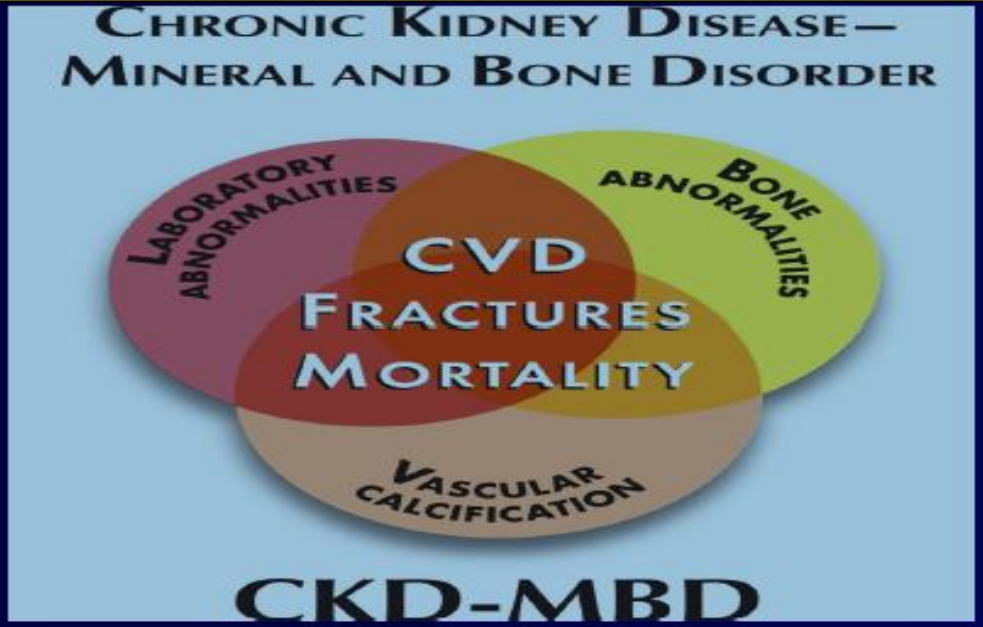
CKD-MBD: Classifications and Diagnosis

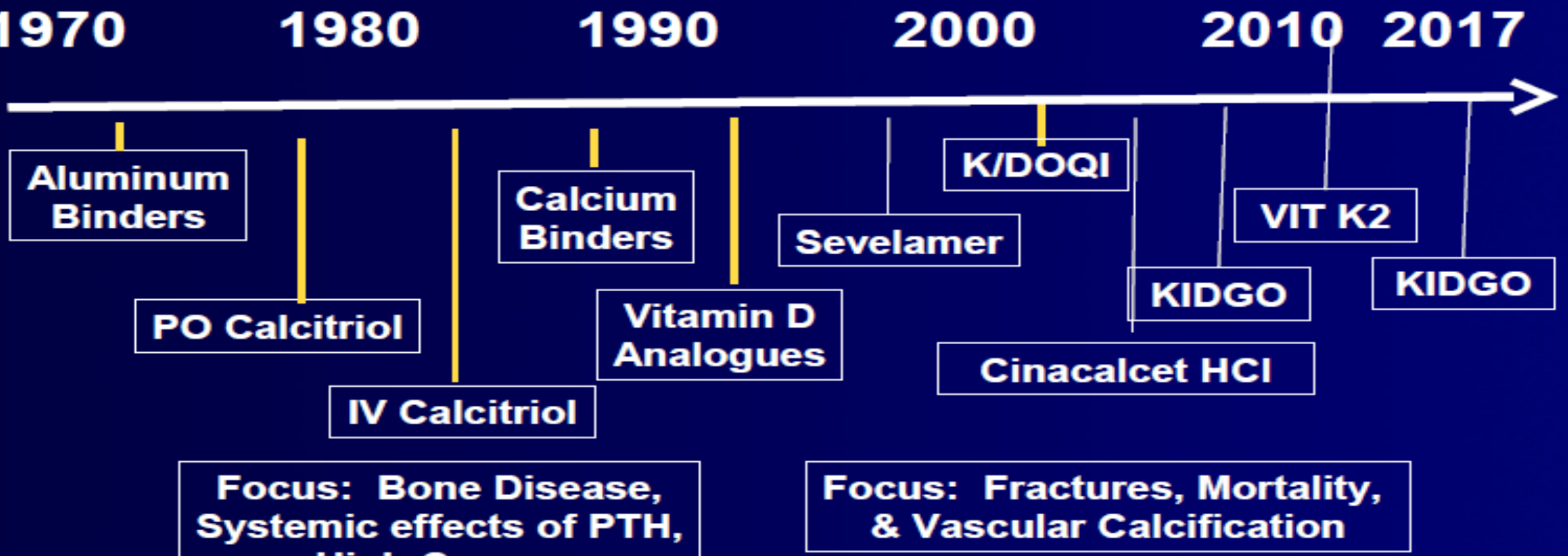


Dr. Houshang – Sanadgol
Prof of Internal Medicine and Nephrology
Tehran_ Iran
Jul.2020

Agenda

- The size of the problem (CKD-MBD)
- Definitions & Classifications
- Bone disease in CKD (B)
- Vascular calcifications/CVD (V/C)
- Role of Calcium and Phosphorus (L)
- Importance of Vitamin D in CKD-MBD (L)
- CKD & SHPT (L)
- Frequency of Monitoring
- CKD-MBD 2017 Guidelines (Diagnosis of CKD-MBD & VC)

History of Treatment Strategies for Secondary Hyperparathyroidism

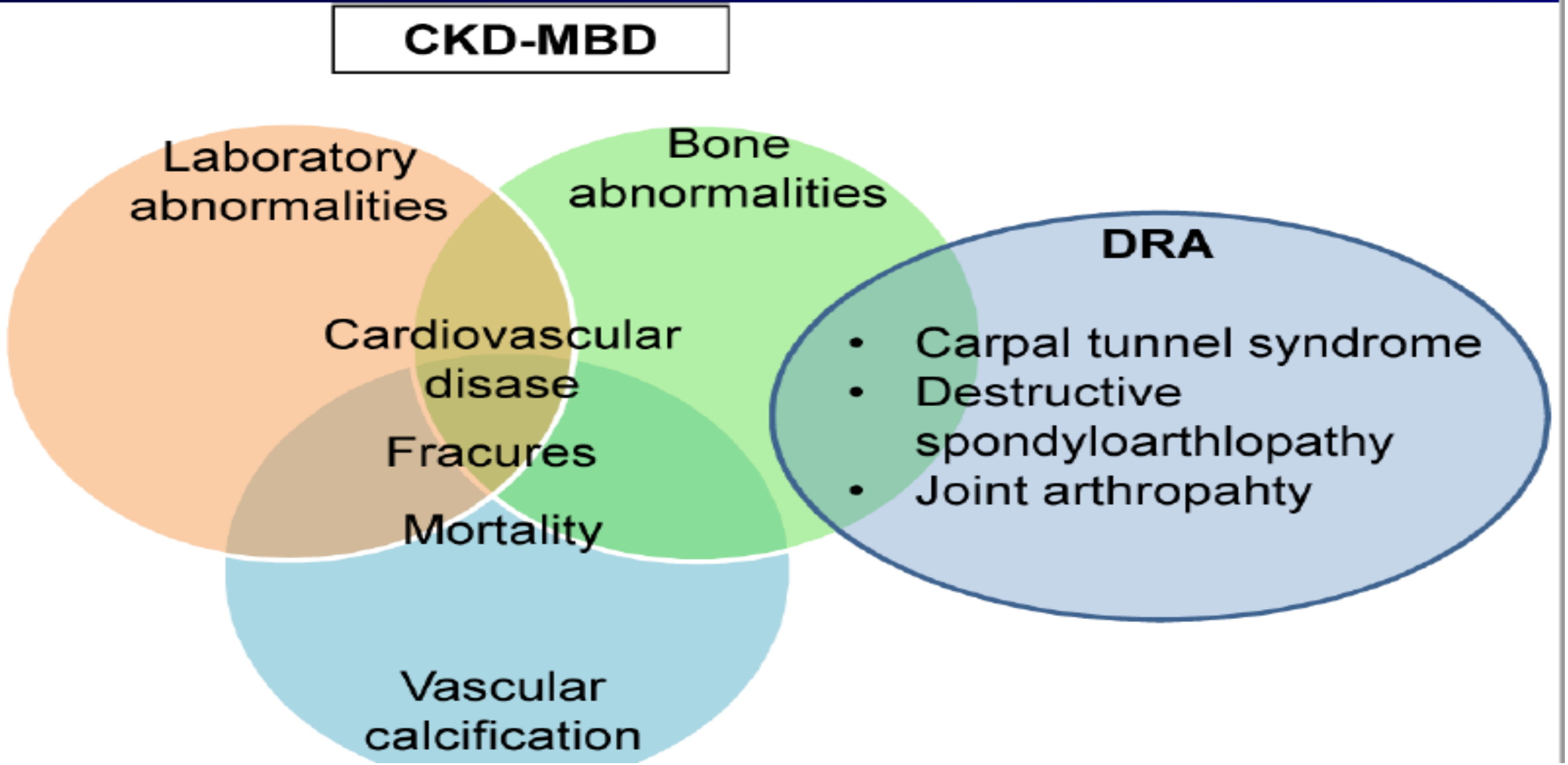


Definition of CKD-MBD And Renal Osteodystrophy

- **Definition of CKD-MBD**
  - A systemic disorder of mineral and bone metabolism due to CKD manifested by either one or the combination of the following:
    - **L**/Abnormalities of calcium, Phosphorus, PTH, or Vitamin D metabolism
    - **B**/ Abnormalities in bone turnover, mineralization, volume, linear growth, or strength.
    - **V/C** : Vascular or other soft-tissue calcification
- **Definition of Renal Osteodystrophy**
  - Renal osteodystrophy is an alteration of bone morphology in patients with CKD.
  - It is one measure of the skeletal component of the systemic disorder of CKD-MBD that is quantifiable by histomorphometry of bone biopsy.

- Uhlig et al, AJKD Vol 55, No 5, May 2010.
- KDIGO classification of CKD-MBD 2009

CKD-MBD components



Pathophysiologic mechanisms of ROD

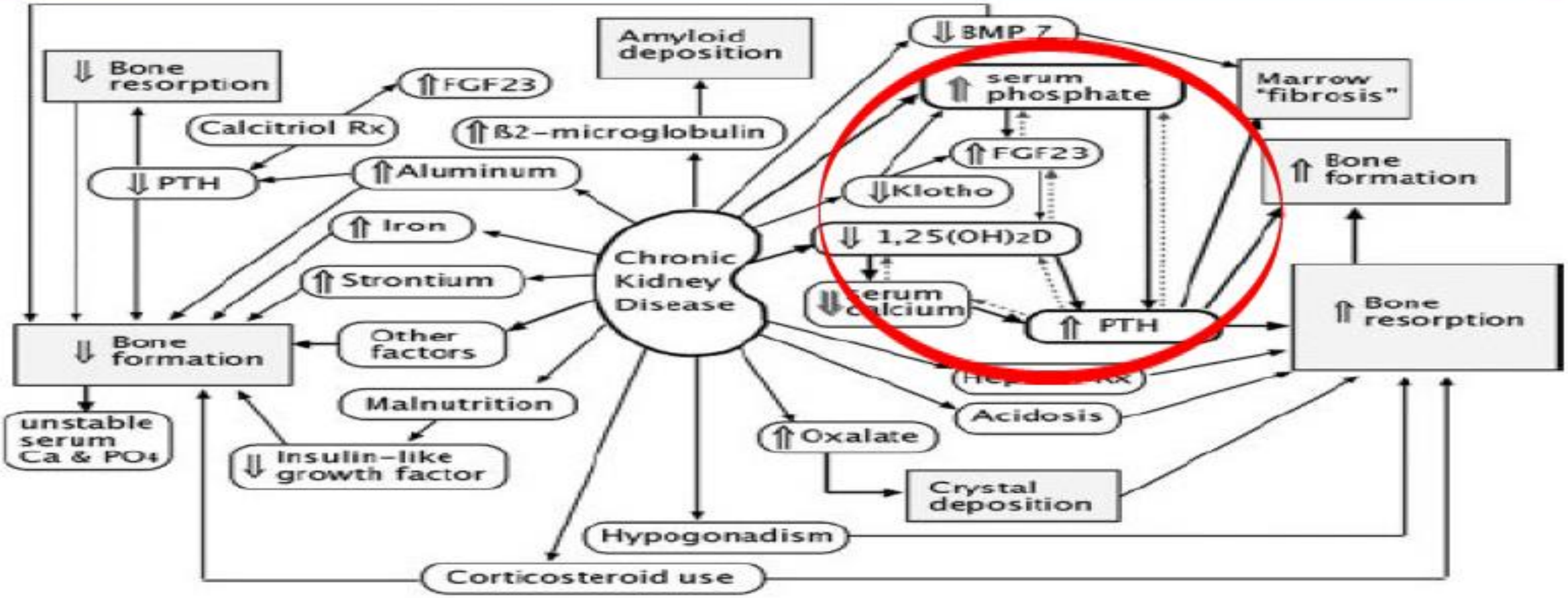


Figure 1. Pathophysiologic mechanisms of renal osteodystrophy. The dashed arrows show feedback loops that are "frustrated" by the renal dysfunction.

From the *Primer on the Metabolic Bone Diseases and Disorders of Mineral Metabolism, 7th Edition.*
www.asbmrprimer.org

Table 1. Pathology and Diagnosis of Bone Turnover in CKD

I. Predominant hyperparathyroidism, high-turnover ROD
   a. Intact PTH > 500 pg/ml
   b. Elevated alkaline phosphatase or bone-specific alkaline phosphatase
II. Low-turnover disease
   a. Adynamic bone disorder
      1. Intact PTH < 100 pg/ml
      2. Normal alkaline phosphatase or bone-specific alkaline phosphatase
      3. Low osteocalcin
   b. Osteomalacia
      1. Intact PTH < 100 pg/ml
      2. Normal alkaline phosphatase or bone-specific alkaline phosphatase
      3. Low osteocalcin
      4. Elevated Al^{3+}
III. Mixed uremic osteodystrophy
   a. PTH > 300 pg/ml
   b. Elevated Al^{3+}
V. Unknown
   a. PTH > 100 < 500 pg/ml

Bone Turnover:
Biomarkers and Images

Significance Statement

Abnormal bone turnover of renal osteodystrophy in advanced CKD can only be diagnosed using bone biopsy (gold standard). However, this is an invasive and painful procedure, and thus, it is rarely performed. This study found that three bone biomarkers (bALP, intact PINP, and TRAP5b) and high-resolution bone imaging of distal radius can discriminate patients with low bone turnover from those with nonlow bone turnover as assessed by bone histomorphometry. Hence, the biomarkers and bone imaging may have the potential to replace bone biopsy, particularly in discriminating patients with low bone turnover. They may also be useful in selecting patients for future clinical trials that aim to reduce their fracture risk.

CKD-MBD:
Changes in Plasma Mineral Parameters

Chronic Renal Disease, Second Edition, 2020

2nd Edition, 2020

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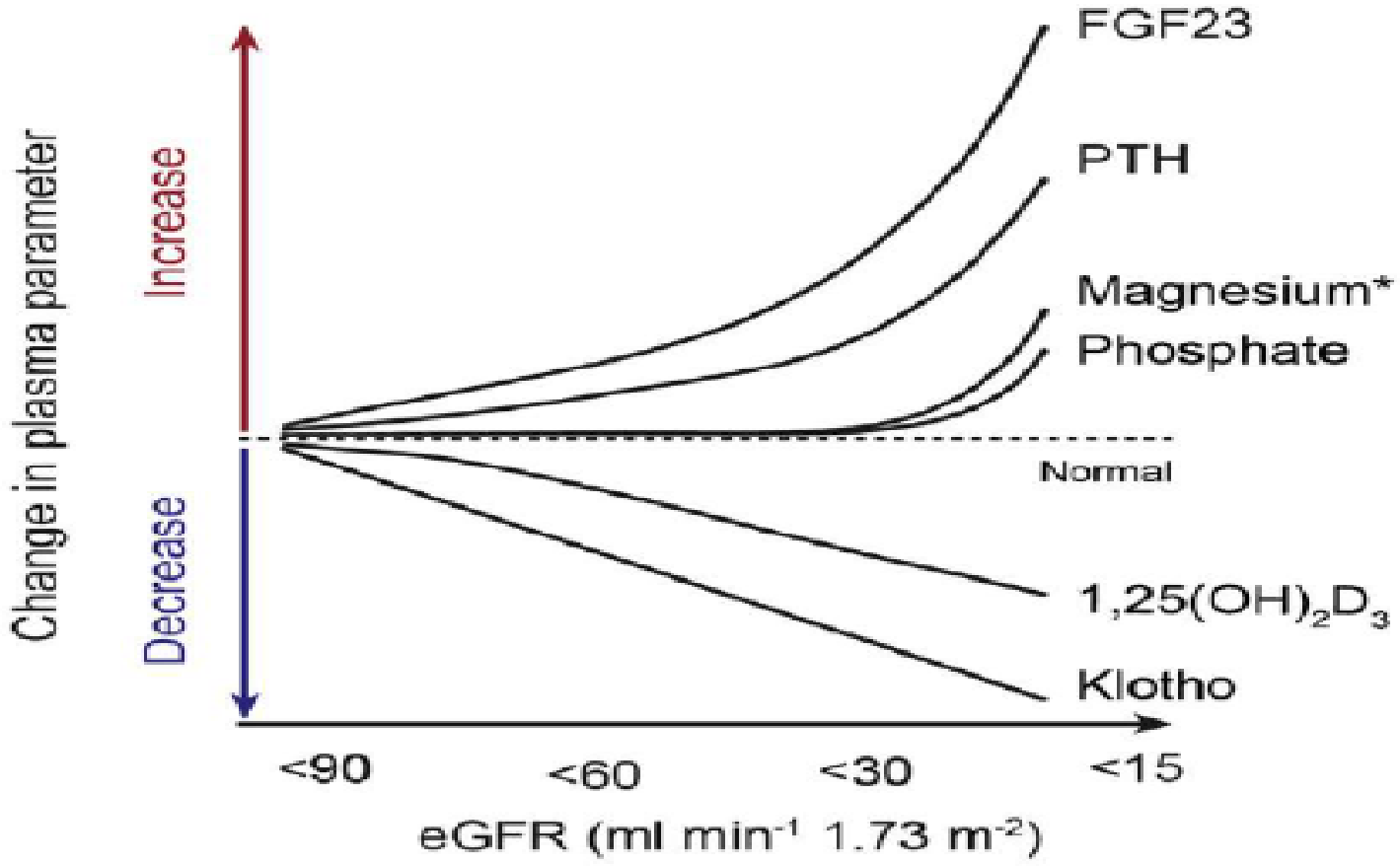
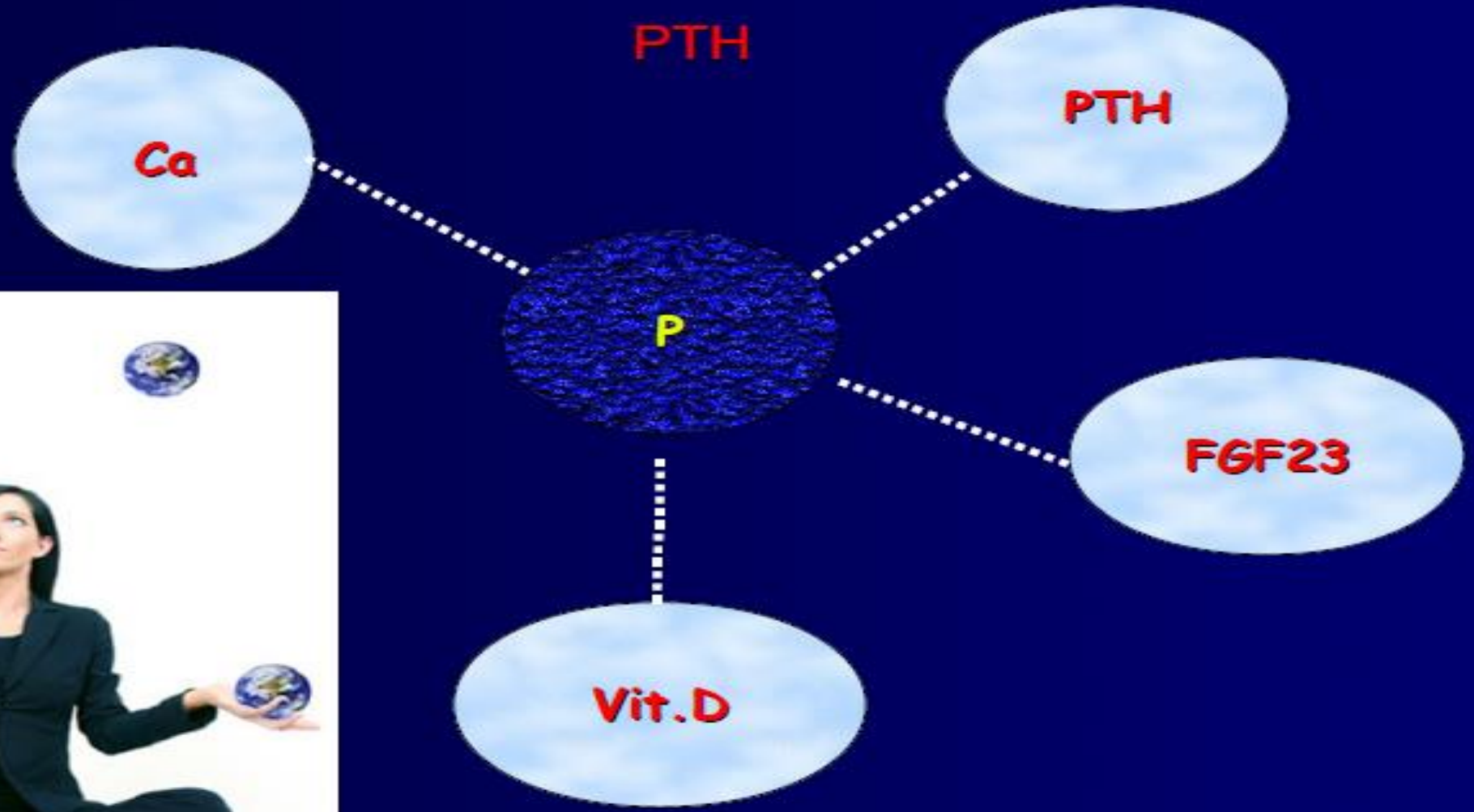


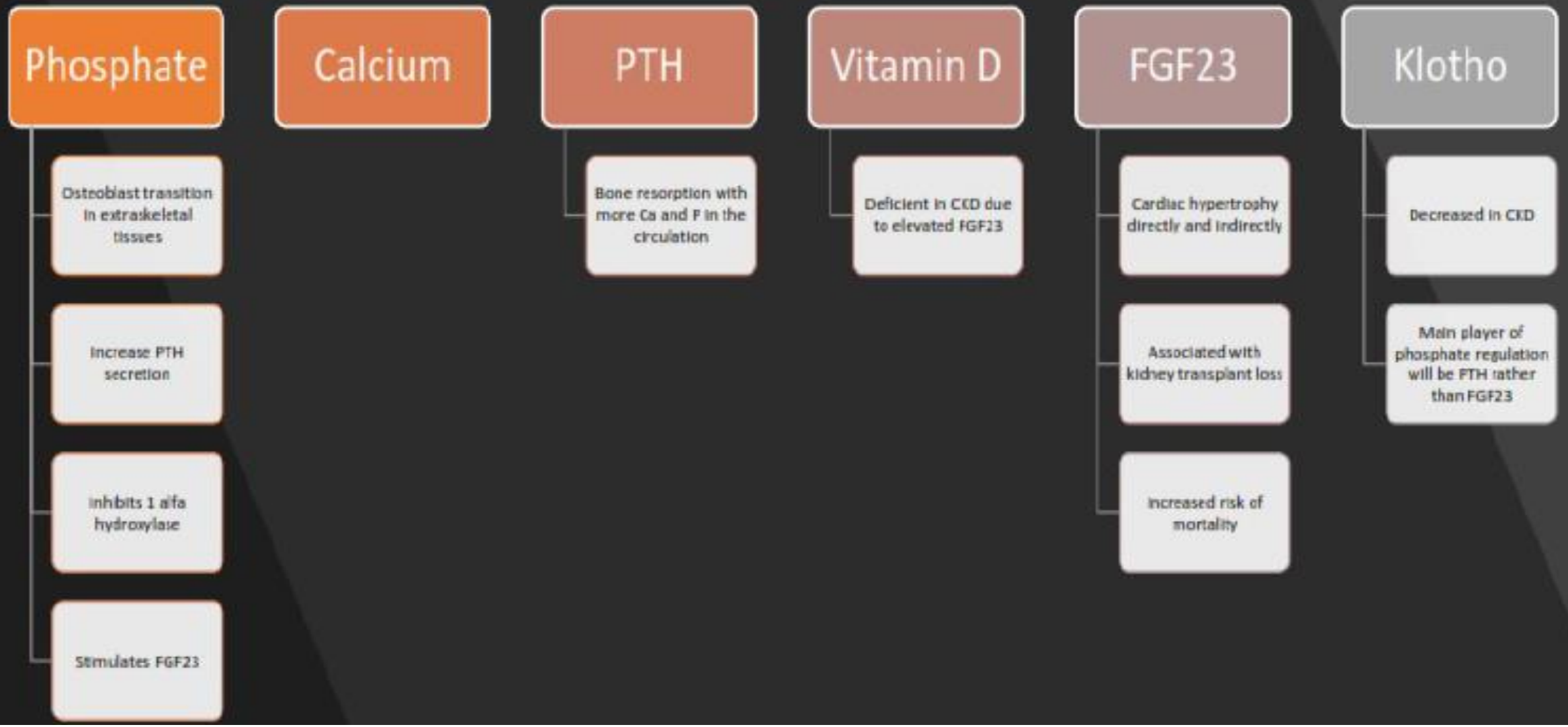
CKD-M(B/V)D Key Players

Complex interdependence of calcium, phosphorus, vitamin D, FGF23 & PTH

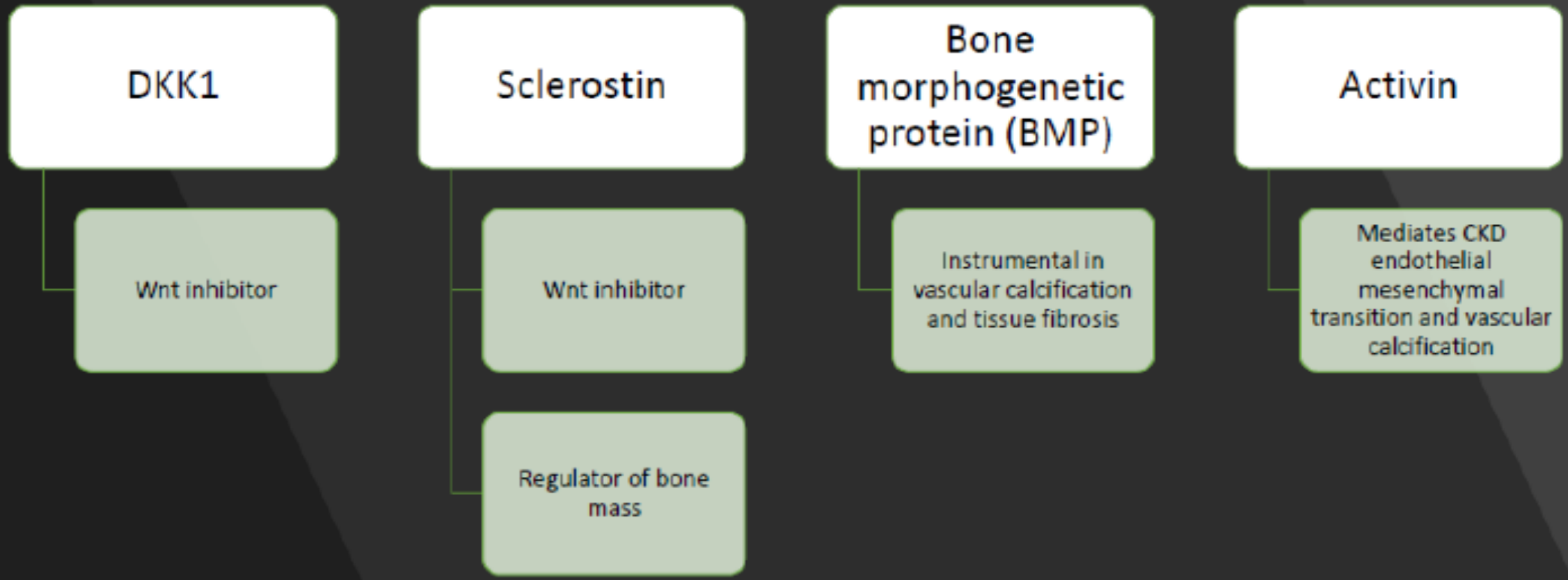


Bone and Mineral Balance

Recognized Players of CKD-MBD



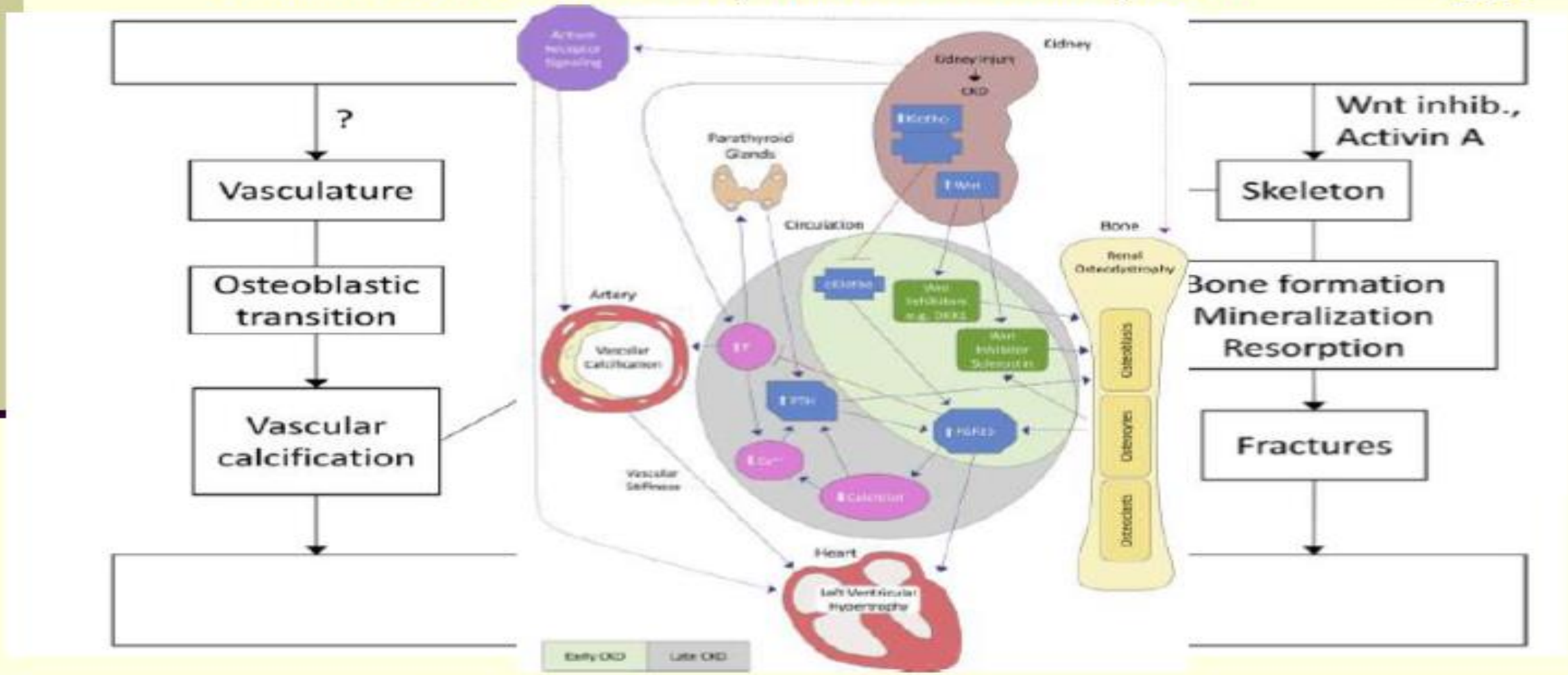
New Players in CKD-MBD



CKD-MBD: An Overview

2nd Edition, 2020

Chronic Renal Disease, Second Edition, 2020



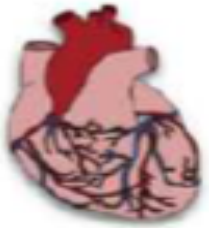
CKD-MBD:
Changes in Plasma Mineral Parameters

Chronic Renal Disease, Second Edition, 2020, Chapter 41

Uremic cardiomyopathy

Traditional risk factors
- Diabetes
- Hypertension
- Dyslipidemia
- Smoking

CKD-specific risk factors
- sHPT
- Volume overload
- Anemia
- Hypoalbuminemia



Novel risk factors
- ↑ Pi
- ↑ FGF23
- ↓ Mg
- ↓ α-Klotho

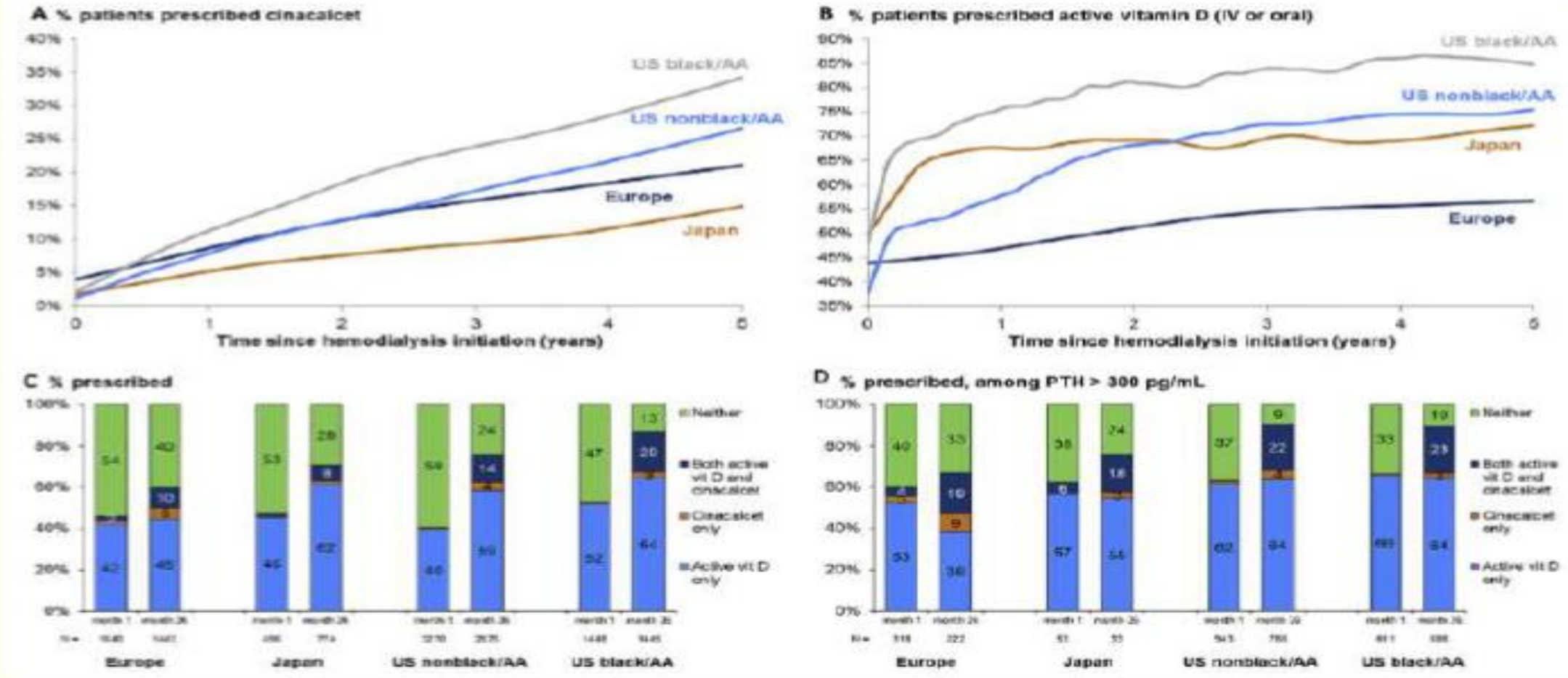
α-Klotho attenuates uremic cariomyopathy via:
- ↓ TRPC6 channel-mediated abnormal Ca signaling
- ↓ Phosphorylation of Smad2/3 and Erk pathways
- ↓ Oxidative stress

Pathological cardiac remodeling

Hypertrophy **Fibrosis**

CKD-MBD:
International and Racial Differences

Kidney Med Vol 1 | Iss 3 | May/June 2019



Grades of EBM	KDIGO 2009	KDIGO 2017
1A	0	0
1B	2	0
2A	0	0
2B	3	3
2C	10	8
2D	9	3
NOT GRADED	6	8
Total	30	22

CHAPTER 3.1:

DIAGNOSIS OF CKD-MBD: BIOCHEMICAL ABNORMALITIES

ASSESSMENT

3.1.1: We recommend monitoring serum levels of calcium, phosphate, PTH, and alkaline phosphatase activity beginning in CKD G3a *(1C)*. In children, we suggest such monitoring beginning in CKD G2 *(2D)*.

3.1.2: In patients with CKD G3a–G5D, it is reasonable to base the frequency of monitoring serum calcium, phosphate, and PTH on the presence and magnitude of abnormalities, and the rate of progression of CKD *(Not Graded)*.

ASSESSMENT

3.1.2 (cont'd.): Reasonable monitoring intervals would be:

- In CKD G3a–G3b: for serum calcium and phosphate, every 6–12 months; and for PTH, based on baseline level and CKD progression.
- In CKD G4: for serum calcium and phosphate, every 3–6 months; and for PTH, every 6–12 months.
- In CKD G5, including G5D: for serum calcium and phosphate, every 1–3 months; and for PTH, every 3–6 months.
- In CKD G4–G5D: for alkaline phosphatase activity, every 12 months, or more frequently in the presence of elevated PTH (see Chapter 3.2).

In CKD patients receiving treatments for CKD-MBD, or in whom biochemical abnormalities are identified, it is reasonable to increase the frequency of measurements to monitor for trends and treatment efficacy and side effects *(Not Graded)*.

ASSESSMENT

3.1.3: In patients with CKD G3a–G5D, we suggest that 25(OH)D (calcidiol) levels might be measured, and repeated testing determined by baseline values and therapeutic interventions *(2C)*.

We suggest that vitamin D deficiency and insufficiency be corrected using treatment strategies recommended for the general population *(2C)*.

3.1.4: In patients with CKD G3a–G5D, we recommend that therapeutic decisions be based on trends rather than on a single laboratory value, taking into account all available CKD-MBD assessments *(1C)*.

ASSESSMENT

3.1.5: In patients with CKD G3a–G5D, we suggest that individual values of serum calcium and phosphate, evaluated together, be used to guide clinical practice rather than the mathematical construct of calcium-phosphate product (Ca x P) *(2D)*.

3.1.6: In reports of laboratory tests for patients with CKD G3a–G5D, we recommend that clinical laboratories inform clinicians of the actual assay method in use and report any change in methods, sample source (plasma or serum), or handling specifications to facilitate the appropriate interpretation of biochemistry data *(1B)*.

CHAPTER 3.2:

DIAGNOSIS OF CKD-MBD: BONE

TESTING FOR CKD-MBD

3.2.1: In patients with CKD G3a-G5D with evidence of CKD-MBD and/or risk factors for osteoporosis, we suggest bone mineral density (BMD) testing to assess fracture risk if results will impact treatment decisions *(2B)*.

3.2.2: In patients with CKD G3a-G5D, it is reasonable to perform a bone biopsy if knowledge of the type of renal osteodystrophy will impact treatment decisions *(Not Graded)*.

ASSESSMENT

3.2.3: In patients with CKD G3a–G5D, we suggest that measurements of serum PTH or bone-specific alkaline phosphatase can be used to evaluate bone disease because markedly high or low values predict underlying bone turnover *(2B)*.

3.2.4: In patients with CKD G3a–G5D, we suggest not routinely measuring bone-derived turnover markers of collagen synthesis (such as procollagen type I C-terminal propeptide) and breakdown (such as type I collagen cross-linked telopeptide, cross-laps, pyridinoline, or deoxypyridinoline) *(2C)*.

3.2.5: We recommend that infants with CKD G2–G5D have their length measured at least quarterly, while children with CKD G2–G5D should be assessed for linear growth at least annually *(1B)*.

CHAPTER 3.3:

DIAGNOSIS OF CKD–MBD: VASCULAR CALCIFICATION

ASSESSMENT

3.3.1: In patients with CKD G3a–G5D, we suggest that a lateral abdominal radiograph can be used to detect the presence or absence of vascular calcification, and an echocardiogram can be used to detect the presence or absence of valvular calcification, as reasonable alternatives to computed tomography-based imaging *(2C)*.

3.3.2: We suggest that patients with CKD G3a–G5D with known vascular or valvular calcification be considered at highest cardiovascular risk *(2A)*.

It is reasonable to use this information to guide the management of CKD-MBD *(Not Graded)*.

CKD-MBD:

Q

Chronic Renal Disease, Second Edition, 2020, Chapter 41

Which of the following statements about bone examination in CKD is false?

A. Bone examination in patients with CKD stages ≥3 and evidence of CKD-MBD and/or risk factors for osteoporosis is recommended for diagnosis and prognosis

B. In patients with advanced CKD and low or normal PTH, DXA measures of BMD predict pathologic fracture risk

X

C. Noninvasive examination of bone disease yields high negative predictive values for differentiating low-turnover vs. nonlow-turnover

D. Noninvasive examination of bone disease yields low positive predictive values for differentiating high-turnover vs. nonhigh-turnover bone disease

E. Bone biopsy should be considered in patients with pathological fractures, suspicion of osteomalacia, and refractory hypercalcemia

CKD-MBD: Chinese CPG

Kidney Dis 2019, Published online: July 9, 2019

Guidelines

Kidney Diseases

Kidney Dis
DOI: 10.1159/000500053

Received: March 31, 2019
Accepted: April 1, 2019
Published online: July 9, 2019

Executive Summary: Clinical Practice Guideline of Chronic Kidney Disease – Mineral and Bone Disorder (CKD-MBD) in China

Zhi-Hong Liu[a] Guisen Li[b] Ling Zhang[c] Jianghua Chen[d] Xiaonong Chen[e] Jinghong Zhao[f] Xinling Liang[g] CKD-MBD Guideline Working Group and National Clinical Research Center for Kidney Disease

[a]Department of Nephrology, Nanjing General Hospital, National Clinical Research Center of Kidney Diseases, Nanjing, China; [b]Sichuan Academy of Medical Science and Sichuan Provincial People's Hospital, School of Medicine, University of Electronic Science, Chengdu, China; [c]Department of Nephrology, Sino-Japanese Friendship Hospital, Beijing, China; [d]Department of Nephrology, The First Affiliated Hospital, Zhejiang University School of Medicine, Hangzhou, China; [e]Department of Nephrology, Ruijin Hospital, Shanghai Jiao Tong University School of Medicine, Shanghai, China; [f]Department of Nephrology, Third Military Medical University, Chongqing, China; [g]Department of Nephrology, Guangdong General Hospital, Guangzhou, China

CKD-MBD: Chinese CPG

CKD stage	Serum phosphorus	Serum calcium	ALP	iPTH	25(OH)D
G1–G2	6–12 months	6–12 months	6–12 months	Determine based on the baseline level and CKD progression	
G3a/G3b	6–12 months	6–12 months	6–12 months	Determine based on the baseline level and CKD progression	Determine based on the baseline level and treatment interventions
G4	3–6 months	3–6 months	6–12 months, which can be shortened if iPTH is elevated	6–12 months	Determine based on the baseline level and treatment interventions
G5	1–3 months	1–3 months	6–12 months, which can be shortened if iPTH is elevated	3–6 months	Determine based on the baseline level and treatment interventions

MBD, mineral and bone disorder; CKD, chronic kidney disease; ALP, alkaline phosphatase; iPTH, intact parathyroid hormone. CKD G5 includes CKD G5D; CKD G1–G5T refers to CKD G1–G5.

CKD-MBD: Chinese CPG

Kidney Dis 2019, Published online: July 9, 2019

2.2 Assessment of Bone Diseases (BMD/ Biopsy)?

2.2.3 For patients with CKD G3a–G5, we recommend that measurements of serum iPTH and ALP or bone-specific ALP can be used to evaluate bone disease because markedly high or low values predict underlying bone turnover. (*2B*)

2.2.4 For patients with CKD G3a–G5, where conditions permit, bone-derived collagen metabolism markers can be detected to assess the severity of bone disease. (*2C*)

CKD-MBD: Chinese CPG

Kidney Dis 2019, Published online: July 9, 2019

Chapter 3: Prevention and Treatment of CKD-MBD

3.2 Treatment of SHPT

3.2.4 For patients with CKD G5D requiring PTH-lowering therapy, we recommend calcimimetics, calcitriol, or vitamin D analogs, or a combination of calcimimetics with calcitriol or vitamin D analogs. (*2B*)

CKD-MBD: Chinese CPG

Kidney Dis 2019, Published online: July 9, 2019

Chapter 4: Prevention and Treatment of Osteoporosis in Patients with CKD

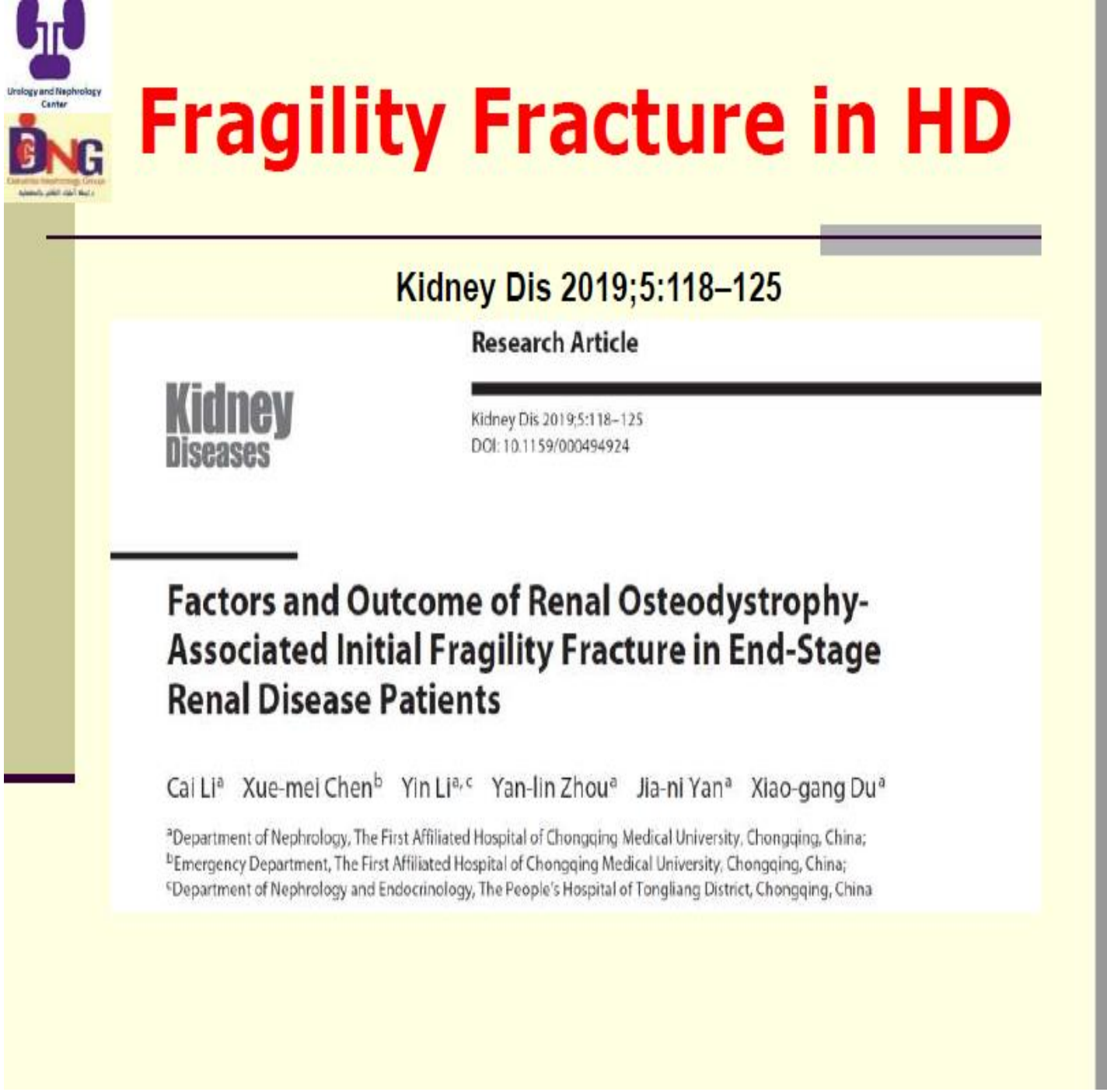
4.1 Diagnosis and Evaluation of Osteoporosis

4.1.2 We suggest measuring the BMD of the lumbar spine and hip in patients with CKD G1–G2 regularly to evaluate patients with osteoporosis. (*Not Graded*)

4.1.3 We recommend measuring the BMD in CKD G3a–G5D patients with CKD-MBD and/or risk of osteoporosis to evaluate the risk of fracture. (*2B*)

Fragility Fracture in HD

Key Messages: Patients with hypertension, diabetes, excessive suppression of PTH, and poor nutritional status are more prone to fractures. Serum corrected calcium and ALP were independent risk factors of fragility fracture. Patients with initial fragility fracture had more CV events and higher mortality.



Kidney Dis 2019;5:118–125

Research Article

Kidney Diseases

Kidney Dis 2019;5:118–125
DOI: 10.1159/000494924

Factors and Outcome of Renal Osteodystrophy-Associated Initial Fragility Fracture in End-Stage Renal Disease Patients

Cai Li[a] Xue-mei Chen[b] Yin Li[a,c] Yan-lin Zhou[a] Jia-ni Yan[a] Xiao-gang Du[a]

[a]Department of Nephrology, The First Affiliated Hospital of Chongqing Medical University, Chongqing, China;
[b]Emergency Department, The First Affiliated Hospital of Chongqing Medical University, Chongqing, China;
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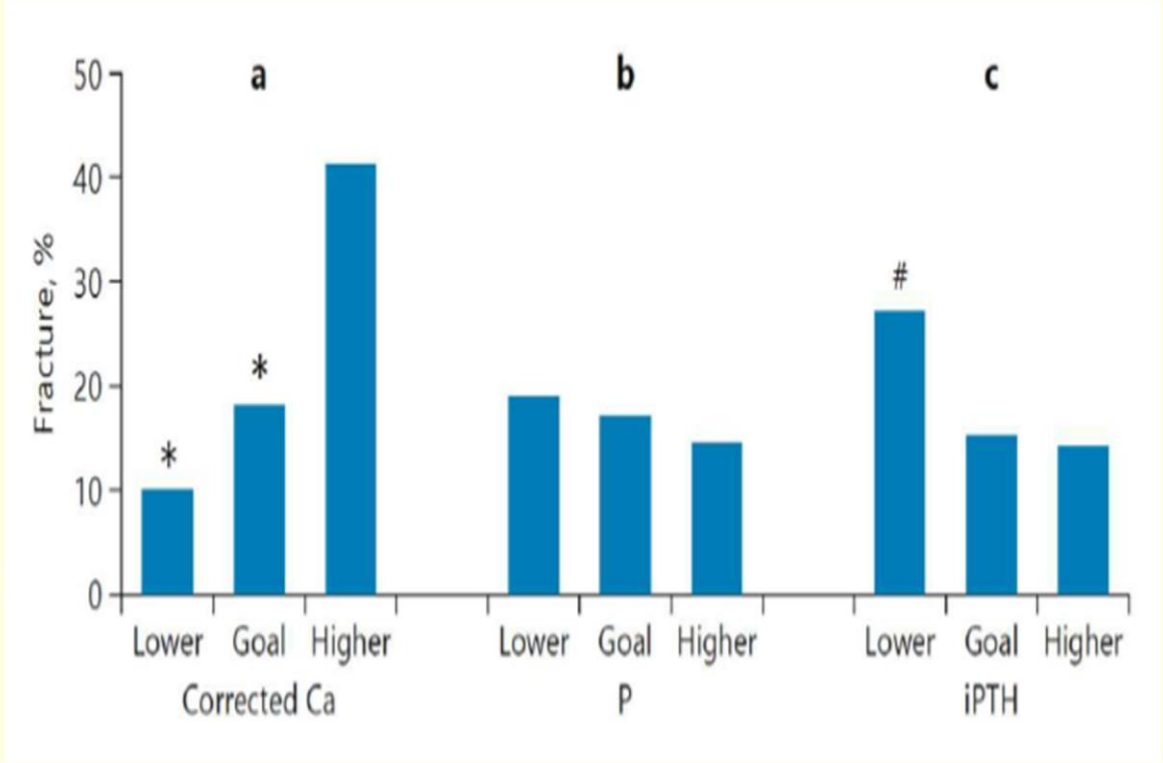
Fragility Fracture in HD: Which is Correct?

Kidney Dis 2019;5:118–125



Alterations of mineral-bone metabolism are associated with increased risk of fracture. In this study, we analyzed the changes of mineral-bone metabolism-associated parameters in ESRD patients with initial fragility fracture. Higher serum ALP, corrected calcium, and lower serum iPTH levels were found in the FF group compared with the control group ($p < 0.05$).

No significant differences in phosphorus and calcium-phosphorus product were found between the two groups.

We further assessed the incidence of initial fragility fracture in patients with different levels of serum corrected calcium, phosphorus, and iPTH. According to the KDIGO recommendations regarding target corrected calcium (2.1–2.5 mmol/L) and phosphorus (1.13–1.78 mmol/L) or K/DOQI guideline recommendations about target iPTH (150–300 pg/mL) in CKD5 patients, the 354 patients were divided into three subgroups: lower, target, and higher level subgroups, respectively. As shown in Figure 2, fractures were more likely to occur in the higher level subgroups by corrected calcium levels as well as in the lower iPTH group ($p < 0.05$). However, no differences were found among the various serum phosphorus subgroups ($p > 0.05$).

Phosphate Binders

Chronic Renal Disease, Second Edition, 2020, Chapter 41

TABLE 41.2 Phosphate Binders in Clinical Use

Cation	Formulation	Adverse Effects	Cost per Dose
Al^{3+}	Aluminum hydroxide	Osteomalacia Encephalopathy Microcytic anemia	
La^{3+}	Lanthanum carbonate	GI upset Unknown effect on bone	
Ca^{2+}	Calcium acetate Calcium carbonate	Hypercalcemia Ectopic calcification Adynamic bone disease	
Mg^{2+}	Magnesium carbonate	Diarrhea Hypermagnesemia	
Fe^{2+}	Sucroferric oxyhydroxide Ferric citrate	Diarrhea Nausea	
Sevalemar	Sevelamer hydrochloride Sevelamer carbonate	Diarrhea Constipation Metabolic acidosis	

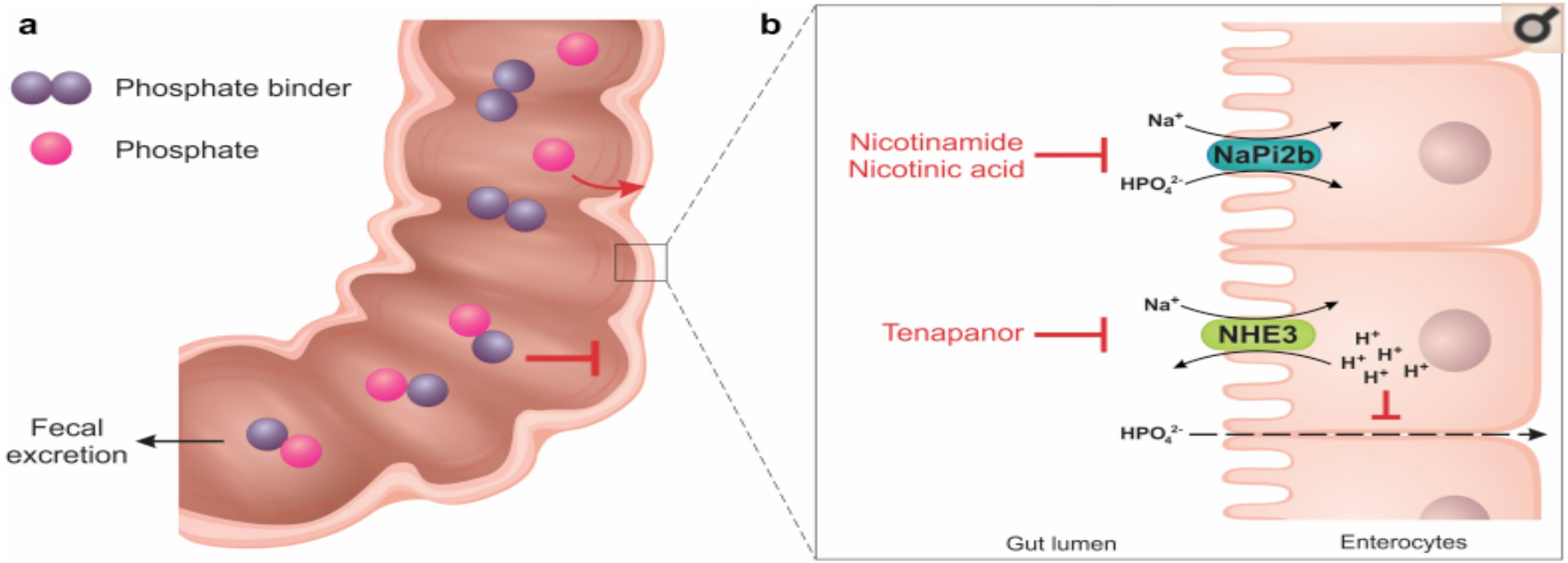
Phosphate Binders

Kidney Int Rep. 2019 Jun 20;4(8):1043-1056

Drug	Usual dose (pill burden)°	Advantages	Disadvantages
Calcium carbonate	500–1250 mg (3–6 tablets)	Lower pill burden	Calcium overload
Calcium acetate	667 mg (6–12 capsules)	As effective as calcium carbonate	Calcium overload High pill burden
Magnesium carbonate	63 mg (2–6 capsules)	Good GI tolerance, lower pill burden	Hypermagnesemia
Sevelamer hydrocloride	800 mg (6–12 capsules)	↓ LDL-cholesterol levels, better survival in HD	High pill burden, GI side effects, metabolic acidosis
Sevelamer carbonate	800 mg (6–12 capsules)	↓ LDL-cholesterol levels, better survival in HD	High pill burden, GI side effects
Bixalomer	250 mg (6–14 capsules)	Good GI tolerance	High pill burden
Lanthanum carbonate	250–1000 mg (3–6 chewable tablets)	Lower pill burden, good GI tolerance	Low solubility Tissue accumulation, eg, bone
Ferric citrate	210 mg (4–5 tablets)	Lower pill burden, ↓ iron suplementation ↓ ESA doses	GI side effects (mild)
Sucroferric oxyhydroxide	500 mg (2–6 chewable tablets)	Lower pill burden	GI side effects (mild)

Published online 2019 Jun 20. doi: 10.1016/j.ekir.2019.06.002

Figure 1



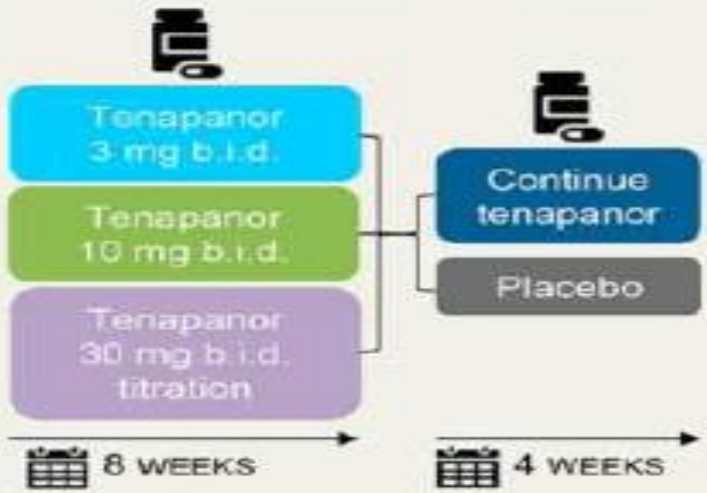
Mechanisms of action of phosphate-lowering pharmacological agents. (a) Phosphate binders reduce the intestinal absorption of dietary phosphate by forming a nonabsorbable compound in the gastrointestinal tract lumen that is excreted in the feces. (b) Nicotinic acid (niacin) and nicotinamide (niacinamide) inhibit sodium-dependent, active intestinal phosphate absorption via a reduction in NaPi2b expression; tenapanor reduces intestinal sodium and phosphate absorption by inhibiting the sodium/hydrogen ion-exchanger isoform 3 (NHE3), leading to intracellular proton accumulation and inducing a conformational change in tight junction proteins, thereby decreasing permeability to paracellular phosphate transport.

Phosphate Control in HD: Tenapanor Scenario

J Am Soc Nephrol. 2019 Apr;30(4):641-652

METHODS

219 patients across 41 US sites



RESULTS

Change in serum phosphate

CONCLUSION

Tenapanor significantly reduced elevated serum phosphate in patients on hemodialysis with hyperphosphatemia.

Conclusion

The PCT showed to be efficient in the maintenance of serum phosphorus in the individuals who adhered well to the tool, without the administration of phosphate binders. Such a method can assist in patient adherence to treatment and enables better diet flexibility

Phosphorus Control in HD: Effect of PCT

Clin Nutr ESPEN. 2019 Aug;32:153-157

Contents lists available at ScienceDirect

Clinical Nutrition ESPEN

journal homepage: http://www.clinicalnutritionespen.com

Original article

Phosphorus Counting Table for the control of serum phosphorus levels without phosphate binders in hemodialysis patients

Vivianne Rêis Bertonsello-Catto [a, *], Leandro Junior Lucca [b], José Abrão Cardeal da Costa [c]

[a] Graduate Program in Science, Department of Clinical Medicine, Ribeirão Preto Medical School – São Paulo University, Brazil
[b] CKD-MBD Unit, Nephrology Division, Department of Clinical Medicine, Ribeirão Preto Medical School – University of São Paulo, Brazil
[c] Nephrology Division, Department of Clinical Medicine, Ribeirão Preto Medical School – University of São Paulo, Brazil

Phosphorus Control in CKD3b/4 CKD: COMBINE Trial

EDITORIAL www.jasn.org

Dual Inhibition of Gastrointestinal Phosphate Absorption: More Questions Than Answers

Wing-Chi G. Yeung,[1] Nigel D. Toussaint,[2,3] and Sunil V. Badve[1,4]

[1]Department of Renal Medicine, St. George Hospital, Sydney, Australia; [2]Department of Nephrology, The Royal Melbourne Hospital, Melbourne, Victoria, Australia; [3]Department of Medicine, University of Melbourne, Parkville, Victoria, Australia; and [4]Renal and Metabolic Division, The George Institute for Global Health, University of New South Wales Medicine, Sydney, New South Wales, Australia

Paricalcitol Vs. Calcitriol in Dialysis Patients

Therapeutic Apheresis and Dialysis Feb 2019; 23(1):73–79

Therapeutic Apheresis and Dialysis

Therapeutic Apheresis and Dialysis 2019; 23(1):73–79
doi: 10.1111/1744-9987.12760

Comparison of Paricalcitol and Calcitriol in Dialysis Patients With Secondary Hyperparathyroidism: A Meta-Analysis of Randomized Controlled Studies

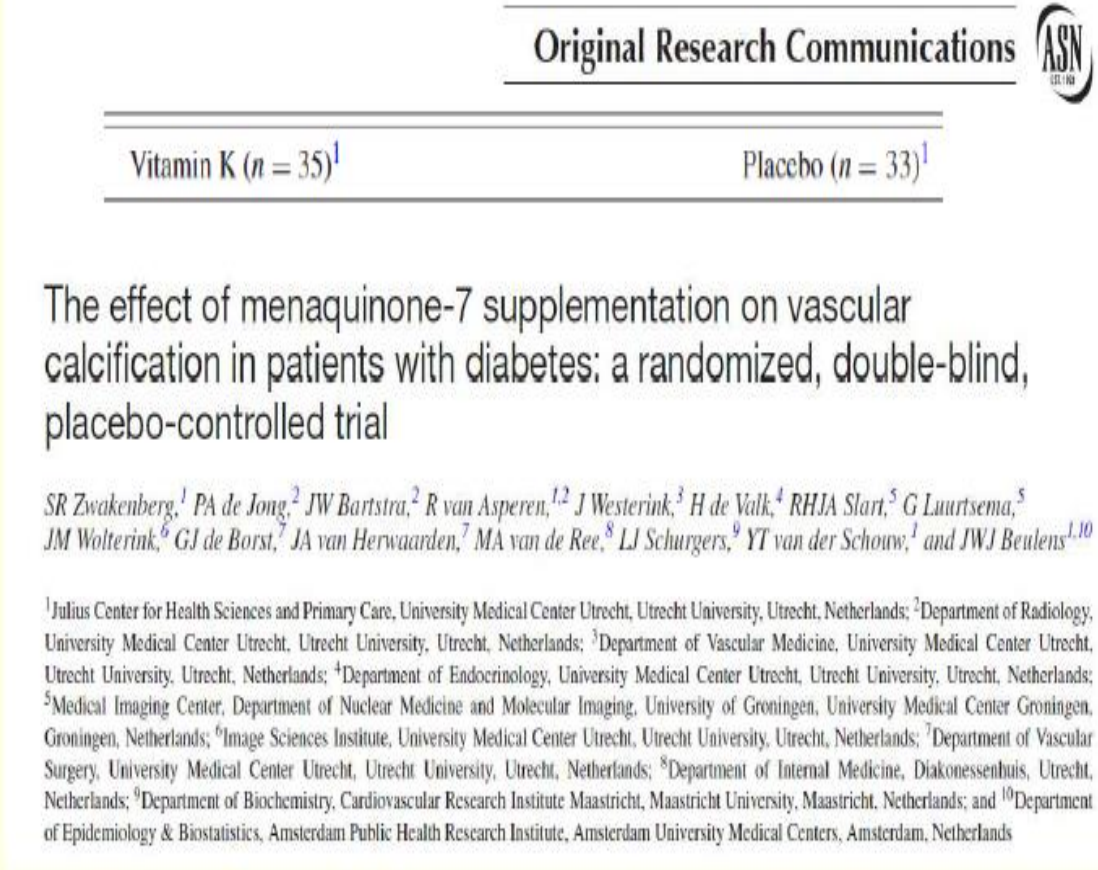
Tong Zhang,[1] Hongbo Ju,[2] Haojun Chen,[2] and Wen Wen[3]

Departments of [1]Gastroenterology, [3]Nephrology, The First Affiliated Hospital of Chongqing Medical University, Chongqing, and [2]Nephrology Department, Fenghua People's Hospital, Ningbo, China

Paricalcitol and calcitriol result in similar ≥50% reduction of parathyroid hormone, calcium concentration, phosphate concentration, calcium phosphate, alkaline phosphatase, hypercalcemia, adverse events, and serious adverse events for secondary hyperparathyroidism in dialysis patients.

Vitamin K2 and Vascular Calcification

Am J Clin Nutr. 2019 Aug 6. pii: nqz147



Original Research Communications

Vitamin K ($n = 35$)[1]	Placebo ($n = 33$)[1]

The effect of menaquinone-7 supplementation on vascular calcification in patients with diabetes: a randomized, double-blind, placebo-controlled trial

SR Zwakenberg,[1] PA de Jong,[2] JW Bartstra,[2] R van Asperen,[1,2] J Westerink,[3] H de Valk,[4] RHJA Slart,[5] G Luurtsema,[5] JM Wolterink,[6] GJ de Borst,[7] JA van Herwaarden,[7] MA van de Ree,[8] LJ Schurgers,[9] YT van der Schouw,[1] and JWJ Beulens[1,10]

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Discussion

In contrast to our hypothesis, active vascular calcification on 18F-NaF PET scan tended to increase after MK-7 supplementation compared with placebo during 6-mo intervention. In addition, no effect of MK-7 supplementation on CT calcification mass was found. Therefore, this study does not support that MK-7 supplementation inhibits vascular calcification

Case Scenario

JBMR Plus. 2019 Feb 27;3(7):e10176.

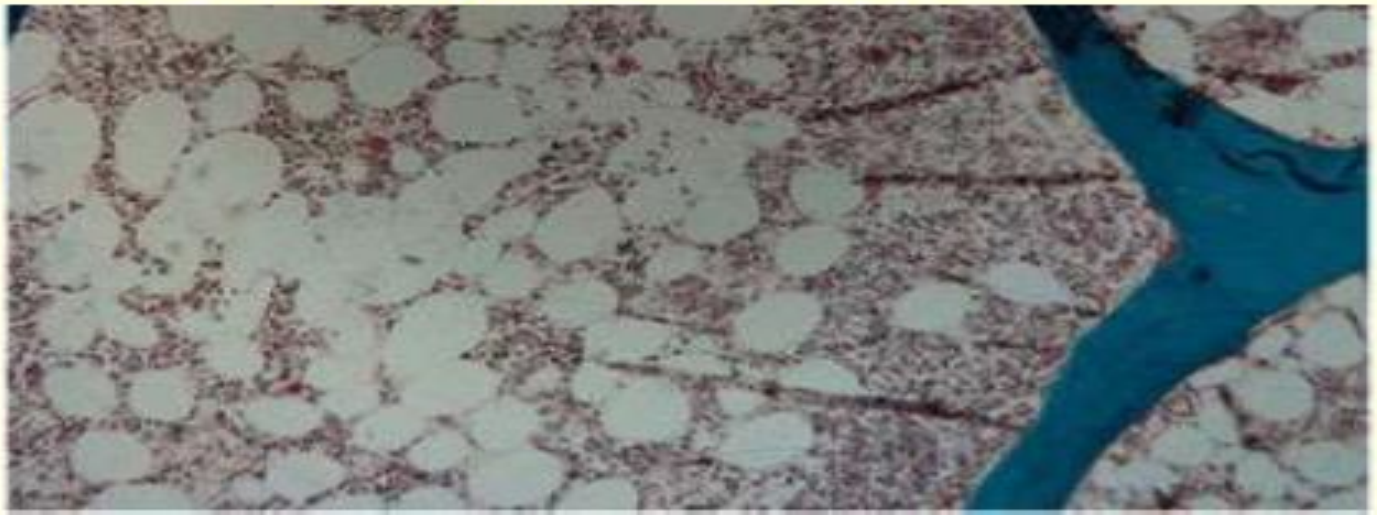
- A 51-year-old woman on dialysis with persistent hypercalcemia despite low calcium intake and no vitamin D supplements.

Case Scenario

JBMR Plus. 2019 Feb 27;3(7):e10176.

Do you agree to use teriparatide to treat this case?

Demeclocycline-labeled trans-iliac bone biopsy with Goldner's stain



Parathyroidectomy:
Long-term Outcomes

Semin Dial. 2019, in press

DOI: 10.1111/sdi.12833

REVIEW ARTICLE

Seminars in Dialysis WILEY

Long-term outcomes and management considerations after parathyroidectomy in the dialysis patient

TABLE 1 Survival outcomes after PTX in dialysis patients

Author	Year	Population	Time period	Study design	Result
Li-Chun Ho et al[59]	2016	Nationwide dialysis cohort, Taiwan	1998-2010	Case-control study with matching for propensity and for radionuclide PTH imaging	PTX had significant 20%-25% lower risk for all-cause mortality
Ivarsson et al[58]	2015	Swedish Renal Registry	1991-2009	Nested case-control study matched for gender, age, cause of ESRD (N: 423/1234).	RR of death for PTX: 0.80 (95% CI 0.65-0.99)
Komaba et al[179]	2015	Registry - Japanese Society for Dialysis Therapy	1-year follow up	4420 with PTX vs 4420 propensity matched controls	PTX reduced all cause mortality by 34% and cardiovascular mortality by 41%.
Kestenbaum et al[180]	2004	USRDS	1998-2001	Case-control study matched by age, race, gender, cause of ESRD, dialysis duration, prior transplant status, dialysis modality (N: 8556/8556)	PTX 30-day postoperative mortality rate 3.1%; higher short-term, and lower long-term mortality rates; Median survival PTX: 53.4 mo (95% CI: 51.2-56.4); Control 46.8 mo (95% CI: 44.7-48.9)
Aperrii et al[139]	2017	MEDLINE Cochrane Library Clinicaltrials.gov EMBASE	Inception to October 2016	Meta-analysis: 15 retrospective cohort studies including 24 048 patients	PTX decreased all-cause mortality (RR 0.74; 95% CI of 0.66-0.83) bi cardiovascular mortality (RR 0.59)
Chen et al[166]	2016	MEDLINE Cochrane Library EMBASE	1974-2015	Meta-analysis: 13 retrospective studies; 30 052 patients treated with PTX vs 12 001 medically treated.	PTX: ~20% reduction in all-cause mortality; ~27% in cardiovascular mortality.

TABLE 1 Survival outcomes after PTX in dialysis patients

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Komaba et al[129]	2015	Registry - Japanese Society for Dialysis Therapy	1-year follow up	4428 with PTX vs 4428 propensity matched controls	PTX reduced all-cause mortality by 34% and cardiovascular mortality by 41%.
Kestenbaum et al[160]	2004	USRDS	1998-2001	Case-control study matched by age, race, gender, cause of ESRD, dialysis duration, prior transplant status, dialysis modality. (N: 4558/4558)	PTX 30-day postoperative mortality rate 3.1%; higher short-term, and lower long-term mortality rates; Median survival PTX: 53.4 mo (95% CI: 51.2-56.4); Control: 46.8 mo (95% CI: 44.7-48.9).
Apetrii et al[128]	2017	MEDLINE Cochrane Library Clinicaltrials.gov EMBASE	Inception to October 2016	Meta-analysis: 15 retrospective cohort studies including 24 048 patients	PTX decreased: a) all-cause mortality (RR 0.74; 95% CI of 0.66-0.83) b) cardiovascular mortality (RR 0.59)
Chen et al[161]	2016	MEDLINE Cochrane Library EMBASE	1974-2015	Meta-analysis: 13 retrospective studies; 10 052 patients treated with PTX vs 12 001 medically treated.	PTX −28% reduction in all-cause mortality; 37% in cardiovascular mortality.

Parathyroidectomy: Long-term Outcomes

Semin Dial. 2019 Sep;32(5):444-451

DOI: 10.1111/sdi.12772

REVIEW ARTICLE

WILEY Seminars in Dialysis

Parathyroidectomy in dialysis patients: Indications, methods, and consequences

María E. Rodríguez-Ortiz[1,2,3,4] | María V. Pendón-Ruiz de Mier[1,2,3,4] | Mariano Rodríguez[1,3,4,5]

Parathyroidectomy:
Timing

Original Scientific Report

Timing of Parathyroidectomy Does Not Influence Renal Function After Kidney Transplantation

Willemijn Y. van der Plas, Mostafa El Moumni...

» Download PDF (491KB) » View Article Pages 1972-1980

Original Scientific Report

Cardiovascular and Cerebrovascular Events After Parathyroidectomy in Patients on Renal Replacement Therapy

Kerstin M. Ivarsson, Shehriar Akaberi, Elin Isaksson...

» Download PDF (239KB) » View Article Pages 1981-1988

Invited Commentary

Is There an Optimal Time for Parathyroidectomy in Patients with Secondary Hyperparathyroidism?

Tracy S. Wang

» Download PDF (167KB) » View Article Pages 1989-1990

August 2019

Parathyroidectomy

Ren Fail. 2019 Nov;41(1):921-929

182 dialysis patients who underwent PTX between February 2012 and January 2018

RENAL FAILURE
2019, VOL. 41, NO. 1, 921–929
https://doi.org/10.1080/0886022X.2019.1666724

Taylor & Francis
Taylor & Francis Group

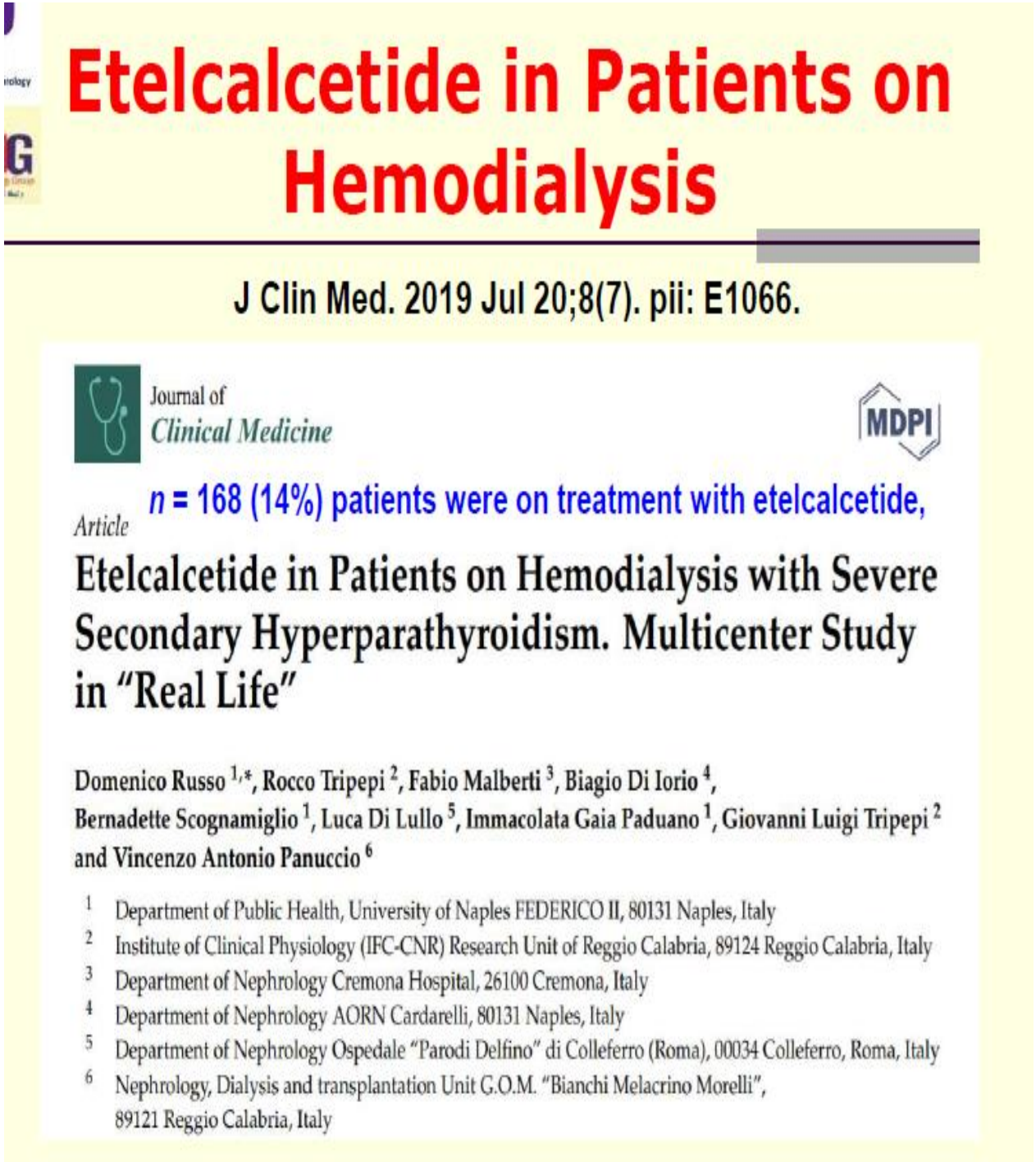
CLINICAL STUDY

Evaluation of laboratory parameters and symptoms after parathyroidectomy in dialysis patients with secondary hyperparathyroidism

Yi Zhang*, Ying Lu*, Sheng Feng, Zhoubing Zhan and Huaying Shen

Department of Nephrology, The Second Affiliated Hospital of Soochow University, Suzhou, China

Conclusion: PTX is a safe and effective therapy for treating SHPT that is refractory to medical therapies and accompanied by related signs and symptoms in dialysis patients. All three operative techniques were effective in controlling SHPT.



Etelcalcetide in Patients on Hemodialysis

J Clin Med. 2019 Jul 20;8(7). pii: E1066.

Journal of *Clinical Medicine*

MDPI

n = 168 (14%) patients were on treatment with etelcalcetide,

Article

Etelcalcetide in Patients on Hemodialysis with Severe Secondary Hyperparathyroidism. Multicenter Study in "Real Life"

Domenico Russo [1,*], Rocco Tripepi [2], Fabio Malberti [3], Biagio Di Iorio [4], Bernadette Scognamiglio [1], Luca Di Lullo [5], Immacolata Gaia Paduano [1], Giovanni Luigi Tripepi [2] and Vincenzo Antonio Panuccio [6]

1 Department of Public Health, University of Naples FEDERICO II, 80131 Naples, Italy
2 Institute of Clinical Physiology (IFC-CNR) Research Unit of Reggio Calabria, 89124 Reggio Calabria, Italy
3 Department of Nephrology Cremona Hospital, 26100 Cremona, Italy
4 Department of Nephrology AORN Cardarelli, 80131 Naples, Italy
5 Department of Nephrology Ospedale "Parodi Delfino" di Colleferro (Roma), 00034 Colleferro, Roma, Italy
6 Nephrology, Dialysis and transplantation Unit G.O.M. "Bianchi Melacrino Morelli", 89121 Reggio Calabria, Italy

n = 1190 patients on the charge.

From this cohort, n = 168 (14%) patients were on treatment with etelcalcetide,

A median weekly dose of etelcalcetide was 15 mg

PTH declined median value of 636 pg/mL to 357 pg/mL.

The median time for responders was 53 days; the percentage of responders increased (from baseline 27% to 63%)

Few patients had symptomatic hypocalcemia requiring etelcalcetide withdrawal (four cases (3%) at 30-day control, two cases (2%) at 60-day, one case (1%) at 90-day control).

Side effects with etelcalcetide were lower.

Etelcalcetide is a new therapeutic option for SHPT with low side effects and pills burden. Etelcalcetide may improve adherence to therapy, avoiding unremitting SHP. It remains to be assessed whether etelcalcetide may reduce parathyroidectomy, vascular calcification, or mortality. Being etelcalcetide very potent in suppressing PTH levels, even in severe SHPT, future studies should evaluate the potential risk of more adynamic bone disease during long-term therapy.

Secondary Hyperparathyroidism: Overview

Therapeutic Apheresis and Dialysis Aug 2019; 23(4):309–318

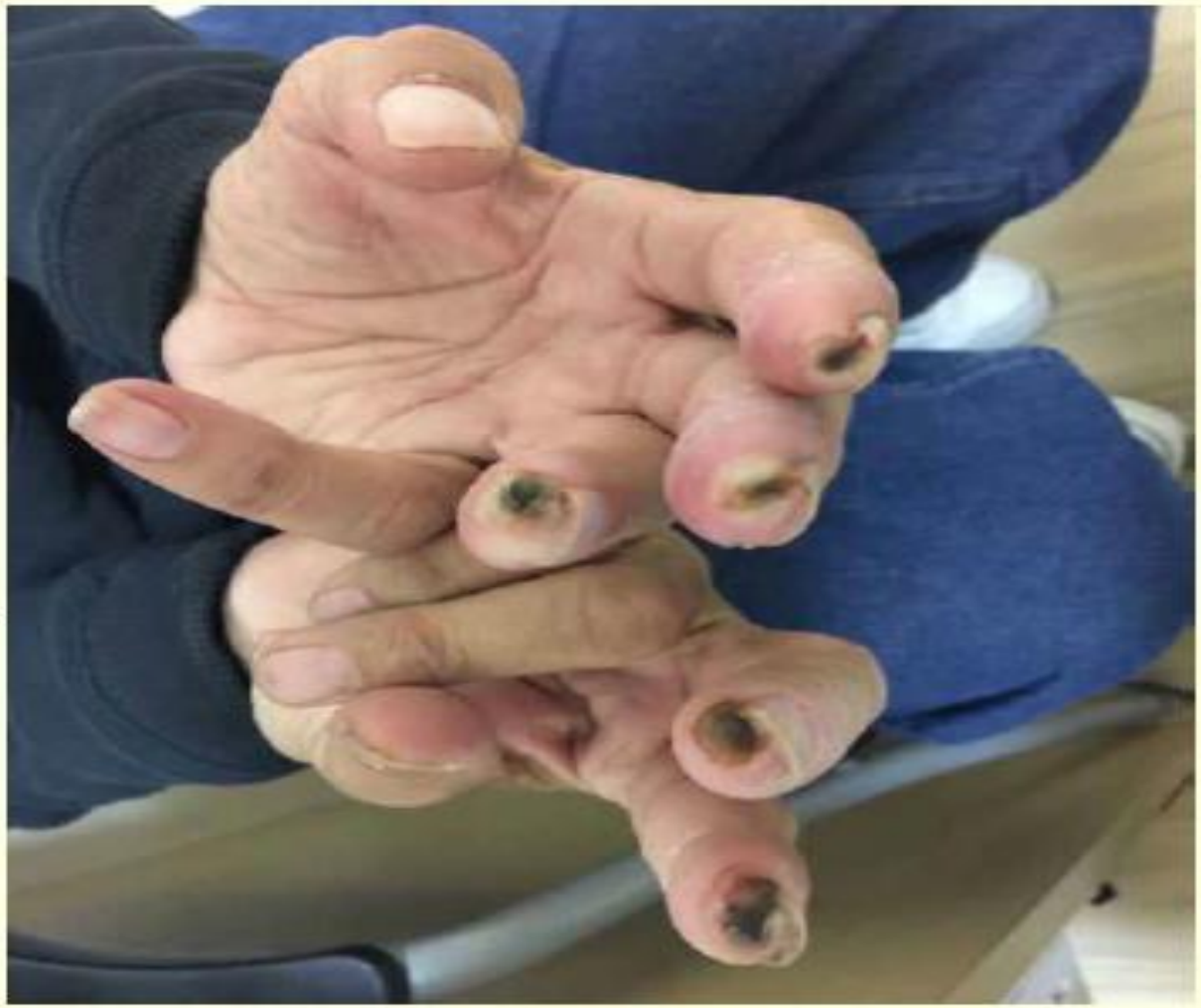
TABLE 3. *Pharmacokinetic properties of calcimimetics*

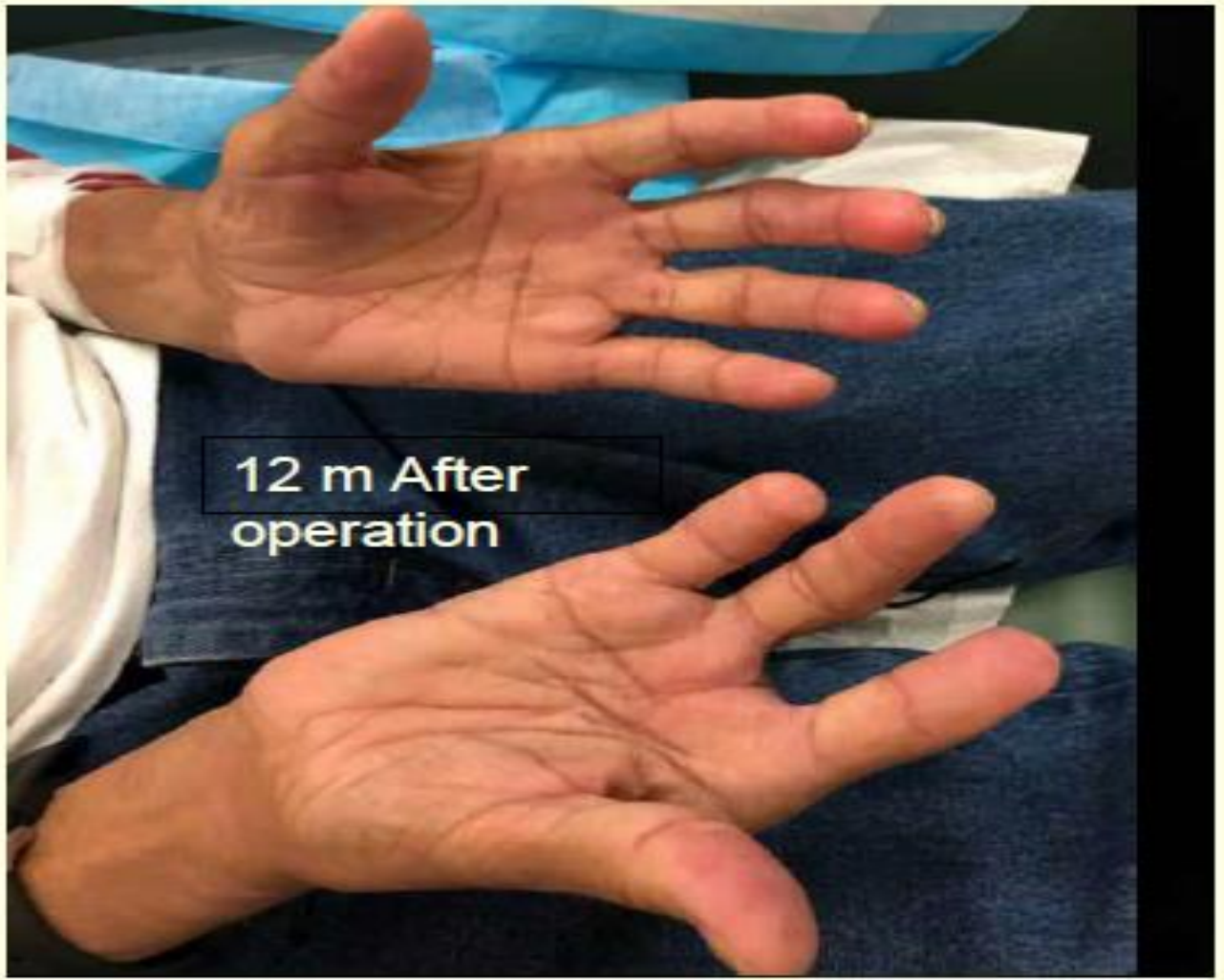
	Cinacalcet	Etelcalcetide	Evocalcet
Binding site	Transmembrane	Extracellular	Transmembrane
Half-life[†]	30–40 h	15.6 days	20–33 h
Period with a maximal decrease of PTH[‡]	4–12 h	0.5–24 h	4–12 h
Period with a maximal decrease of Ca[‡]	8–12 h	8 h–8 days	12–24 h
Metabolic organ	Liver	None	Liver
Risk of drug–drug interaction	High	Low	Low
Elimination in dialysis	0	Approximately 60%	0
CaSR activation concentration (EC_{50})	5.1×10^{-8} M	5.3×10^{-7} M	6.7×10^{-8}–1.6×10^{-7} M

[†]In dialysis patients (dialytic half-life for etelcalcetide [after three times per week of 5 mg for 12 weeks administration]). [‡]Single administration. CaSR, Ca-sensing receptor; PTH, parathyroid hormone.

Case Scenario

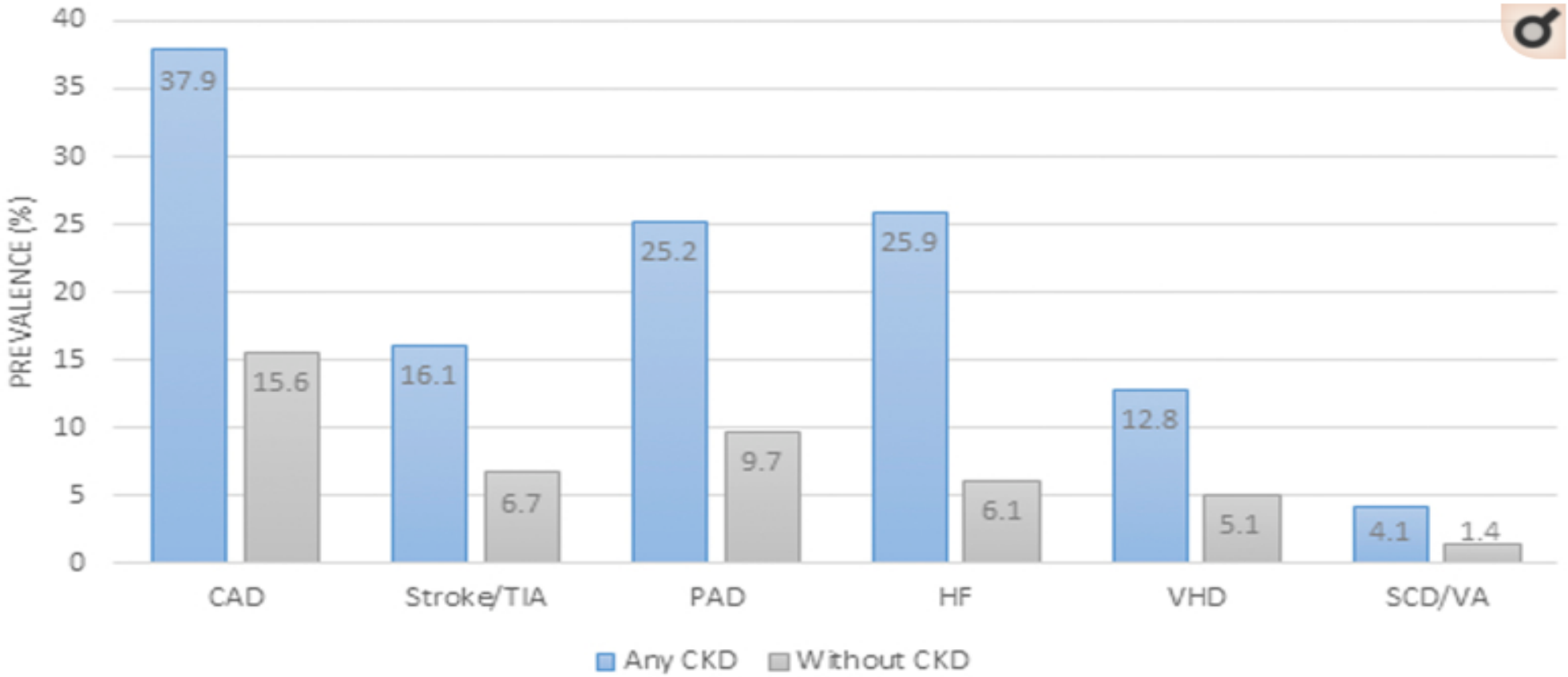
Am J Case Rep. 2019 Aug 9;20:1170-1174





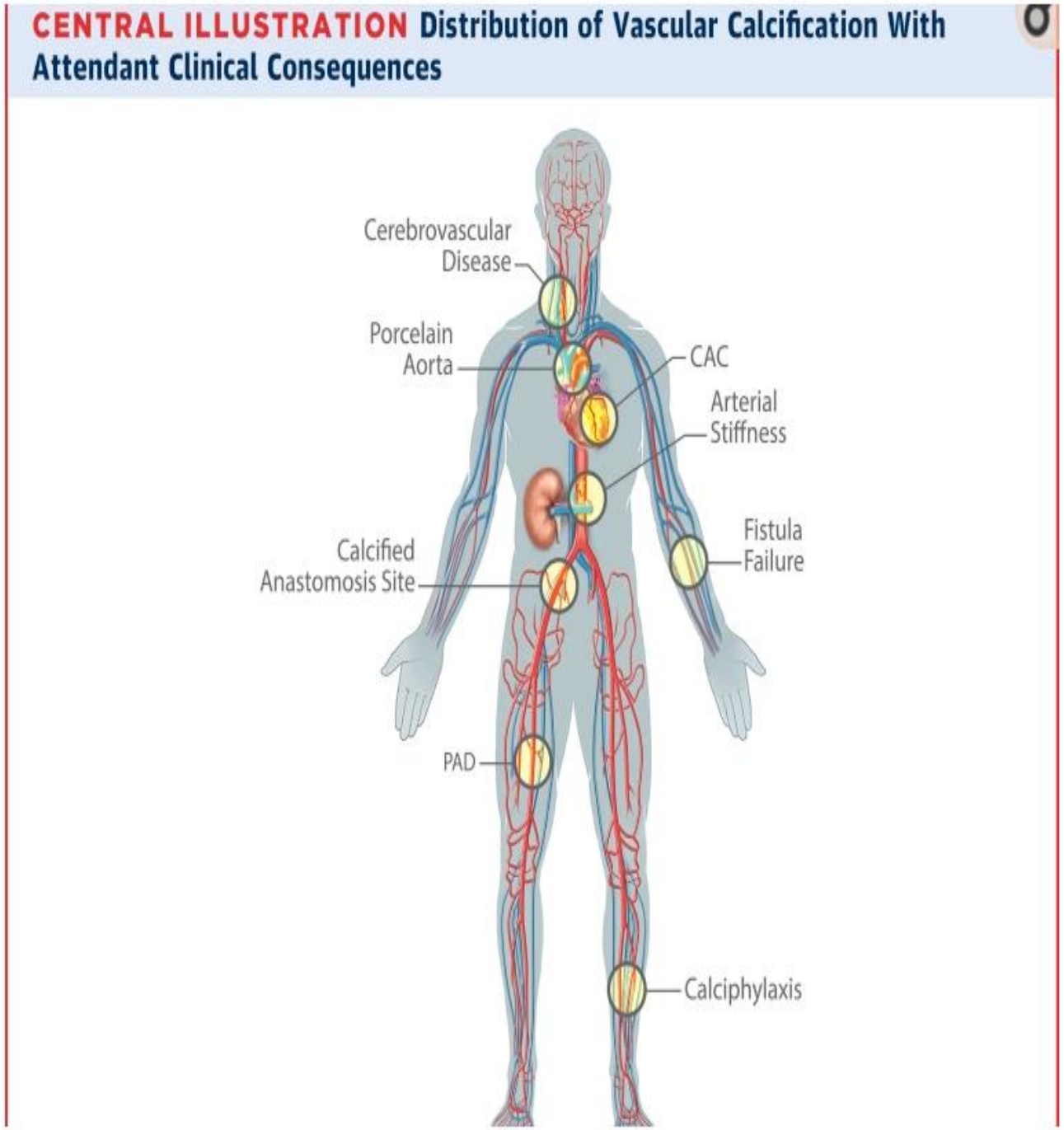
PMC full text: JACC Basic Transl Sci. 2020 Apr; 5(4): 398–412.
Published online 2020 Apr 27. doi: 10.1016/j.jacbts.2020.02.002

Figure 2



Cardiovascular Disease Burden in a Sample of Medicare Beneficiaries

Cardiovascular disease burden in a sample of Medicare beneficiaries in the United States Renal Data System 2016 sample. CAD = coronary artery disease; PAD = peripheral arterial disease; SCD = sudden cardiac death; TIA = transient ischemic attack; VA = ventricular arrhythmia;



Distribution of Vascular Calcification

Vascular calcification at the carotid vessels is associated with increased risk of stroke .

proximal aorta can cause a porcelain aorta that can prohibit cardiothoracic surgery.

Calcification of the coronary linked to increased cardiovascular mortality & increased atherothrombosis.

Calcification of the aorta and the distal vessels is associated with increased arterial stiffness.

Calcification of the iliofemoral vessels at the site of anastomosis has been associated with graft failure and worse transplantation outcomes
Calcification of the radial artery and fistula site is more generally associated with early fistula failure

. Calcification of the lower limb arteries : peripheral arterial disease (PAD) (claudication, limb ischemia) as well as arterial stiffness

. **Calciphylaxis** is a severe and accelerated form of calcification, predominantly localized in the medial layer of skin arterioles and commonly affects the lower limbs but can occur anywhere.

Calciphylaxis: Overview

Adv Skin Wound Care. 2019 May;32(5):205-215.

MAY 2019

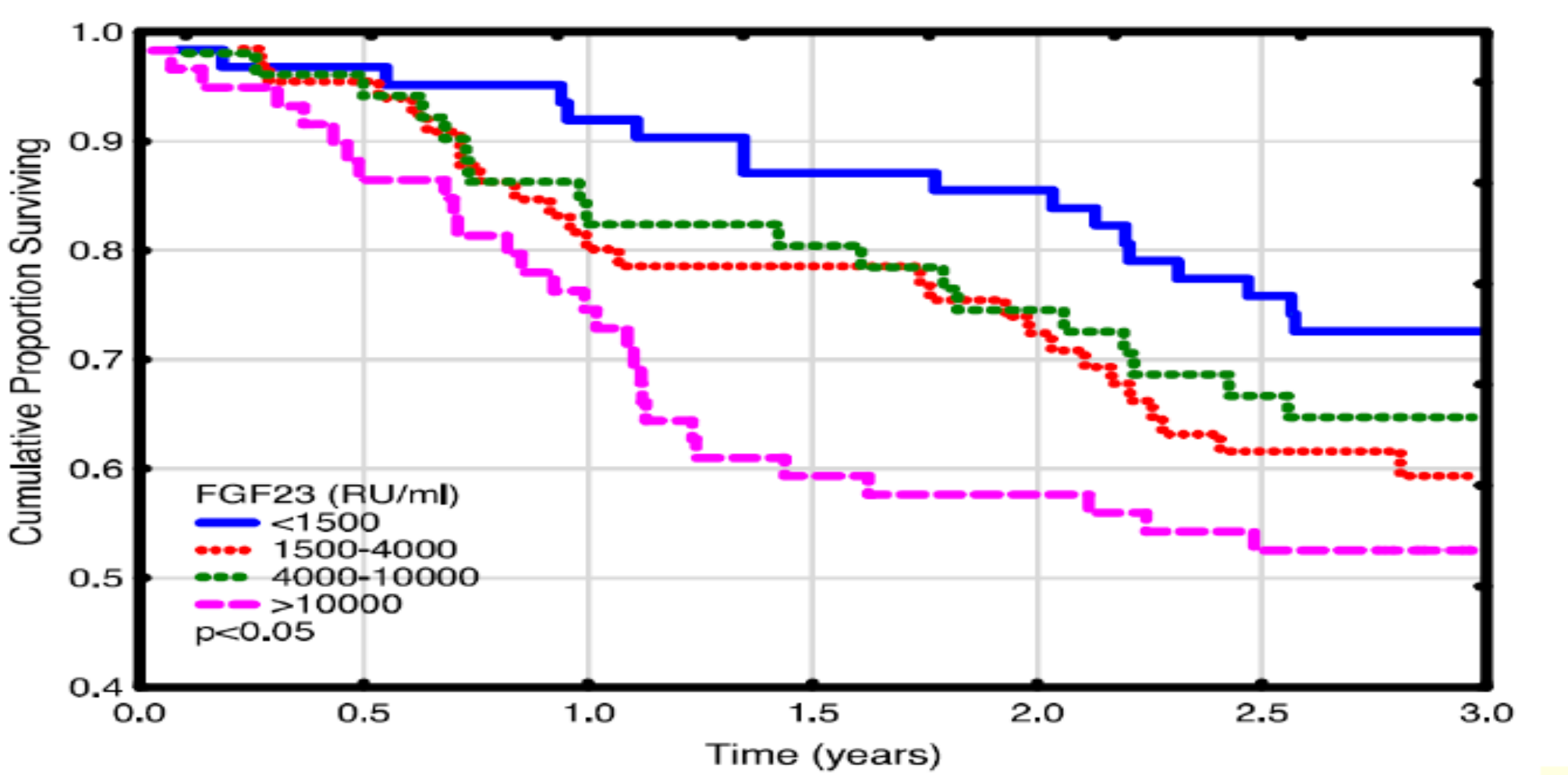
CLINICAL MANAGEMENT

extra

Calciphylaxis: Diagnosis, Pathogenesis, and Treatment

FGF23 in HDPatients: LVH, EF and Survival

Nefrologia. 2019 May - Jun;39(3):258-268



FGF-23 in Hemodialysis Patients: Effect of Low-Phosphate Diets

CJASN 14: 1475–1483, October 2019

What are the short-term effects of low-phosphate diets on FGF23 level?

CJASN
Clinical Journal of American Society of Nephrology

Cohort

35 Patients on HD

64 years old

40% male

Phosphate 5 mg/dL

Methods

Very-low phosphate → 5-day washout → Low phosphate

Low phosphate → 5-day washout → Very-low phosphate

Primary Outcome

Change in intact FGF23

NS difference

Secondary Outcomes

Very-low phosphate diet → Serum Phosphate 0.6 mg/dL CI 0.2 to 1.0

PTH: NS

C-terminal FGF23: NS

Conclusions The very-low-phosphate diet offered no benefit for FGF23 reduction but provided a greater phosphate-lowering effect.

Wan-Chuan Tsai, Hon-Yen Wu, Yu-Sen Peng, et al. ***Short-Term Effects of Very-Low-Phosphate and Low-Phosphate Diets on Fibroblast Growth Factor 23 in Hemodialysis Patients: A Randomized Crossover Trial.*** CJASN doi: https://doi.org/10.2215/CJN.04250419. **Visual Abstract by Pablo Garcia, MD**

Burosumab Therapy

CJASN 14: 1097–1099, July 2019

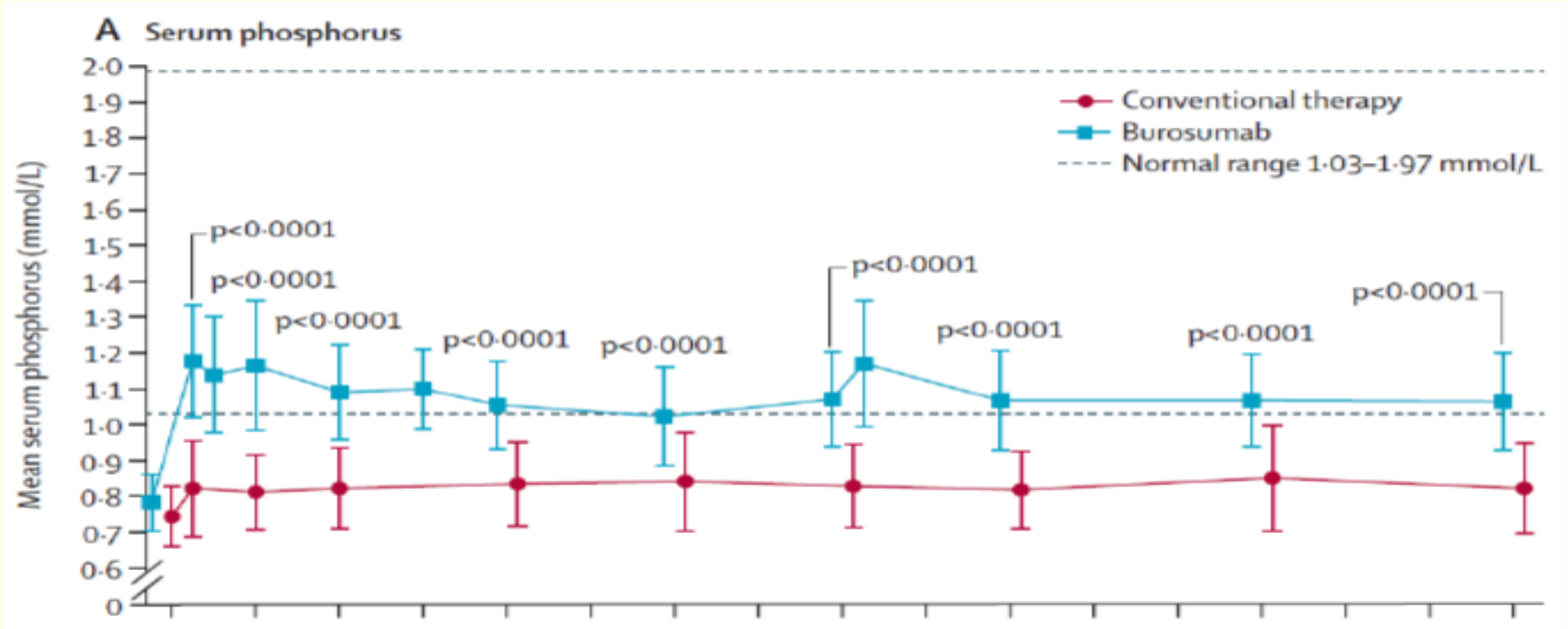
Perspective

Burosumab Therapy for X-Linked Hypophosphatemia and Therapeutic Implications for CKD

Farzana Perwad and Anthony A. Portale

X Linked Hypophosphatemia: Burosumab Therapy

Lancet, 2019; 2019 Jun 15;393(10189):2416-2427



FGF23 and Inflammation: Translational Statement

Kidney International (October 2019) 96, 890–905

basic research www.kidney-international.org

Tumor necrosis factor stimulates fibroblast growth factor 23 levels in chronic kidney disease and non-renal inflammation

Daniela Egli-Spichtig[1,2,3,14], Pedro Henrique Imenez Silva[1,2,14], Bob Glaudemans[1,2], Nicole Gehring[1,2], Carla Bettoni[1,2], Martin Y.H. Zhang[3], Eva M. Pastor-Arroyo[1,2], Désirée Schönenberger[1,2], Michal Rajski[1,2], David Hoogewijs[1,2], Felix Knauf[4], Benjamin Misselwitz[5], Isabelle Frey-Wagner[5], Gerhard Rogler[5], Daniel Ackermann[6], Belen Ponte[7], Menno Pruijm[8], Alexander Leichtle[9], Georg-Martin Fiedler[9], Murielle Bochud[2,10], Virginia Ballotta[11], Sandra Hofmann[11], Farzana Perwad[3], Michael Föller[12], Florian Lang[13], Roland H. Wenger[1,2], Ian Frew[1,2] and Carsten A. Wagner[1,2]

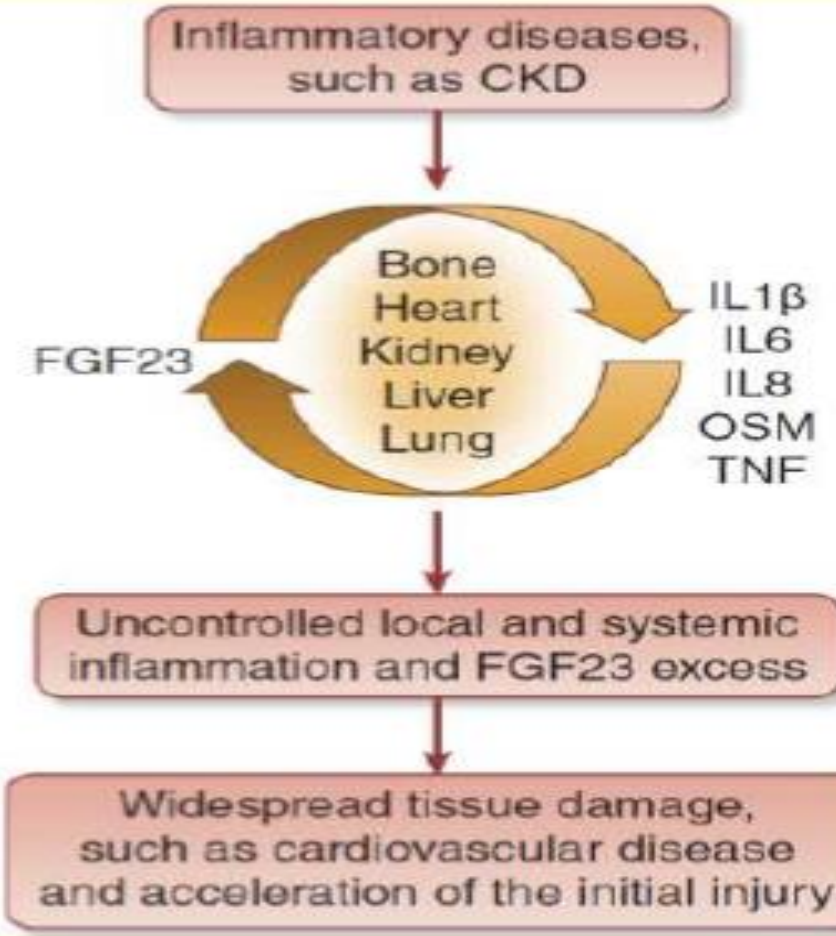
[1]Institute of Physiology, University of Zurich, Zurich, Switzerland; [2]Swiss National Center of Competence in Research NCCR-Kidney.CH, University of Zurich, Zurich, Switzerland; [3]Department of Pediatrics, Division of Nephrology, University of California, San Francisco, San Francisco, California, USA; [4]Division of Nephrology, Charité – Universitätsmedizin Berlin, Berlin, Germany; [5]University Hospital Zurich, Clinic for Gastroenterology and Hepatology, Zurich, Switzerland; [6]Department of Nephrology and Hypertension, Inselspital, Bern University Hospital, University of Bern, Bern, Switzerland; [7]Department of Nephrology, University Hospital of Geneva (HUG), Geneva, Switzerland; [8]Department of Nephrology, Lausanne University Hospital (CHUV), Lausanne, Switzerland; [9]Institute of Clinical Chemistry, Inselspital, Bern University Hospital, University of Bern, Bern, Switzerland; [10]Institute of Social and Preventive Medicine (IUMSP), Lausanne University Hospital (CHUV), Lausanne, Switzerland; [11]Department of Biomedical Engineering and Institute for Complex Molecular Systems, Eindhoven University of Technology, Eindhoven, The Netherlands; [12]Institute of Physiology, University of Hohenheim, Stuttgart, Germany; and [13]Institute of Physiology I, University of Tübingen, Tübingen, Germany

FGF23 and Inflammation: Vicious Coalition

Kidney International (October 2019) 96, 813–815

FGF23 and inflammation—a vicious coalition in CKD

Brian Czaya[1] and Christian Faul[1]



Post-transplant Bone Biopsy

Kidney International (2019) 96, 1100–1104

brief report

Comparison of serum levels with bone content and gene expression indicate a contradictory effect of kidney transplantation on sclerostin

Maria Julia Correa Lima Nepomuceno Araújo[1,2], Igor Denizarde Beckar Marques[1,2], Fabiana Gingeri Graciolli[1], Luiza Fukuhara[1], Luciene Machado dos Reis[1], Melani Custódio[1], Vanda Jorgetti[1], Rosilene Mota Elias[1,3], Elias David-Neto[1] and Rose MA Moysés[1,3]

www.kidney-international.org

Sclerostin		β-catenin		RANKL		OPG		FGF-23	
Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post

Kidney International (November 2019) 96, 1059–1070

Unraveling the osteocyte in CKD-MBD post–renal transplantation

Marciana Laster[1], Renata C. Pereira[1] and Isidro B. Salusky[1]

Transplantation and Bone Disease

Cochrane Database Syst Rev. 2019 Oct 22; in press

Cochrane Library

Cochrane Database of Systematic Reviews

198 pages

Interventions for preventing bone disease in kidney transplant recipients (Review)

Palmer SC, Chung EYM, McGregor DO, Bachmann F, Strippoli GFM

Main results

Authors' conclusions

Bisphosphonate therapy may reduce fracture and bone pain after kidney transplantation, however low certainty in the evidence indicates it is possible that treatment may make little or no difference. It is uncertain whether bisphosphonate therapy or other bone treatments prevent other skeletal complications after kidney transplantation, including spinal deformity or avascular bone necrosis. The effects of bone treatment for children and adolescents after kidney transplantation are very uncertain.

THE TAKE-HOME MESSAGE

- Chronic kidney disease-mineral and bone disorder (CKD-MBD) patients have a huge morbidity and mortality.
- Only relatively minor progress in therapeutic strategies has been made in the past decades.
- This is at least partially due to a lack of predictive diagnostic tools allowing personalized treatment of CKD-MBD patients
- Without precise diagnostic tools a personalized therapy is not possible. This, however, was part of the success story in oncology.

THE TAKE-HOME MESSAGE

- However, there is hope; Researchers highlighted key recommendations in areas of controversy or conjecture in the management of (CKD-MBD) in a recent synopsis of the (KDIGO) 2017 .
- The original update, published in *Kidney International* (2017;7(Suppl 1):1-59), resulted in 15 revised recommendations based on evidence of varying strengths accumulated since the 2009 KDIGO guidelines
- They described the recent progress in the diagnosis of disturbances of the PTH, calcium & phosphate & metabolism in patients with CKD plus the currently available imaging modalities to Dx. different subcategories of CKD-MBD.

- These new tools may have the potential of allowing personalized therapy for the treatment of CKD-MBD and hence improving outcome.

Knowledge is of no value unless you put it into practice.

-Anton Chekhov