Hyperparathyroïdie primitive: Atteinte osseuse et stratégies de prise en charge

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Déclaration d'intérêt

Activités de consultant,
subventions de recherche :

Amgen

1948 : Primary hyperparathyroidism

« A state of increased parathyroid hormone secretion, inappropriate to the prevailing hypercalcemia »

(Albright, 1948)

1991: Hyperparathyroïdie primitive asymptomatique

- Diagnosis and Management of Asymptomatic Primary Hyperparathyroidism: Consensus Development Conference Statement

Ann Intern Med. 1 April 1991;114(7):593-597

2003: Hyperparathyroïdie primitive normocalcémique

Normocalcemic Primary Hyperparathyroidism: Evidence for a Generalized Target-Tissue Resistance to Parathyroid Hormone

GERARD MARUANI, ALEXANDRE HERTIG, MICHEL PAILLARD, AND PASCAL HOUILLIER

J Clin Endocrinol. Metab. 2003; 88: 4641

« Recently, another variant of PHPT (normocalcaemic PHPT) has been described in which the serum calcium is normal but the serum PTH is elevated, in the absence of any secondary cause for PTH elevation. »

J. Bilezikian
J Intern Med. 2005;257(1):6-17

TABLE 1. EVOLUTION OF THE CLINICAL PROFILE OF PRIMARY HYPERPARATHYROIDISM

	Cope et al. 1930–1965 (%)	*Heath et al. 1965–1974 (%)*	*Mallette et al. 1965–1974 (%)*	*Silverberg et al. 1984–2002 (%)*
Nephrolithiasis	57	51	37	17
Hypercalciuria	Not reported	36	40	39
Overt skeletal disease	23	10	14	1.4
Asymptomatic	0.6	18	22	80

Characteristics of 287 patients with primary hyperparathyroidism

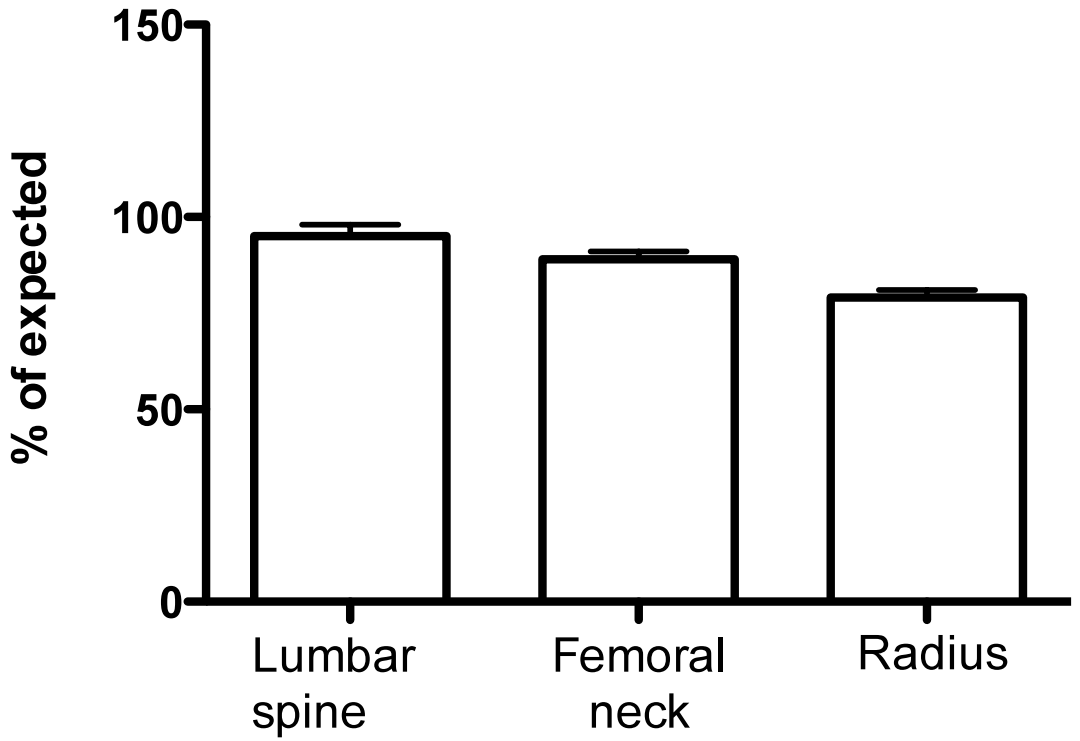
Age (yr)	54 ± 14	
Sex ratio (female/male)	215/72	
Serum Total Calcium (mM)	2.59 ± 0.17	2.09 – 2.52
Serum Ionized Calcium (mM)	1.43 ± 0.10	1.15 – 1.32
Serum PTH (pg/ml)	87 ± 48	11 – 57
25OHvitamin D (nM)	34 (15-121)	
$1,25(OH)_2$vitamin D (pM)	114 ± 36	45 - 110
Plasma Phosphate (mM)	0.80 ± 0.14	0.77 – 1.45
Serum Magnesium (mM)	0.85 ± 0.09	0.71 – 1.04
Fasting U Ca Excretion (mmol/mmol creatinine)	0.57 ± 0.34	0.03 – 0.36

Comparaison de 2 groupes d'hyperparathyroïdie primitive normo et hypercalcémiques

	Hypercalcemic subgroup (n=34)	Normocalcemic subgroup (n=34)
Age (yrs)	55 ± 10	55 ± 11
Sex ratio (female/male)	26/8	26/8
Serum PTH (pg/ml)	75 ± 18	75 ± 19
BMI (Kg/m^2)	23.0 ± 3.5	27.0 ± 8.3**
25OHvitamin D (nmol/L)	31 (15-121)	33 (17-86)
$1,25(OH)_2$vitamin D (pmol/L)	122 ± 39	103 ± 30*
TmPi (mmol/L GF)	0.71 ± 0.13	0.79 ± 0.17*
Serum osteocalcin (ng/mL)	20.2 ± 8.4	15.3 ± 7.1**
Serum Mg concentration (mmol/L)	0.90 ± 0.08	0.90 ± 0.08
Fasting deoxypyridinoline excretion (nmol/mmol creatinine)	8.4 ± 4.1	6.4 ± 2.1*
Fasting UCa/UCr (mmol/mmol creat)	0.62 ± 0.39	0.39 ± 0.25**
Urine Na excretion (mmol/24 hr)	138 ± 53	130 ± 56

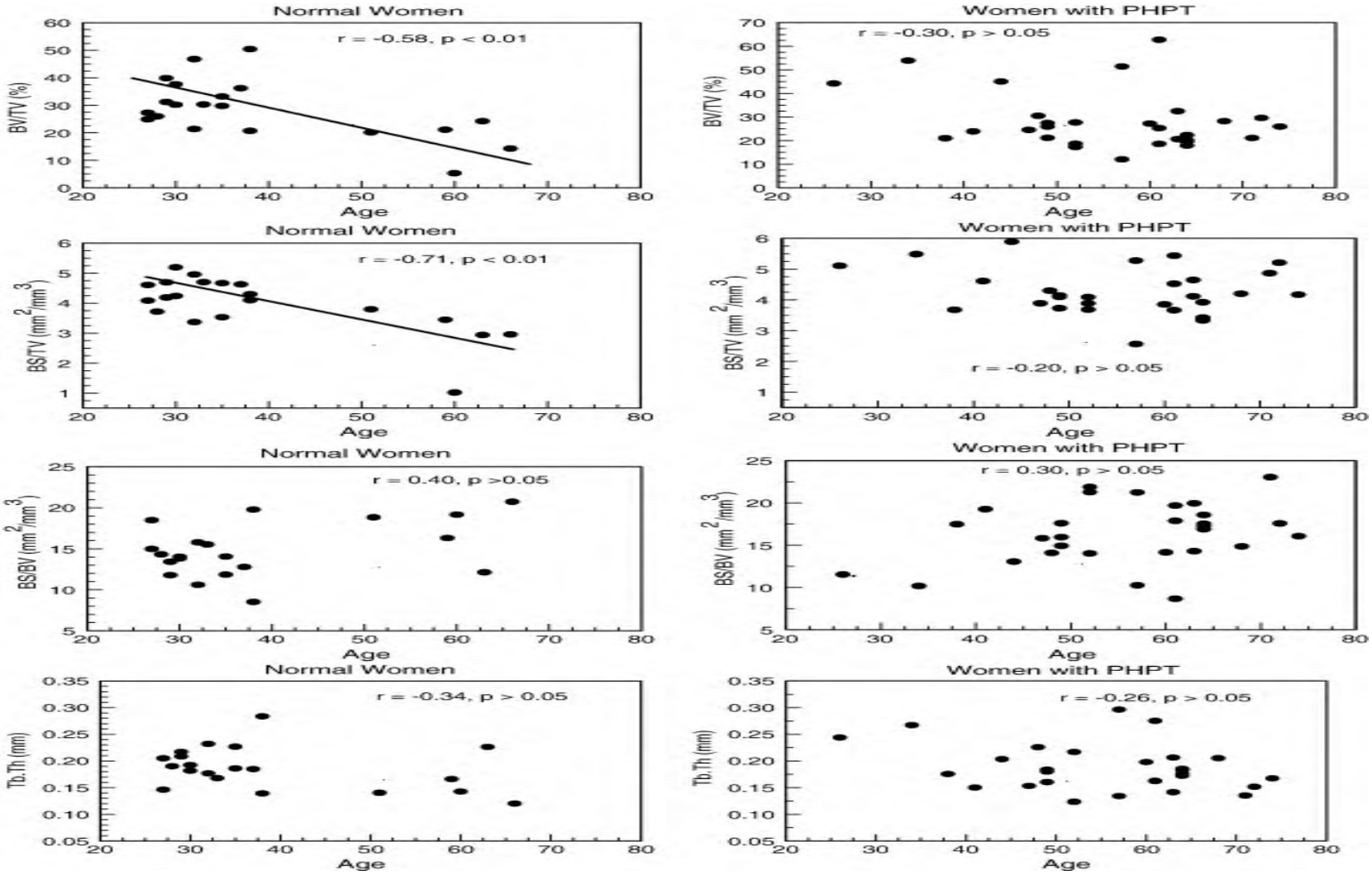
*, p< 0.05 ; **, p< 0.01

Atteinte osseuse



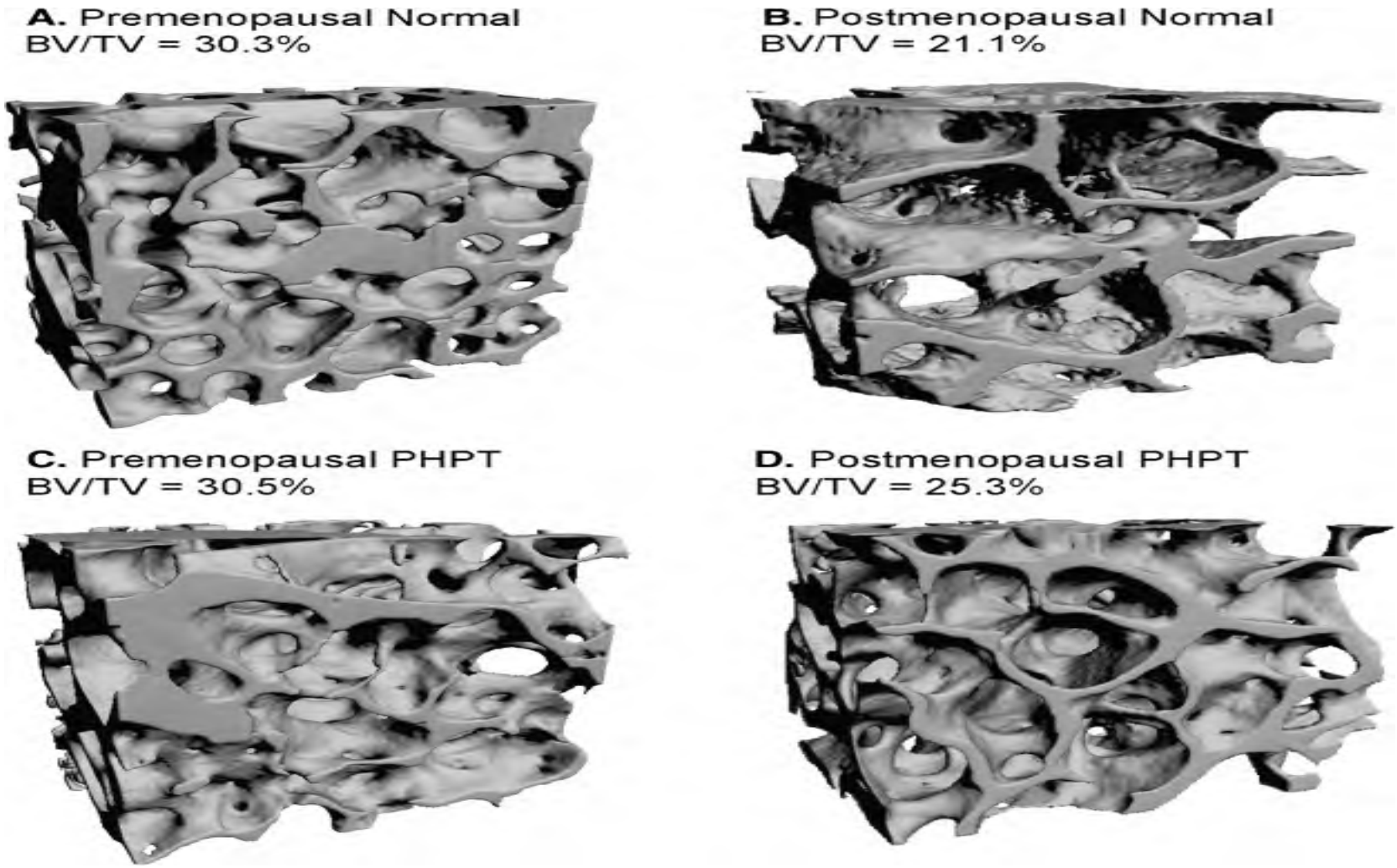
S Silverberg et al, J Bone Miner Res, 1989

Preserved three-dimensional cancellous bone structure in mild primary hyperparathyroidism



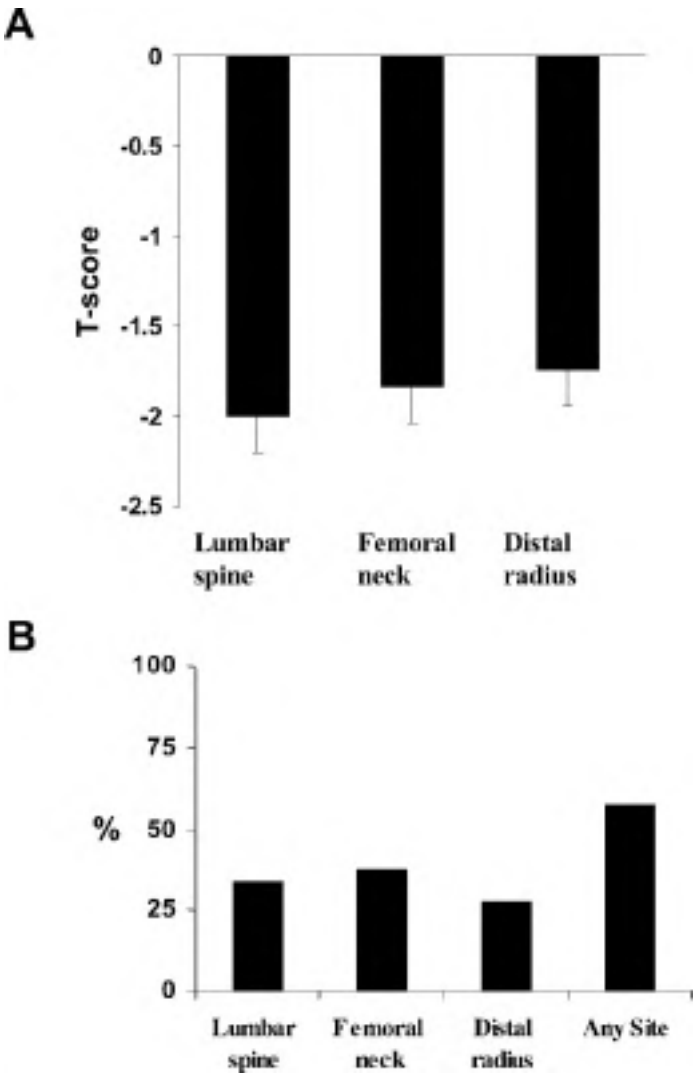
D.W. Dempster , et al, Bone 2007

Preserved three-dimensional cancellous bone structure in mild primary hyperparathyroidism



D.W. Dempster , et al, Bone 2007

BMD in patients with normocalcemic PHPT.



T-Score by site

% of osteoporosis

Lowe H et al. JCEM 2007;92:3001-3005

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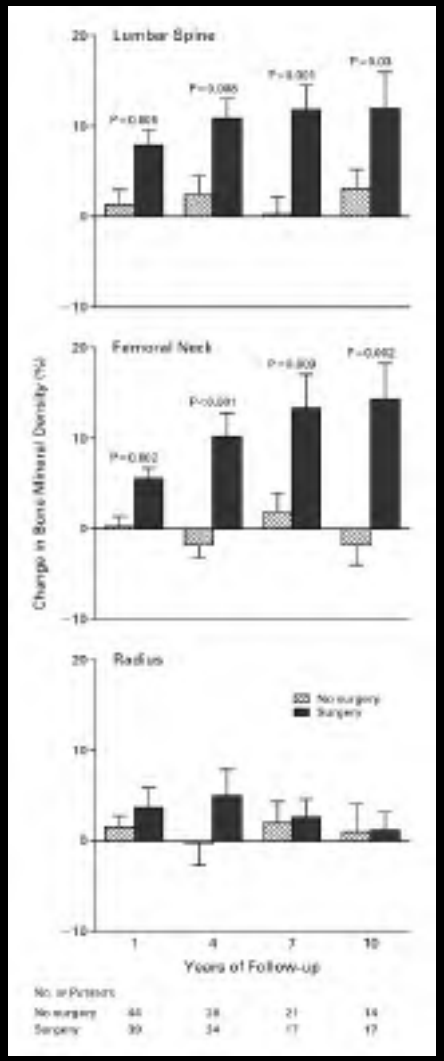
Effect of Primary Hyperparathyroidism on Volumetric Bone Mineral Density and Bone Geometry (pQCT)

Parameter	PH group	Control group	Normocalcemic PH	Hypercalcemic PH	P_{ANOVA}	$P_{ANOVA-adj}$
4% site						
Total BMC (mg)	248.0 ± 36[1] (a)	274.9 ± 36	256.7 ± 36.1[3(c)]	240.8 ± 34.8[1] (a)	<0.001	<0.001
Total vBMD (mg/cm^3)	230.4 ± 31.98[1]	257.78 ± 37.93	233.38 ± 37.5[2]	227.95 ± 27.11[1]	<0.001	
Total CSA (mm^2)	1081.54 ± 119.28	1075.13 ± 116.34	1107.57 ± 106.27	1060.16 ± 126.87	0.34	
Trabecular BMC (mg)	85.6 ± 14.8[1] (a)	98.6 ± 15.2	89.5 ± 14.9[3(c)]	82.5 ± 14.2[1] (a)	<0.001	<0.001
Trabecular vBMD (mg/cm^3)	177.0 ± 31.4[1]	205.0 ± 31.1	181.6 ± 39.4[2]	173.2 ± 23.1[1]	<0.001	
Trabecular CSA (mm^2)	486.5 ± 53.6	483.6 ± 52.3	498.2 ± 47.9	476.9 ± 57.1	0.34	

Charopoulos et al, J Clin Endocrinol Metab, 2006

Evolution osseuse

Mean (±SE) Change in Bone Mineral Density at Three Sites in Patients with Primary Hyperparathyroidism, According to Treatment.



Silverberg SJ et al. N Engl J Med 1999;341:1249-1255.

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Biochemical Values in 52 Asymptomatic Patients with Primary Hyperparathyroidism Who Did Not Undergo Parathyroidectomy.

TABLE 3. BIOCHEMICAL VALUES IN 52 ASYMPTOMATIC PATIENTS WITH PRIMARY HYPERPARATHYROIDISM WHO DID NOT UNDERGO PARATHYROIDECTOMY.*

VARIABLE	BASE LINE (N=52)	YEAR 5 OF FOLLOW-UP (N=35)	YEAR 10 OF FOLLOW-UP (N=14)
Serum calcium (mg/dl)	10.5±0.1	10.6±0.1	10.3±0.2
Serum parathyroid hormone (pg/ml)	118±9	113±67	106±26
Urinary calcium (mg/day)	232±18	193±20	152±34
Alkaline phosphatase (U/liter)	98±6	101±9	110±13
Serum 1,25-dihydroxyvitamin D (pg/ml)	56±2	55±3	53±6

*Values are means ±SD. The base-line values are the means of three measurements in each patient. There were no significant differences from base line in any of the variables shown during follow-up. To convert values for serum calcium to millimoles per liter, multiply by 0.25; to convert values for urinary calcium to millimoles per liter, multiply by 0.025.

Silverberg SJ et al. N Engl J Med 1999;341:1249-1255.

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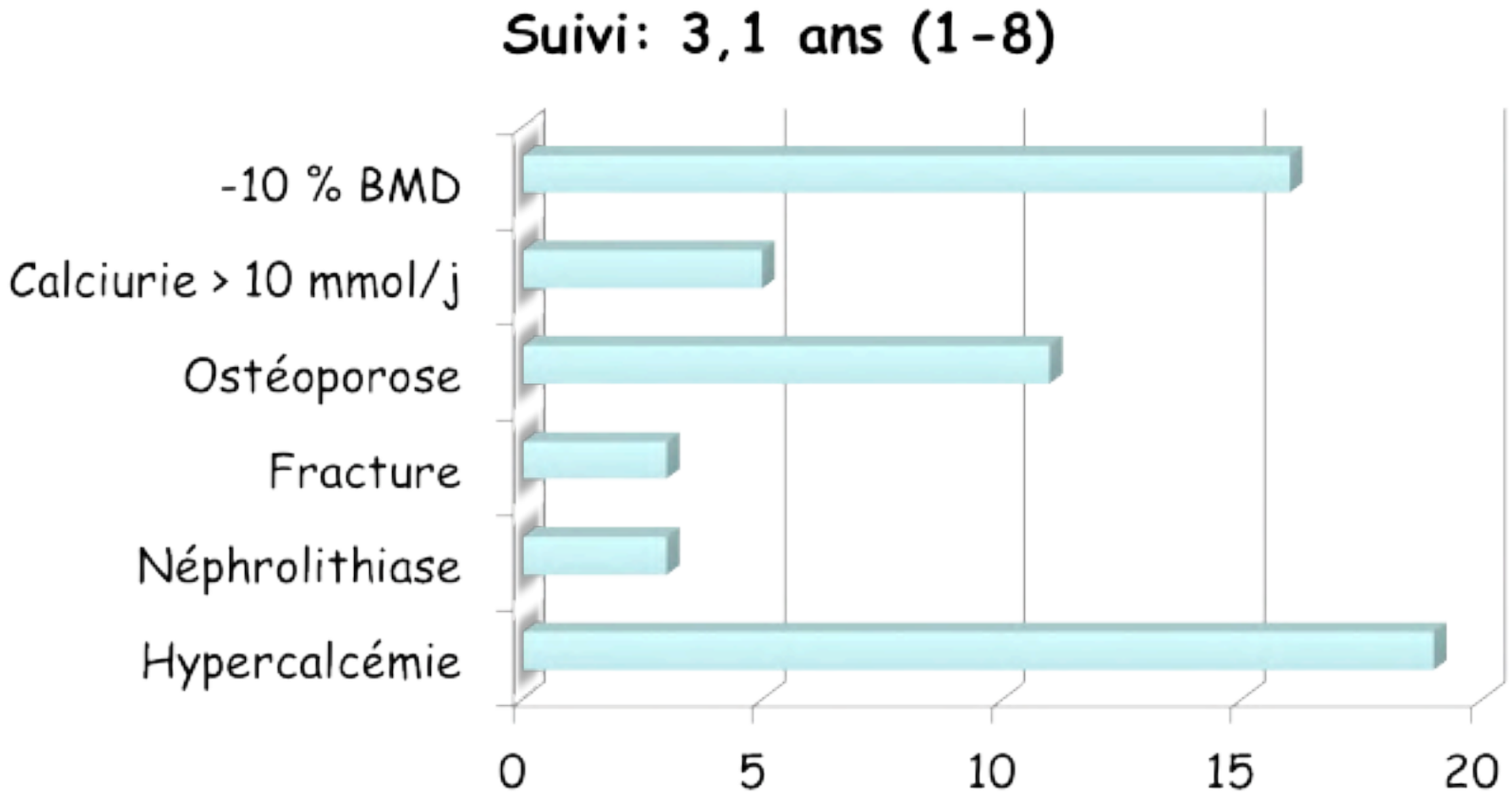
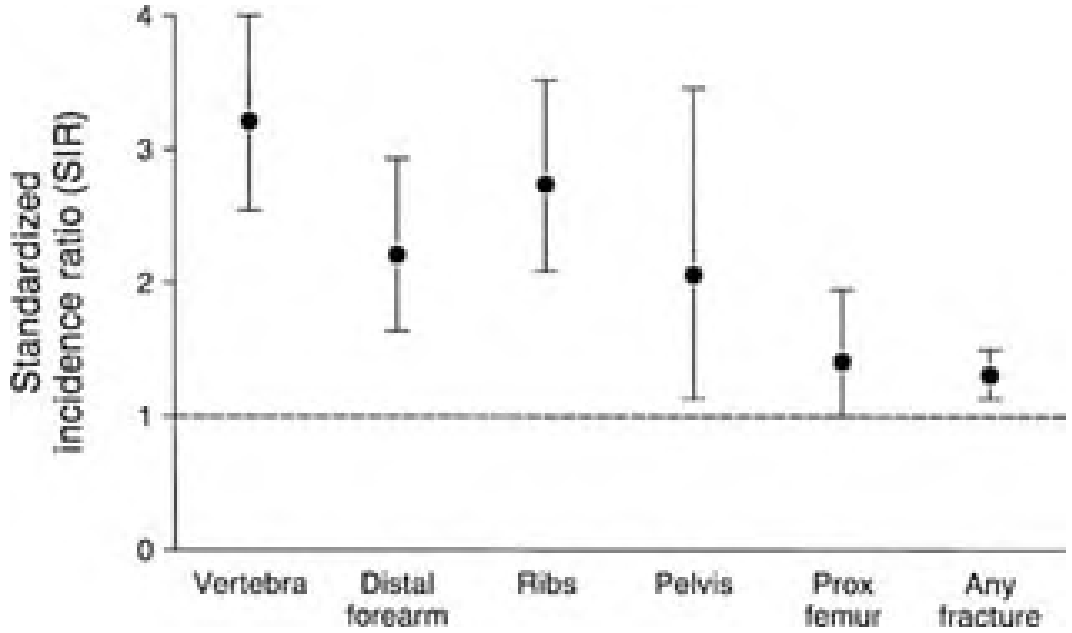
Evolution après le diagnostic des formes normocalcémiques



H Lowe et al, J Clin Endocrinol Metab, 2007

Risque fracturaire

Primary Hyperparathyroidism and the Risk of Fracture: A Population-Based Study

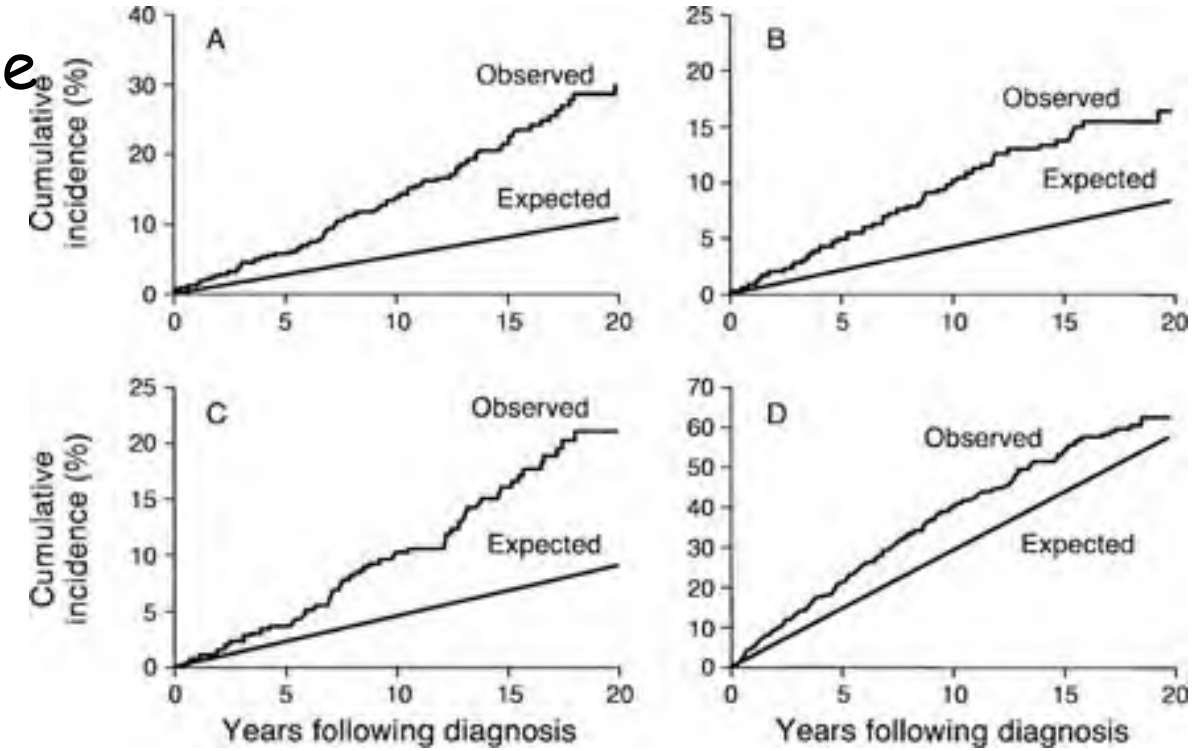


Journal of Bone and Mineral Research
1999

Primary Hyperparathyroidism and the Risk of Fracture: A Population-Based Study

Vertebrae

Colles



Rib

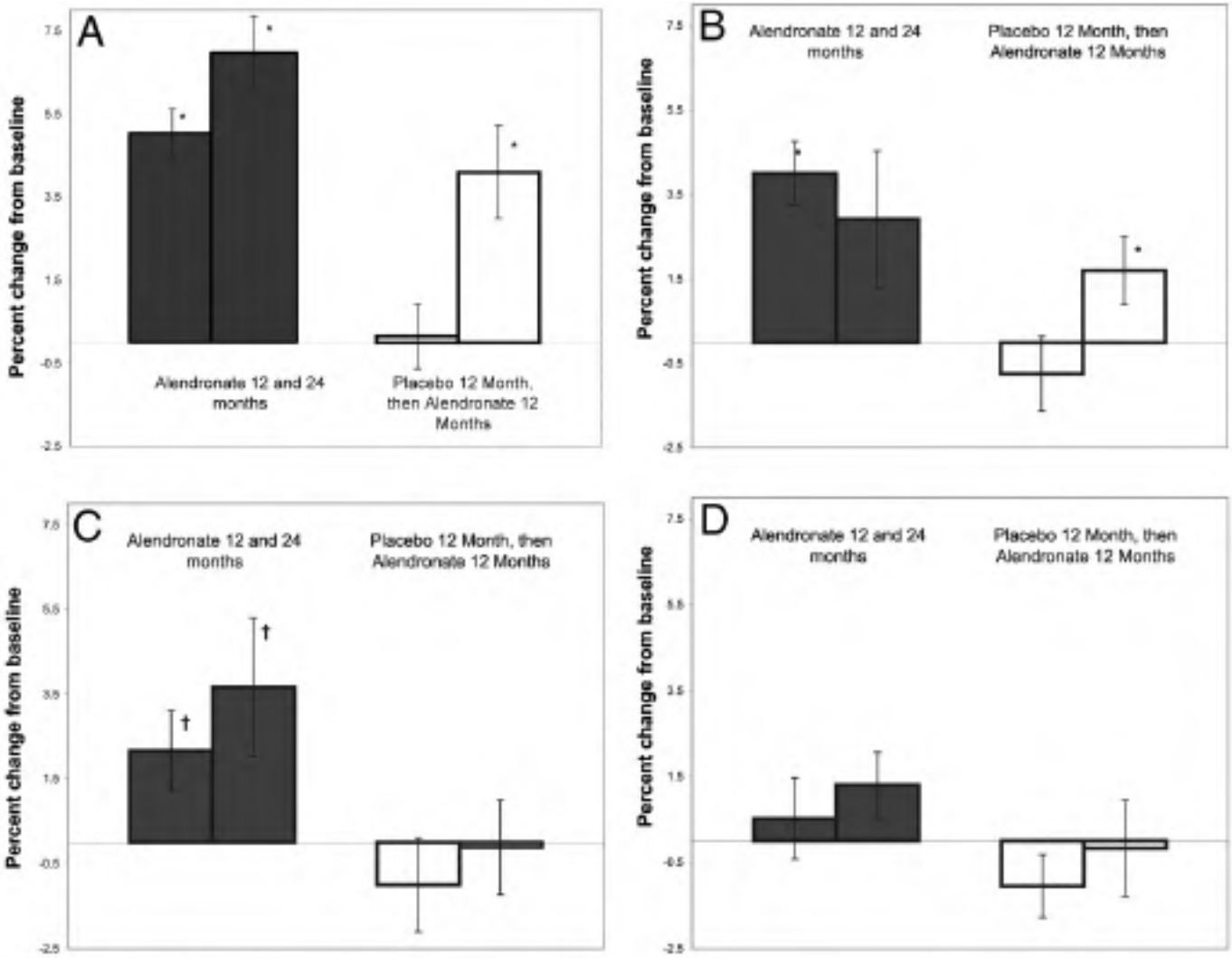
Any

Journal of Bone and Mineral Research
1999

Recommandations pour le traitement chirurgical de l' hyperparathyroïdie primitive asymptomatique

	Recommandations NIH (2002)	Recommandations NIH (2008)
Calcémie (au delà de la limite supérieure de la normale)	0,25 mmol/L	0,25 mmol/L (10 mg/L)
Calciurie (24 h)	> 10 mmol/24 h	Pas de recommandation
Clearance de créatinine (DFG)	Diminuée de 30 %	< 60 mL/min
Densité minérale osseuse	T-score < -2,5	T-score < -2,5
Age	< 50 ans	< 50 ans

Effect of alendronate on lumbar spine (A), total hip (B), femoral neck (C), and one third distal radius (D) BMD



Khan, A. A. et al. J Clin Endocrinol Metab 2004;89:3319-3325

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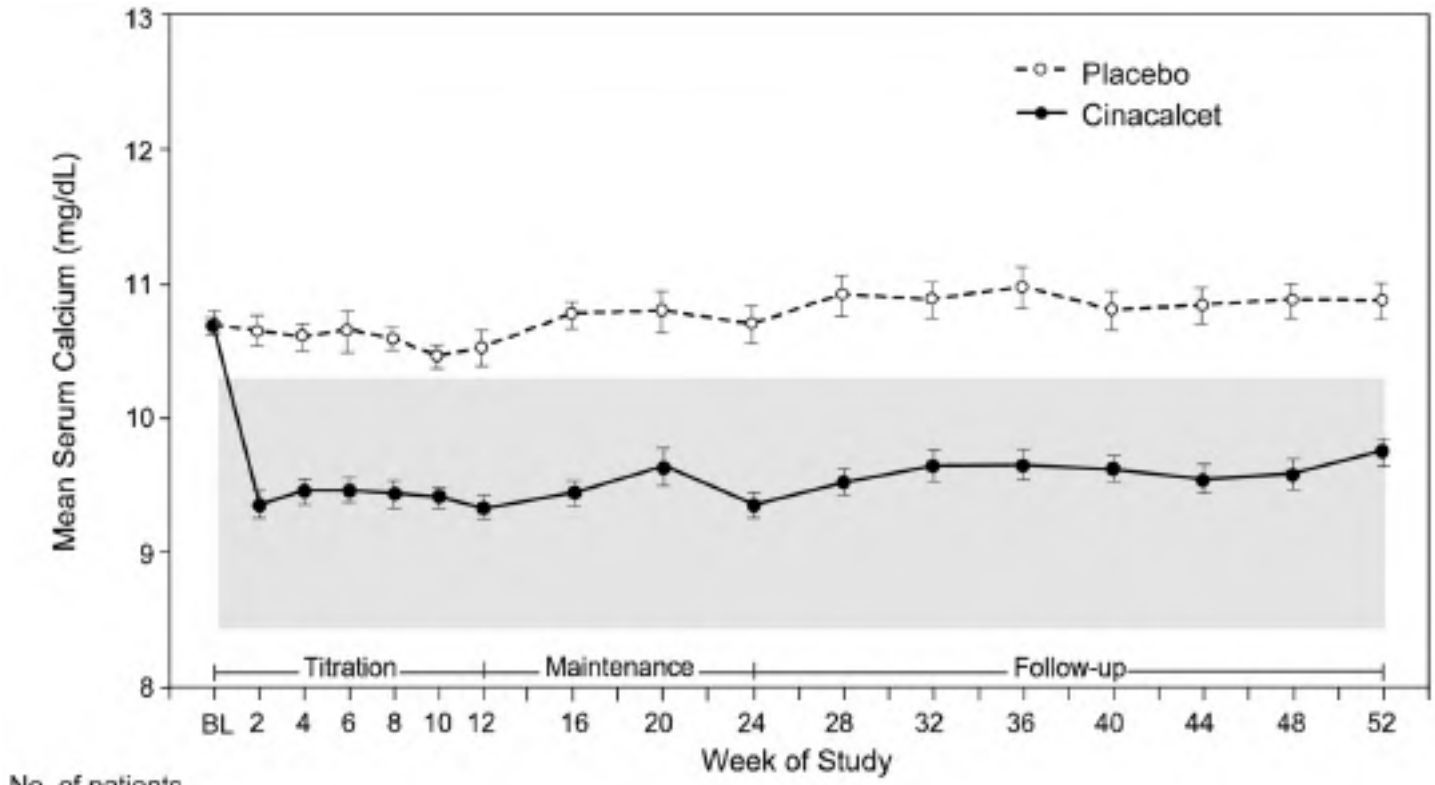
Comparison of predose serum calcium concentrations in patients receiving cinacalcet or placebo

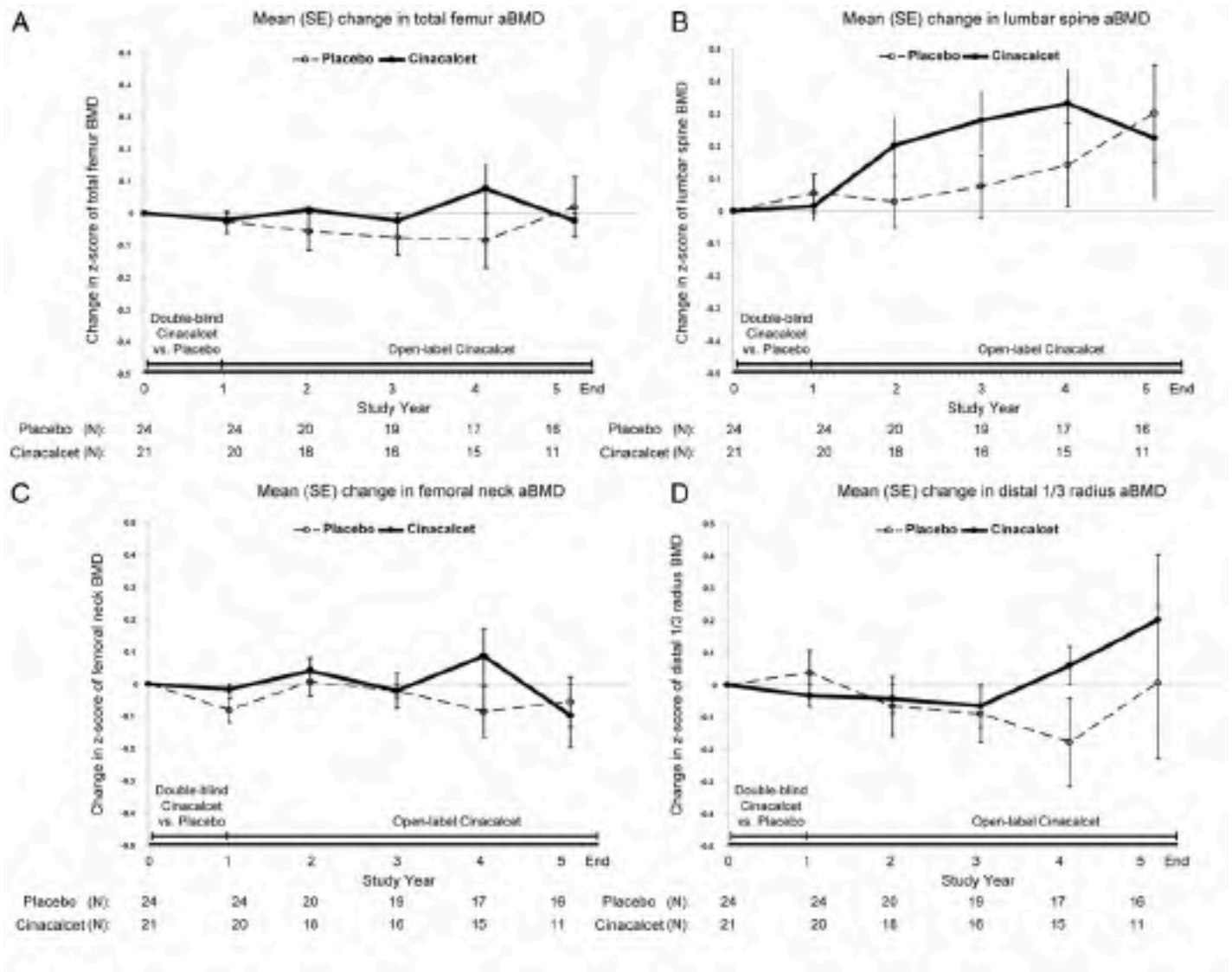


No. of patients				
Placebo	37	31	28	28
Cinacalcet	40	33	31	27

Peacock, M. et al. J Clin Endocrinol Metab 2005;90:135-141

The Journal of Clinical Endocrinology & Metabolism

Treatment by cinacalcet is not a chemical parathyroidectomy



Peacock, M. et al. J Clin Endocrinol Metab 2009

Cas particulier de l'HPTP normocalcémique

- Pas de recommendation consensuelle
- Absence de restriction des apports calciques
- Maintien d' un capital en vitamine D normal

(>75 nmol/L ; 30 ng/mL)

- Œstrogènes ?
- Raloxifène ?
- Bisphosphonates
- PAS DE Calcimimétique

Conclusion

- Atteinte osseuse fréquente dans les formes asymptomatiques
- Augmentation du risque fracturaire
- Préservation de l'os trabéculaire : est-ce un mythe ?
  - Squelette axial vs. périphérique
  - DXA vs. pQCT
- Atteinte osseuse réversible après chirurgie

PHRC : Micros

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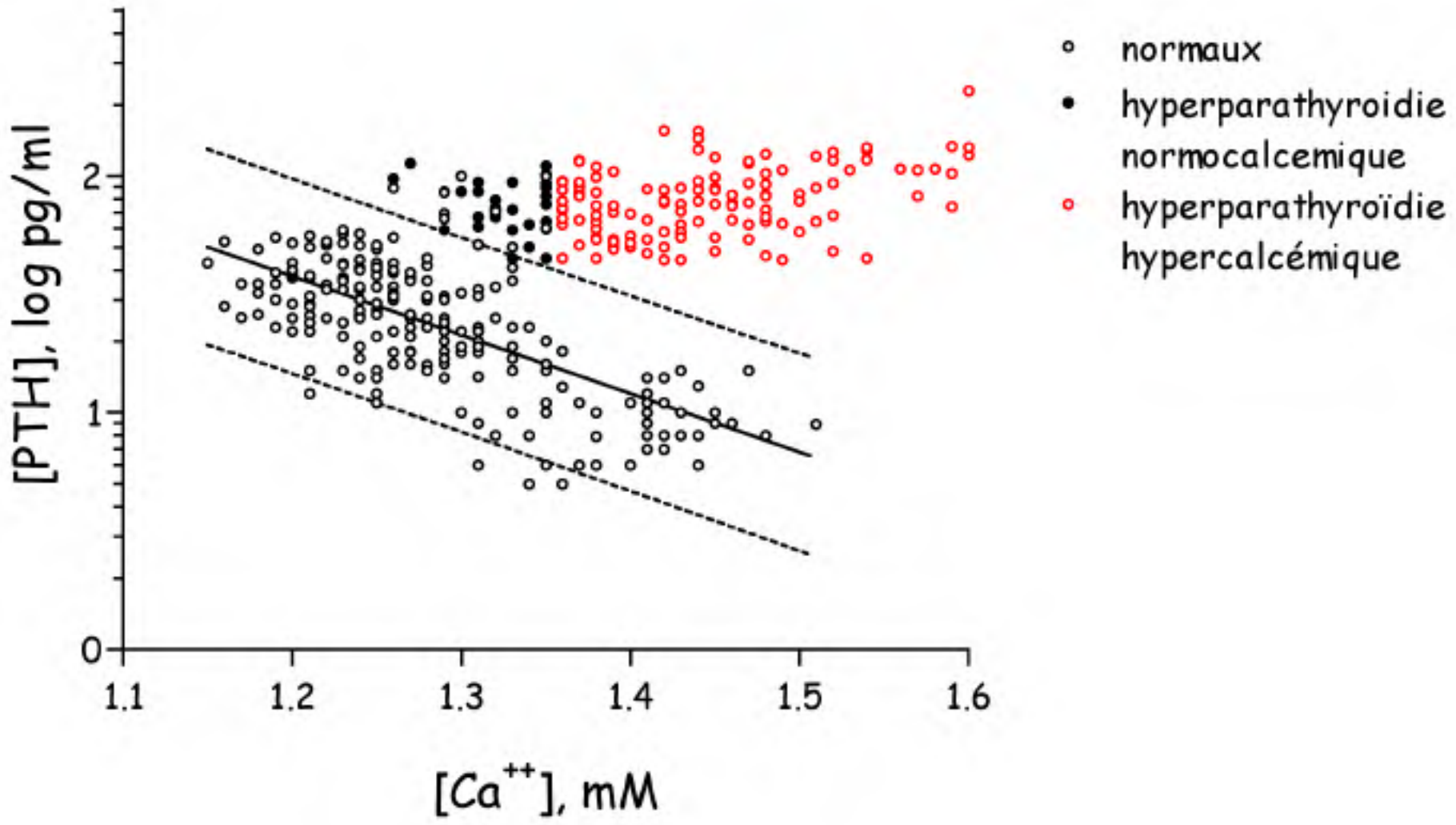
Relation normale et intervalle de confiance à 95 %



Effet du test de charge orale en calcium