurements per pt (1.9% vs 3.7%; P=0.27). The rhPTH(1–84) cohort, compared with the control, had a higher proportion of pts with target range Ca measurements ≥7.5−<9.0 mg/dL (≥1.875−<2.25 mmol/L) for at least 50% of their values (88.7% vs 62.2%; P<0.001). Data interpretation is limited by the differing pt management (ie, trial protocols for the rhPTH[1–84] cohort and clinical practice for the control cohort). Over a 5-yr period, per pt serum Ca levels fluctuated in pts with chronic HypoPT, but levels were more stable in pts treated with rhPTH(1–84) and a lower proportion had hypercalcemia, compared with controls. 1. Ayodele O, et al. ASBMR 2020, 11−15 Sep 2020.

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The Calcium-Sensing Receptor (CaSR) Variants at rs1801725 Increase the Risk of Developing Secondary Malignant Cancers

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The dysregulation of systemic calcium homeostasis during malignancy is common in most patients with high-grade tumors. The associated comorbidity is known as cancer-induced hypercalcemia (CIH) which affects up to 30% of cases, in the absence of metastasis. In the course of breast cancer progression, the secretion of parathyroid hormone-related protein (PTHrP) by tumor cells and the associated destruction of bone tissues, leads to a progressive increase in systemic calcium or CIH. The increase in circulating Ca^{2+} is sensed by the calcium-sensing receptor (CaSR), which plays a significant role in maintaining Ca^{2+} homeostasis. More than 200 mutations and single nucleotide polymorphisms (SNPs) in the CaSR gene have been described, including the A986S CaSR at rs1801725 and Q1011E CaSR at rs1801726 SNPs with reduced sensitivity to Ca^{2+}. Interestingly, high circulating Ca^{2+} is associated with aggressive breast tumors in premenopausal women and larger tumors in postmenopausal women; however, the contribution of the CaSR in breast cancer progression remains poorly understood. Unlike SNPs at rs1801726, up to 20% of breast cancer patients with SNPs at rs1801725 may be predisposed to higher circulating Ca^{2+} in the course of their disease. Since breast cancer frequently metastasizes to Ca^{2+} rich skeletal tissues, we hypothesize that the development of CIH and subsequent desensitization of the CaSR by sustained high Ca^{2+} is critical for both the adaptation of TNBC cells to CIH in Ca^{2+} rich microenvironments and TNBC progression. Our preliminary data reveal that the expression level and mutational status of the CaSR is cell type-specific, and that sustained high Ca^{2+} desensitizes the receptor, but promotes tumor cell growth and motility. Sustained high Ca^{2+} also triggers the expression of metastasis promoting genes, including the cancer/testis antigen, MAGEC2, and Plasminogen Activator Inhibitor, PAI-2, potentially via the early response genes FOS/FOSB. In addition, our preliminary data show that the A986S SNP is associated with hypercalcemia, secondary malignancy of bone and respiratory organs, and deficiency of humoral immunity. This study provides novel insights into not only the