



AT THE FOREFRONT

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Medicine**

Hyperparathyroidism in ESRD Patients

Lee Stratton, MD
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Dr. Stratton does not have any relevant financial relationships with any commercial interests.

Learning Objectives

- Review of Secondary and Tertiary Hyperparathyroidism pathophysiology
- Nonsurgical Options of Hyperparathyroidism in ESRD/Transplant Patients
- Optimal Timing of Operative Intervention
- Decreasing Length of Stay Postoperatively and Reducing Readmissions

Case Description

44 F referred for evaluation of hyperparathyroidism. Creatinine slowly uptrending due to tacrolimus toxicity, relisted for renal transplant with planned liver donor. Has never required dialysis.

- PMH: HTN, DM Type 1 (in remission), CKD, hypothyroidism (levothyroxine 75 mcg daily)
- PSH: simultaneous kidney-pancreas transplant (2014), umbilical hernia repair (2016), tonsillectomy
- Immunosuppression:
 - tacrolimus 1 mg QAM/0.5 mg QPM
 - MMF 350 mg BID
 - Prednisone 5 mg daily
 - Belatacept monthly infusions

Lab Trends

- Pre-Transplant:
 - 2012: PTH 252
 - 2014: PTH 1109
- Post-Transplant:
 - 2014: PTH 186
 - 2015: PTH 99
 - 2019: PTH 1077
 - 2020: PTH 2498, Phos 3.7-5.6, Vitamin D 25-OH 27-38, TSH 1.4, Hgb A1c 4.6%
 - Creatinine: Slowly uptrending. Current baseline 3.2-3.6, eGFR 15 (CKD Stage 5)

Diagnosis?

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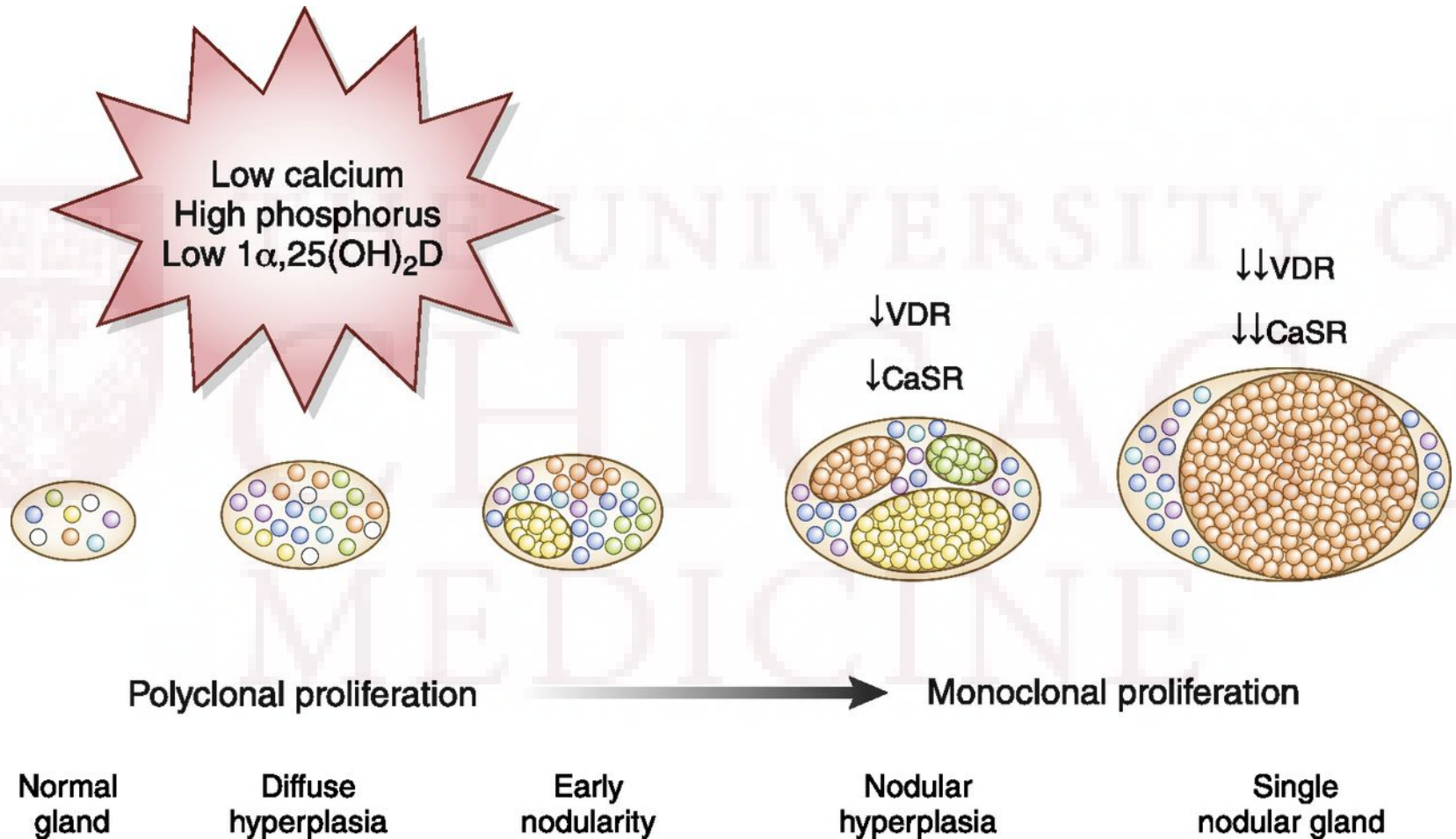
Diagnosis?

Secondary Hyperparathyroidism

Pathophysiology

- eGFR < 45, PTH begins to increase and the glands slowly undergo hyperplasia
- FGF-23 increases, suppressing 1α -hydroxylase, causing Vitamin D deficiency
- Hyperphosphatemia stimulates PTH production and chelates calcium, leading to hypocalcemia
- Elevated PTH
 - A perpetrator and a consequence of decreased BMD
 - Worsens CKD osteodystrophy
 - Anemia resistant to erythropoietin
 - Worsened atherosclerosis in animal models

Pathophysiology of secondary hyperparathyroidism in CKD. Circulating fibroblast growth factor-23 increases early in CKD and suppresses 1α -hydroxylase in the kidney, leading to deficiency of active vitamin D [$1\alpha,25(\text{OH})_2\text{D}$].



Wei Ling Lau et al. CJASN 2018;13:952-961

CJASN

Medical Management

- Trending Calcium, PTH, Vitamin D, phosphorus
 - Abnormalities increase PTH
 - PTH 300-450 increased all-cause mortality and cardiovascular admissions (HR = 1.09)
 - PTH >600 pg/ml (HR 1.23)
- Treating hypocalcemia
 - Most due to vitamin D deficiency
- Treating Vitamin D deficiency
 - Hold until after phosphorus is normalized and hold if calcium elevated
 - Vitamin D3 vs calcitriol
- Calcimimetics
 - PTH reduction 22, Ca reduction 0.7
 - No change in cardiovascular related mortality (EVOLVE Trial)
 - Off label use in tertiary hyperparathyroidism patients
- Treating hyperphosphatemia
 - Significant increase in mortality among dialysis patient
 - Dietary restriction (900mg/day)
 - Phosphate binders (when Phos > 5.5):
 - calcium carbonate, calcium acetate versus sevelamer, lanthanum

KDIGO Guidelines

2017 Kidney Disease: Improving Global Outcomes Guidelines

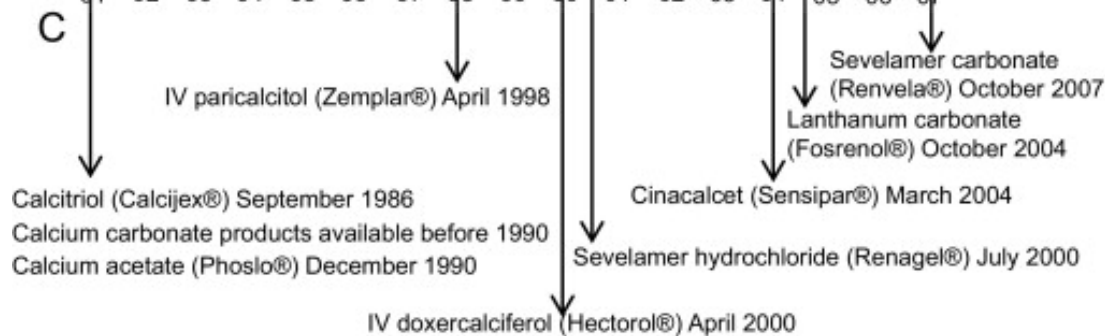
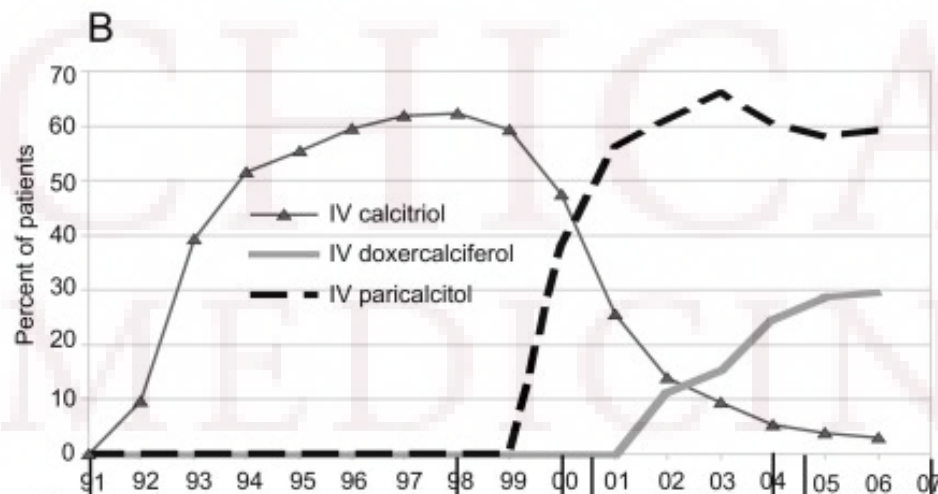
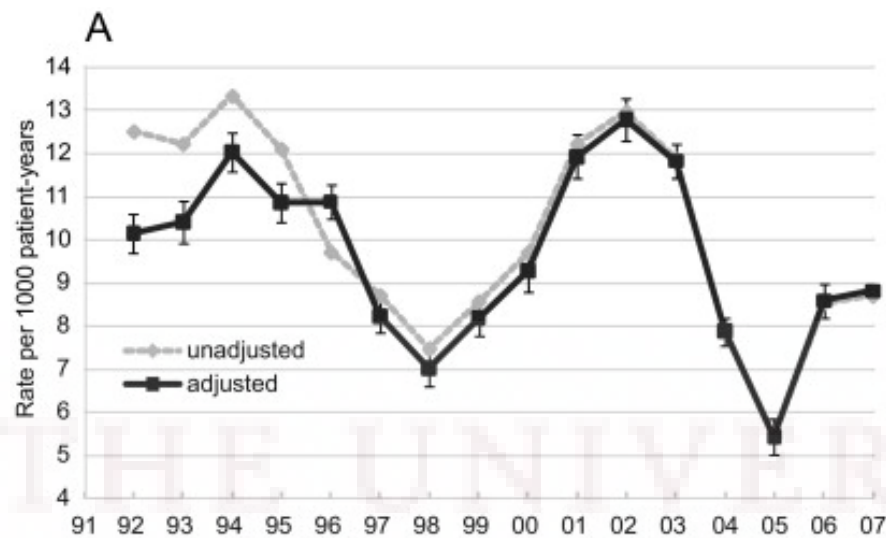
- “Global picture” based recommendations, rather than specific labs
- Calcimimetics vs calcitriol/Vit D: no studies demonstrated a benefit between which to use as first line. Not routinely recommended for patients not yet on dialysis
- BMD testing
- Optimal PTH level unknown: patients with PTH levels progressively rising or persistently elevated be evaluated for modifiable risk factors

Parathyroidectomy

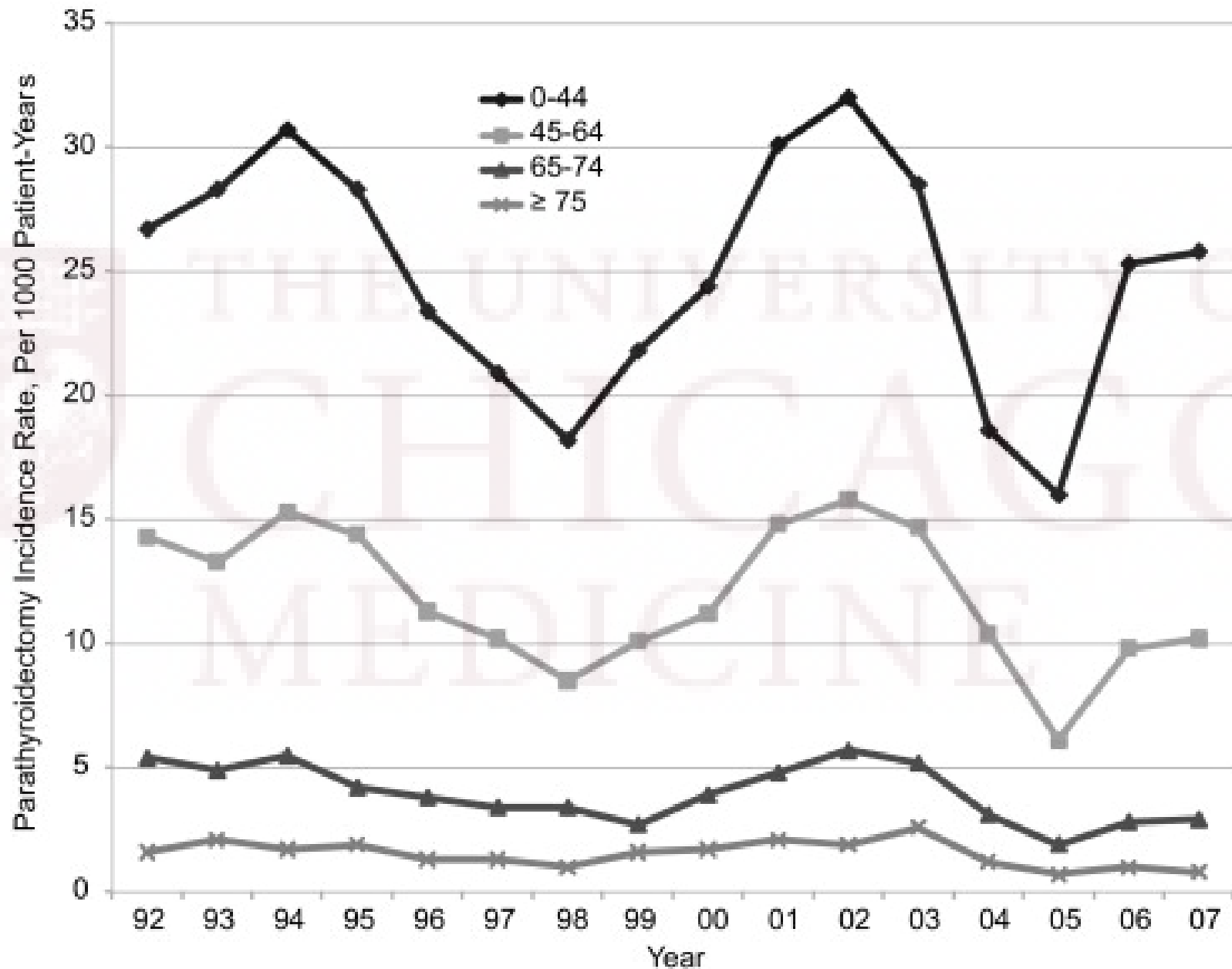
- 30 day readmission rate: 29.3%
- 30 day mortality: 2%
- 15-57% significant increase in median overall survival postoperatively
- Decreased risk of graft-loss in post-transplant patients
 - PTH > 65: 85% increased in graft-loss (ALERT Trial)
 - Persistent hyperparathyroidism post-renal transplant can occur up to 50%
- Increased BMD and decreased risk of fracture (hip fx OR 0.68)
- When do you refer these patients to a surgeon?

Parathyroidectomy

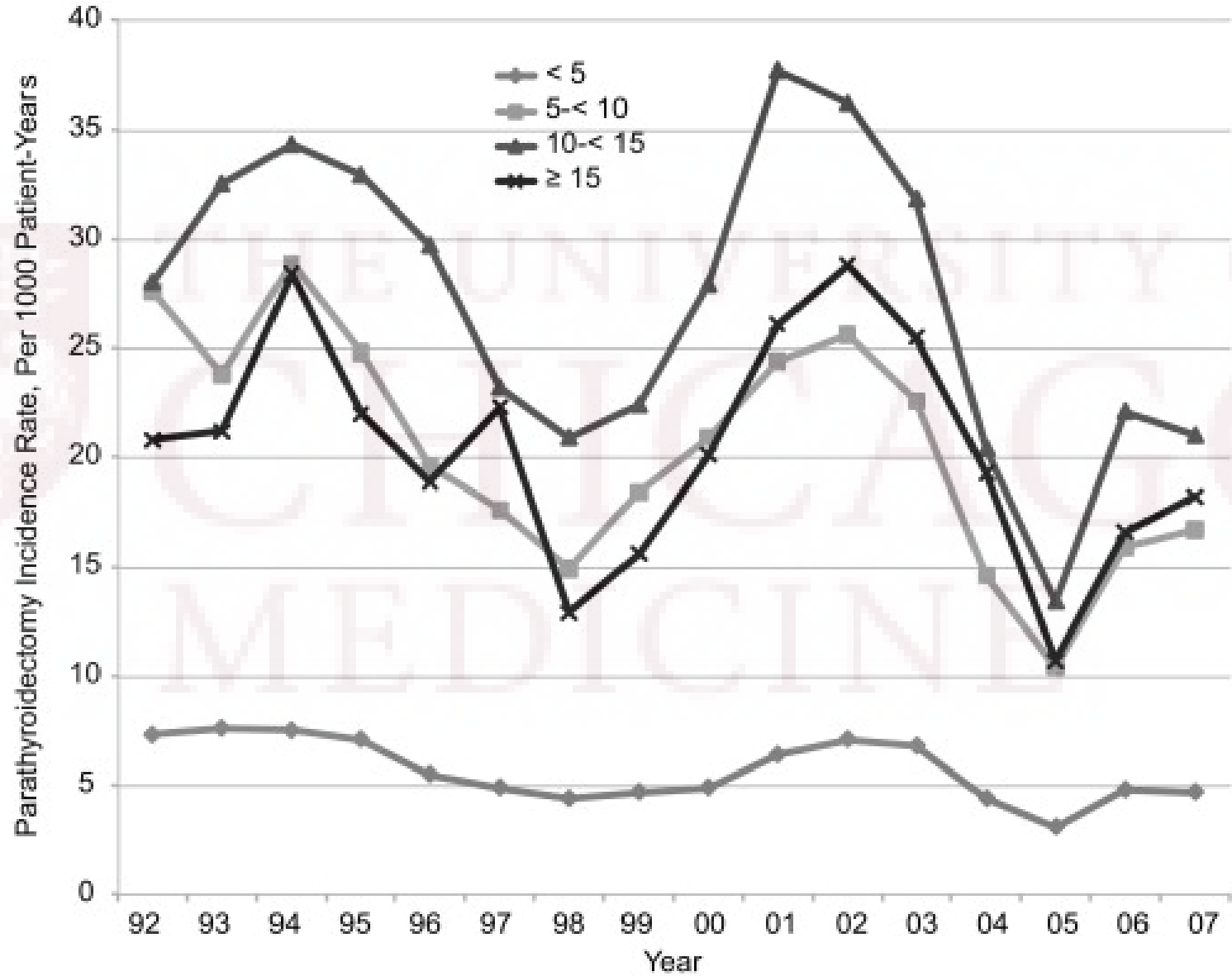
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- Increased BMD and decreased risk of fracture (hip fx OR 0.68)
- Surgical Referral
 - PTH cutoffs: > 800 in some groups (NKF 2003 guidelines)
 - “Failure” of medical management (KDIGO guidelines)
 - PTH 60–240 pg/ml (Japanese Society for Dialysis Therapy 2012 guidelines)
 - x2-9 times the upper normal range (130–600 pg/ml; KDIGO guidelines 2009)



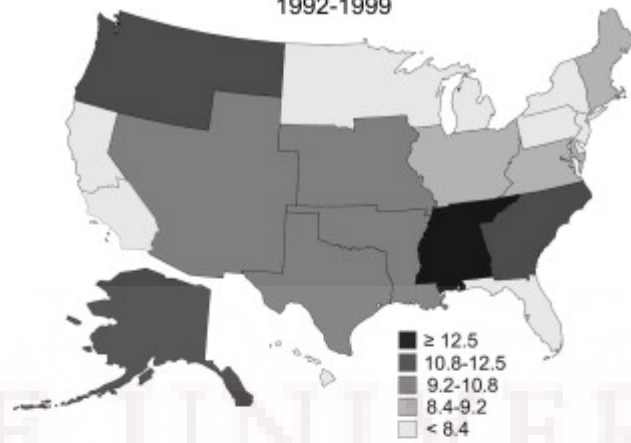
Patient Age



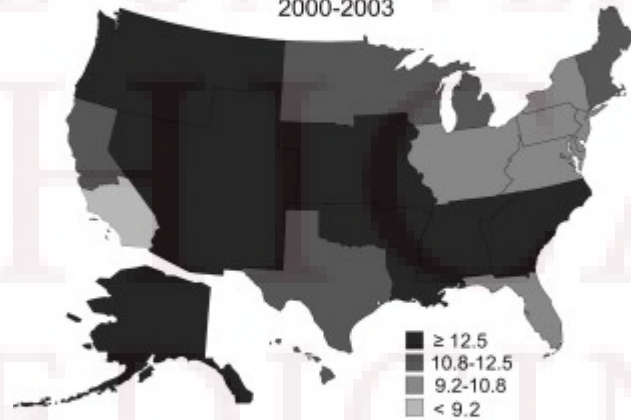
Time on Dialysis



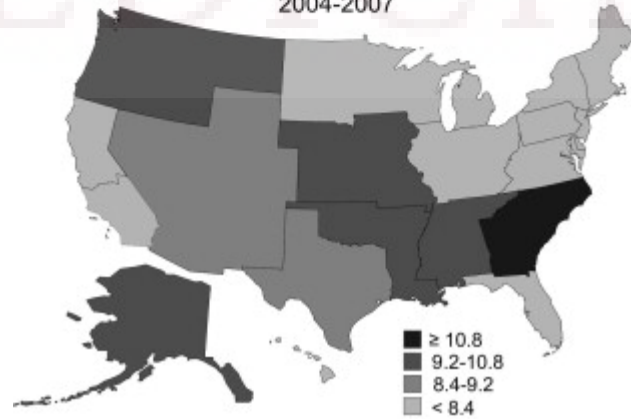
1992-1999



2000-2003



2004-2007



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Parathyroidectomy

When to consider parathyroidectomy in dialysis patients

- Persistent (>6 months) elevated PTH despite maximal management with vitamin D analogs and calcimimetics†
and
- Patient is a surgical candidate
and
- Refractory hypercalcemia or hyperphosphatemia; presence or high risk of calciphylaxis; or anemia hypo-responsive to erythropoietin



Surgical referral

- Parathyroid ultrasound
and/or
- ^{99m}Tc -sestamibi radionuclide scan*
and/or
- Intraoperative blood PTH sampling

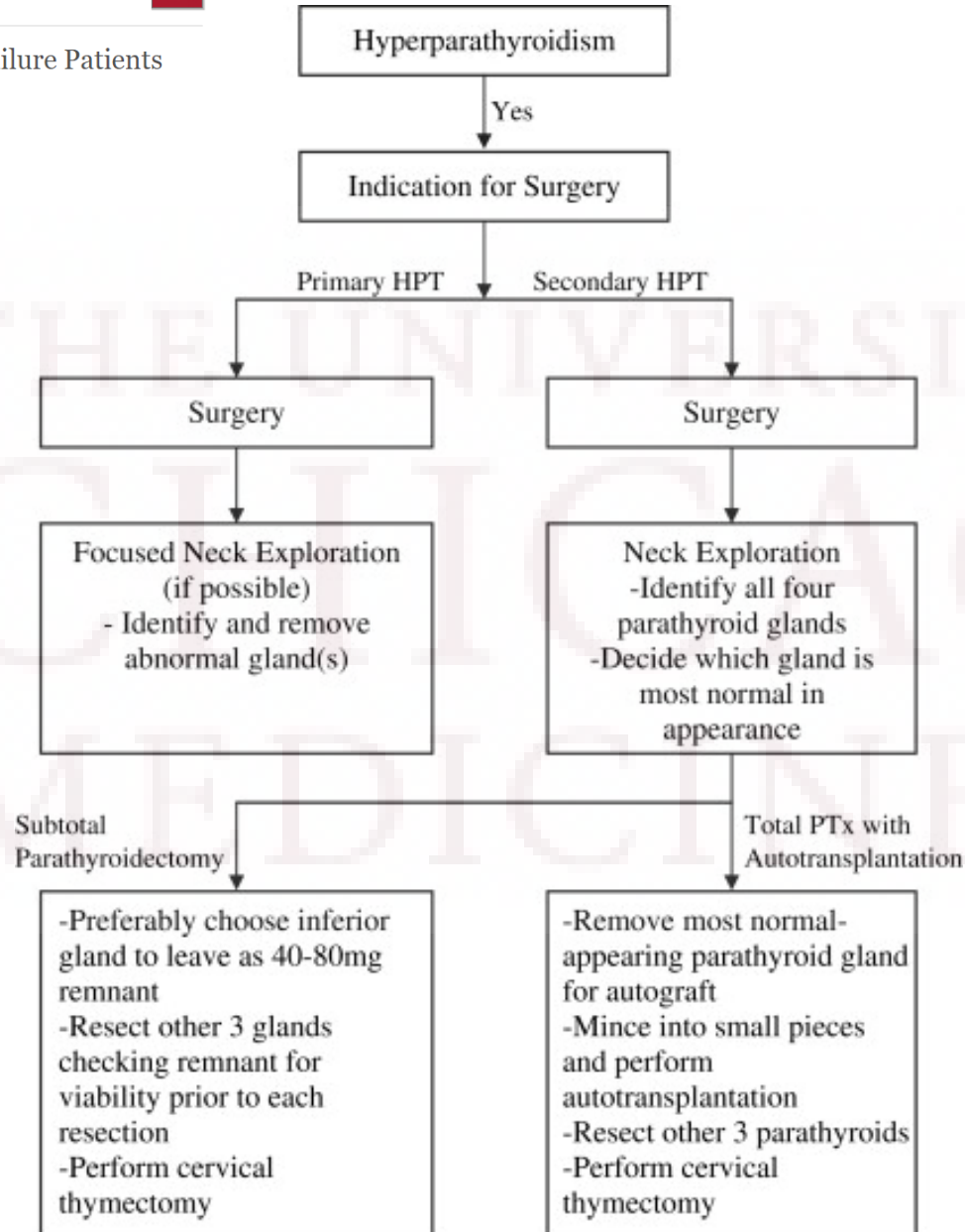
Goals of Surgery

- Subtotal parathyroidectomy vs total parathyroidectomy and autotransplant
 - Identify all four glands
 - Choose the most normal appearing to leave as a remnant (30-40g), ideally inferior gland
 - Marking the remnant gland or autotransplant site
 - Take the remaining three
 - Check PTH levels (goal high normal to high 100s)
- Focused parathyroidectomy
 - Focused exploration and resection
 - Check PTH levels

 - Utility of Sestamibi scan: help assess for abnormal/ectopic location. Weaker relationship with imaging detection and anatomic size compared to adenomas
 - Utility of US: identification of parathyroids, but also identify any thyroid pathology prior to surgery
- Patients with significant calciphylaxis: consider total thyroidectomy alone



Parathyroid Surgery in Renal Failure Patients

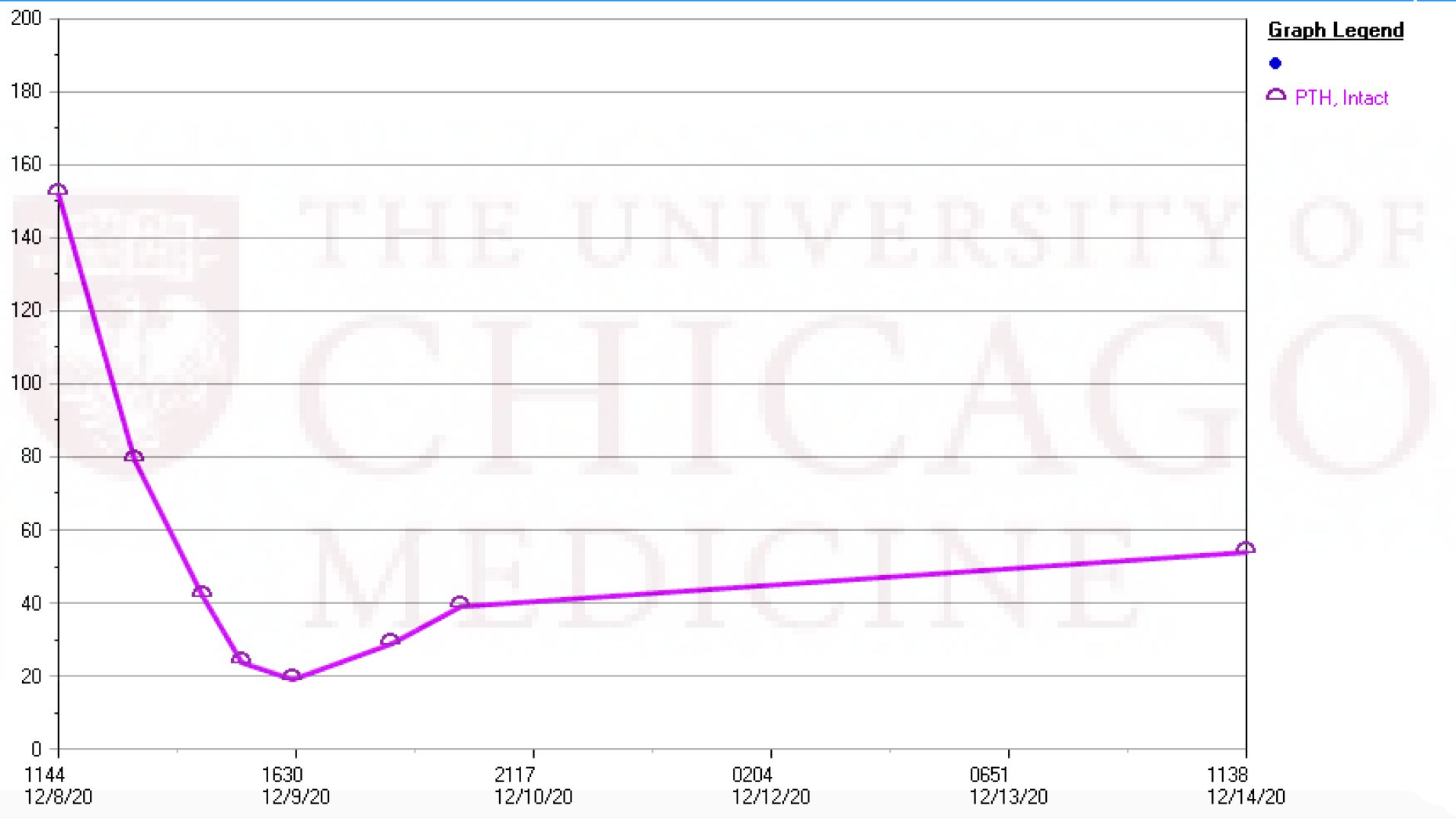
Vidas Dumasius MD, Peter Angelos MD, PhD 

Operative Course

- Preoperative workup
 - Thyroid US: Well-circumscribed hypoechoic extrathyroidal lesions posterior to the bilateral thyroid lobes are nonspecific and may be compatible with parathyroid adenoma
 - Sestamibi: Findings compatible with bilateral parathyroid adenomas at the inferior pole of the thyroid
- Preoperative calcitriol
- Subtotal parathyroidectomy (remnant gland left superior, atypical location in carotid sheath)
 - ioPTH levels dropped from 1369 to 370 post-excision
 - Goal PTH
 - Goal remnant size/location
- Required postoperative calcium IV, transitioned to PO and observed 24 hours prior to discharge

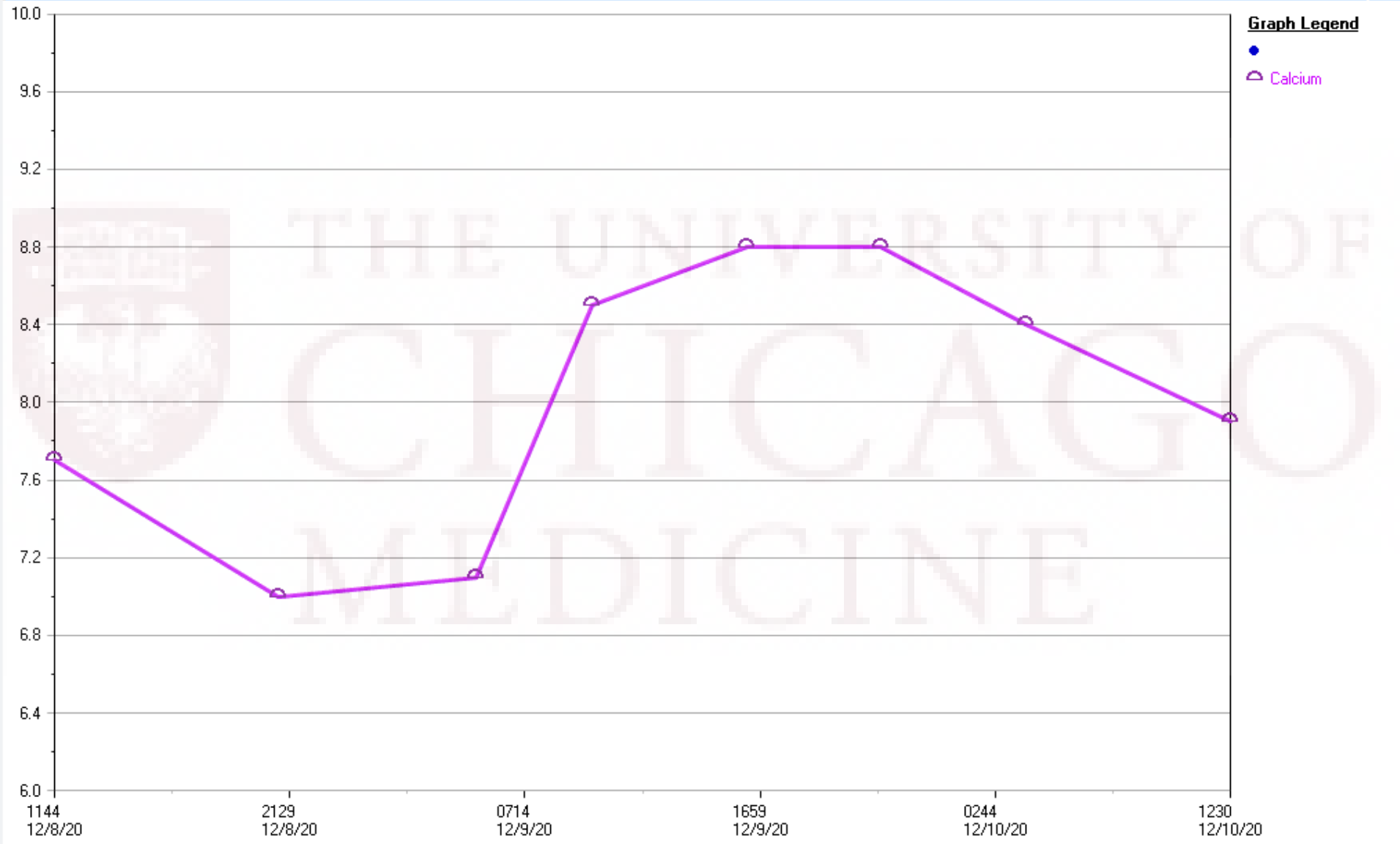
Graph (12/8/20 1144 - 12/14/20 1138)

Close



Graph (12/8/20 1144 - 12/10/20 1230)

Close



Postop Considerations

Monitor for Hungry Bone Syndrome

- Occurs in >25% of patients; serum calcium nadirs 1-3 weeks post-op
High risk if young age <45 years, post-op calcium 8.4 mg/dL, high alkaline phosphatase >120 IU/L (pre-op PTH level is not predictive)
- Treatment includes high-doses of oral and IV calcium and vitamin D (calcitriol is preferred), and high calcium dialysate (3.0 mmol/L)

Decreasing Length of Stay



Contents lists available at [ScienceDirect](#)

Surgery

journal homepage: www.elsevier.com/locate/surg



Preoperative calcitriol reduces postoperative intravenous calcium requirements and length of stay in parathyroidectomy for renal-origin hyperparathyroidism [☆]



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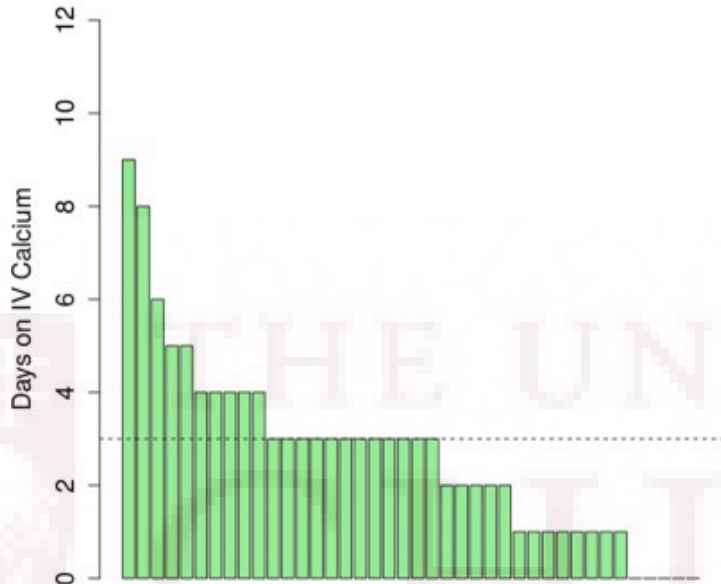
^b Department of Surgery, University of Montreal, QC, Canada

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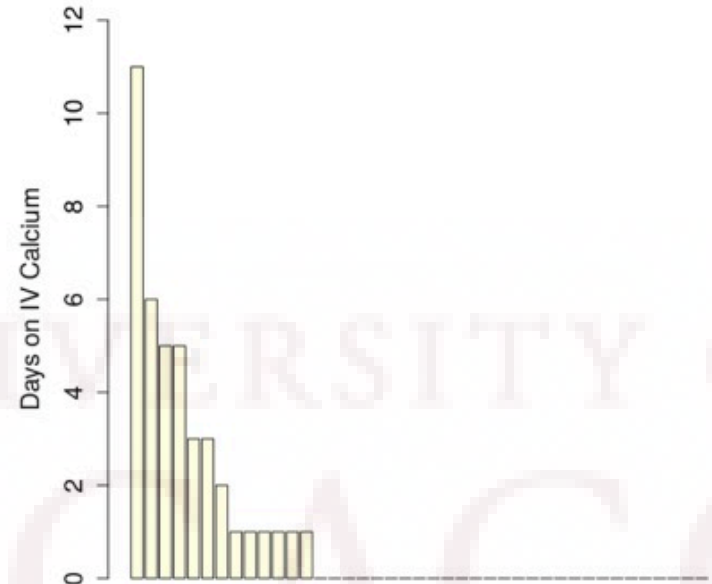
Preoperative Calcitriol

- Preoperative use increased over time (0% 2004–2010, 69% 2011–2016)
- Less often required postoperative administration of IV calcium (34% vs 90% of patients who did not receive preoperative calcitriol treatment, $P < .001$)
- Median length of stay was 2.0 days shorter ($P < .001$)
 - Average LOS 2 vs 4 days between groups
- Factors associated with postoperative administration of IV calcium included:
 - not receiving preoperative calcitriol treatment
 - low preoperative calcium
 - high preoperative parathyroid hormone
- Recommendation: calcitriol 0.5mcg BID 10-14 days prior to surgery

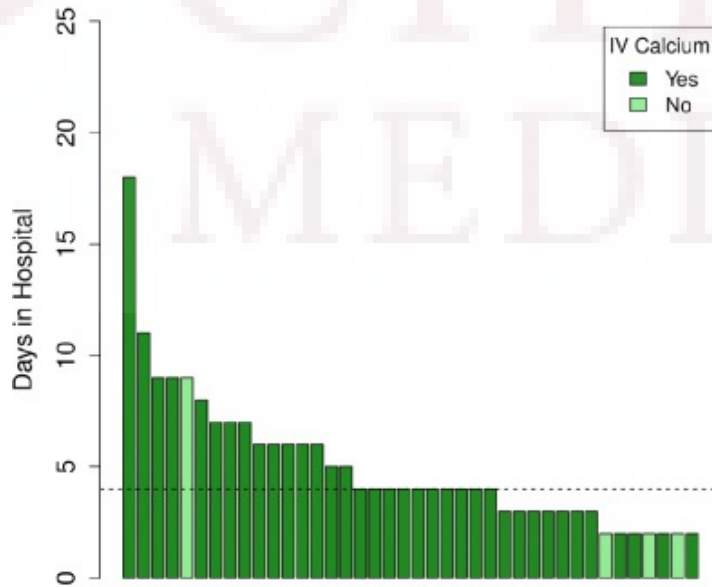
Days on IV Calcium in NPC Group



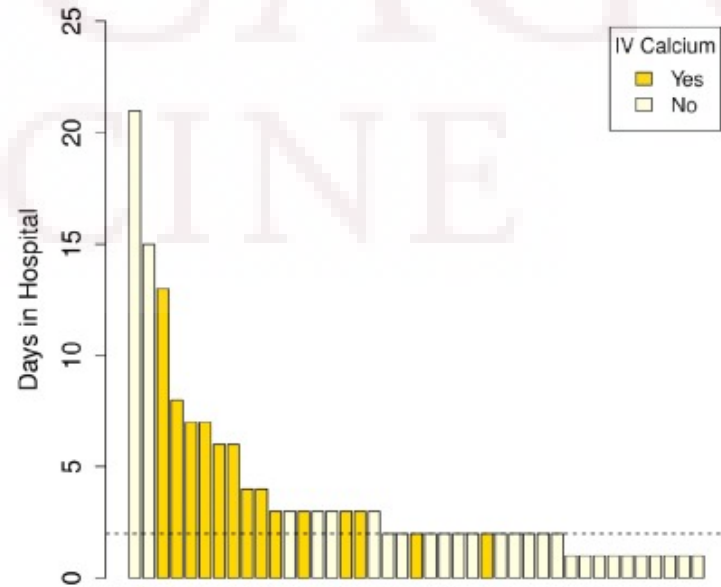
Days on IV Calcium in PC Group



Length of Stay in NPC Group



Length of Stay in PC Group



Patients (n=40)

Patients (n=41)





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