



Associazione Medici Endocrinologi

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ITALIAN CHAPTER

Iperparatiroidismo primario: Presentazione clinica e diagnosi

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AULA 3

AACE Italian Chapter Course 3

Lingua ufficiale: italiano

Guida all'iperparatiroidismo

SESSIONE 1

Chairs: G. Borretta, M. Zini

1. Epidemiologia
F. Saponaro
2. Forme ereditarie e genetiche di iperparatiroidismo primario
A. Falchetti
3. Presentazione clinica e diagnosi
E. Castellano
4. Iperparatiroidismo primario normocalcemico
L. Gianotti
5. Tecniche di localizzazione
A. Festa

L'iperparatiroidismo primitivo (PHPT)
è la terza malattia endocrina più
frequente ed è la causa più comune
di **ipercalcemia**

Melton III LJ. The epidemiology of primary hyperparathyroidism in North America. J Bone Miner Res 2002.

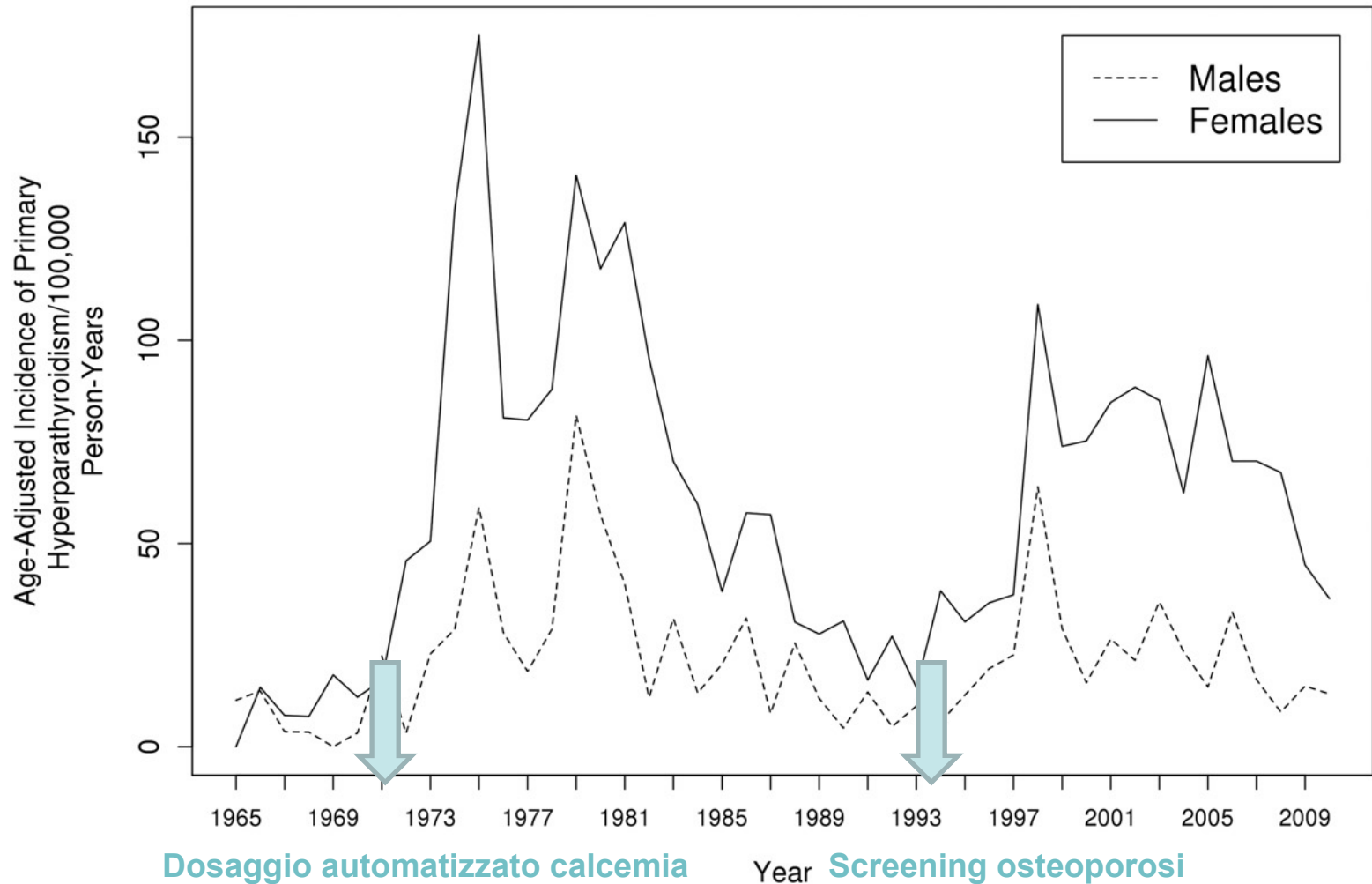
Fraser WD. Hyperparathyroidism. Lancet 2009.

Patogenesi

pHPT sporadico, adenoma singolo	80-85%
pHPT sporadico, adenoma multiplo	10-12%
pHPT carcinoma	< 1%
pHPT associato a sindrome <ul style="list-style-type: none">• <i>MEN 1 – 2</i>• <i>Ipercalcemia Ipocalciurica familiare (FHH)</i>• <i>Iperparatiroidismo severo neonatale</i>• <i>associato a tumore mandibola</i>• <i>Iperparatiroidismo isolato familiare</i>	10% (25%<45 aa)

Secular trends in the incidence of primary hyperparathyroidism over five decades (1965–2010)☆

Marcio L. Griebeler^a, Ann E. Kearns^a, Euijung Ryu^b, Matthew A. Hathcock^b,
L. Joseph Melton III^c, Robert A. Wermers^{a,*}



Dosaggio automatizzato calcemia

Year Screening osteoporosi

Criteria diagnostici

- **Hypercalcemia in the face of increased levels of PTH**
- PTH levels in the normal range, but **inappropriately high** (in the upper range of normal), relative to the hypercalcemia

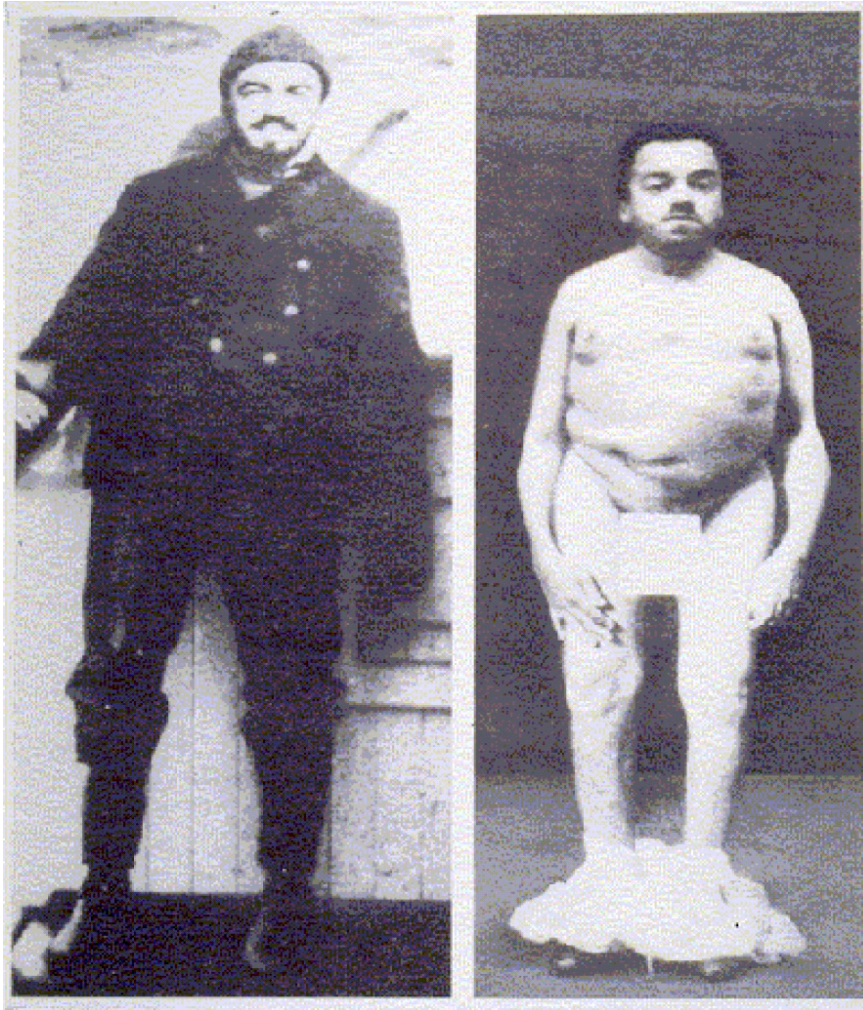
Discriminative power of three indices of renal calcium excretion for the distinction between familial hypocalciuric hypercalcaemia and primary hyperparathyroidism: a follow-up study on methods.

Christensen SE¹, Nissen PH, Vestergaard P, Heickendorff L, Brixen K, Mosekilde L.

Familial Benign Hypocalciuric Hypercalcemia (FHH):

- Mild hypercalcemia (10.5-12 mg/dL [2.7-3 mmol/L])
- PTH level normal or slightly elevated
- Hypocalciuria (usually less than 50 mg/24 h)
- Calcium/creatinine clearance ratio is less than 0.01** and calculated as follows:

Se ratio >0.02 la diagnosi di FHH è esclusa
Ricerca mutazione CASR se ratio tra 0.01 e 0.02



Capitano Charles Martell (1926)
muore per complicanze PHPT
(adenoma paratiroideo ectopico)

XIX-XX secolo

- ❖ **Symptomatic hypercalcemia**
- ❖ **Bone tumours, osteitis fibrosa cystica**
- ❖ **BONES**
- ❖ **Nephrolitiasis** in > 50%
- STONES**
- ❖ **Neuromuscular symptoms, pain**
- MOANS & GROANS**



**Sandra, malattia asintomatica,
guarita dopo asportazione di singolo
adenoma paratiroideo (MIP)**

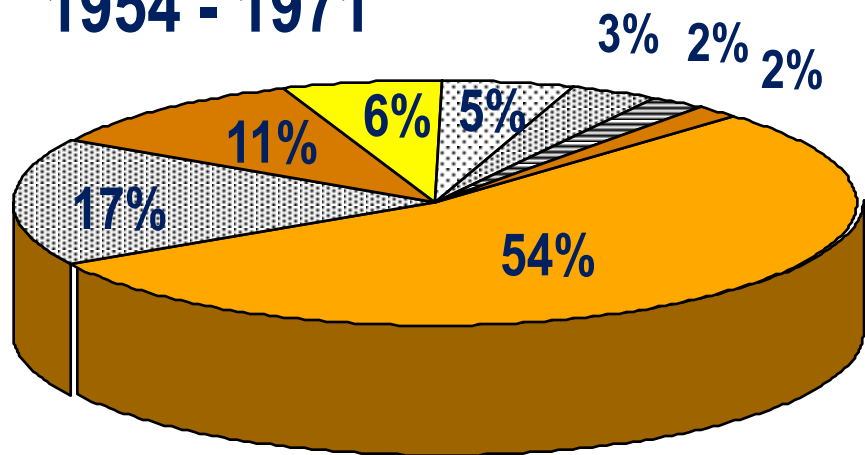
XX-XXI secolo

- ❖ **Slight** hypercalcemia
(sometimes **normal**)
- ❖ **Slight** bone involvement
(osteopenia/osteoporosis)
- ❖ Nephrolitiasis < 25%
- ❖ **Aspecific** neuromuscular
symptoms

ASYMPTOMATIC /MILD

Presentazione clinica nel tempo

1954 - 1971

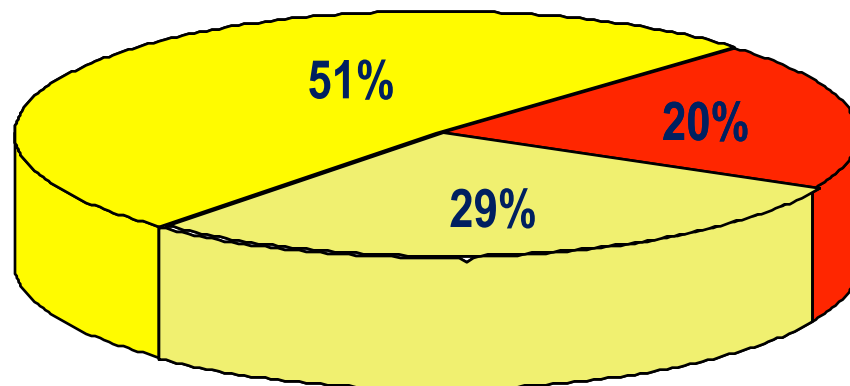


- renali
- ipertensione
- pancreatite
- ulcera
- ossee
- astenia
- neuromuscolari
- asintomatici

Mazzafferri, 1974

1990 - 1996

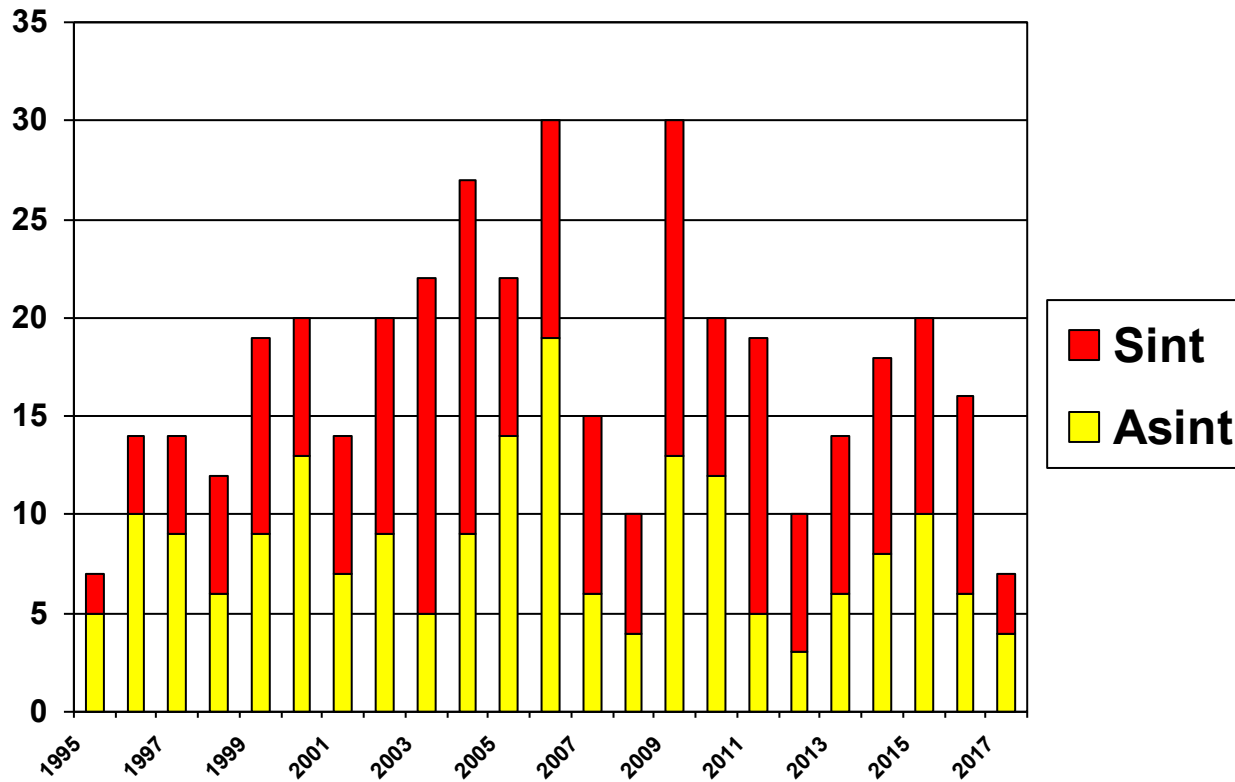
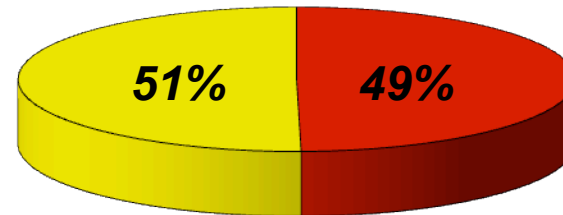
- asintomatici
- asintomatici (elegibili chirurgia)
- sintomatici



Silverberg, 1996

New diagnosis per year in our series 1995- giugno 2017 (n= 443) according to clinical presentation (Cuneo, Italy)

Symptomatic
Asymptomatic



Consensus Development Conference Statement

Asymptomatic PHPT

=

confirmed PHPT without signs and symptoms
commonly attributable to the disease

*(ovvero senza osteite fibroso-cistica, nefrolitiasi-calcinosi,
sintomi correlati a ipercalcemia)*

Italian Society of Endocrinology Consensus Statement: definition, evaluation and management of patients with mild primary hyperparathyroidism

C. Marcocci · M. L. Brandi · A. Scillitani · S. Corbetta ·
A. Faggiano · L. Gianotti · S. Migliaccio · S. Minisola

Table 2 Definition of mild PHPT

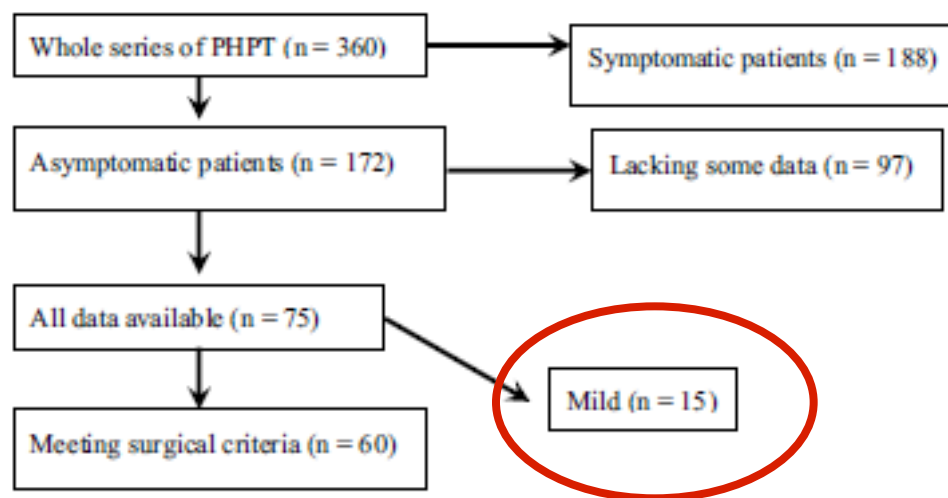
Albumin-corrected serum calcium concentration lower than 1 mg/dL (0.25 mmol/L) above the upper limit of normal
 Bone mineral density by DXA: T score ≥ -2.5 at lumbar spine, femoral neck, total hip, or distal 1/3 radius
 No evidence of vertebral fractures (X-ray, VFA, MRI or CT)
 Estimated creatinine clearance (or eGFR) >60 mL/min
 24-h urinary calcium excretion ≤ 400 mg/day and low renal stone risk by the urinary biochemical stone risk profile
 Absence of nephrolithiasis or nephrocalcinosis (by X-ray or ultrasound)
 Absence of relevant symptoms and complications directly attributable to either hypercalcemia or excess PTH secretion
 Age ≥ 50 years

DXA dual-energy X-ray absorptiometry, *VFA* vertebral fracture assessment (by DXA), *MRI* magnetic resonance imaging, *CT* computed tomography, *eGFR* estimated glomerular filtration rate

Mild \rightarrow aPHPT not meeting surgical criteria

Mild primary hyperparathyroidism as defined in the Italian Society of Endocrinology's Consensus Statement: prevalence and clinical features

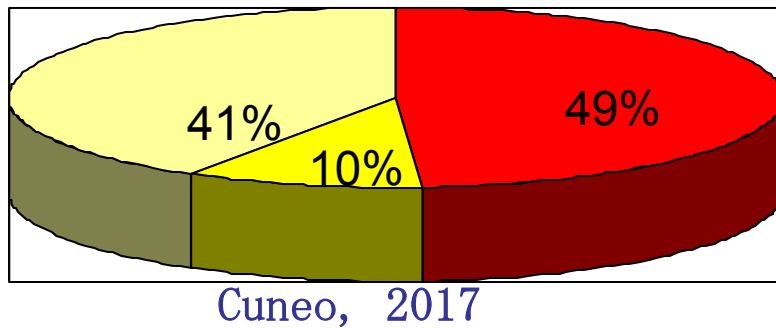
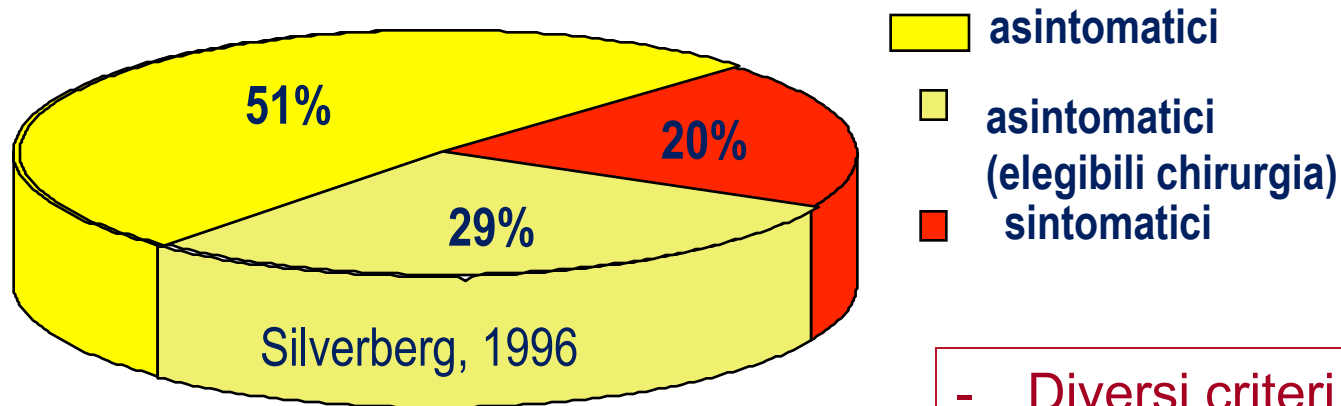
E. Castellano¹ · F. Tassone¹ · R. Attanasio² · L. Gianotti¹ · M. Pellegrino¹ · G. Borretta¹



= 20% dei pazienti asintomatici

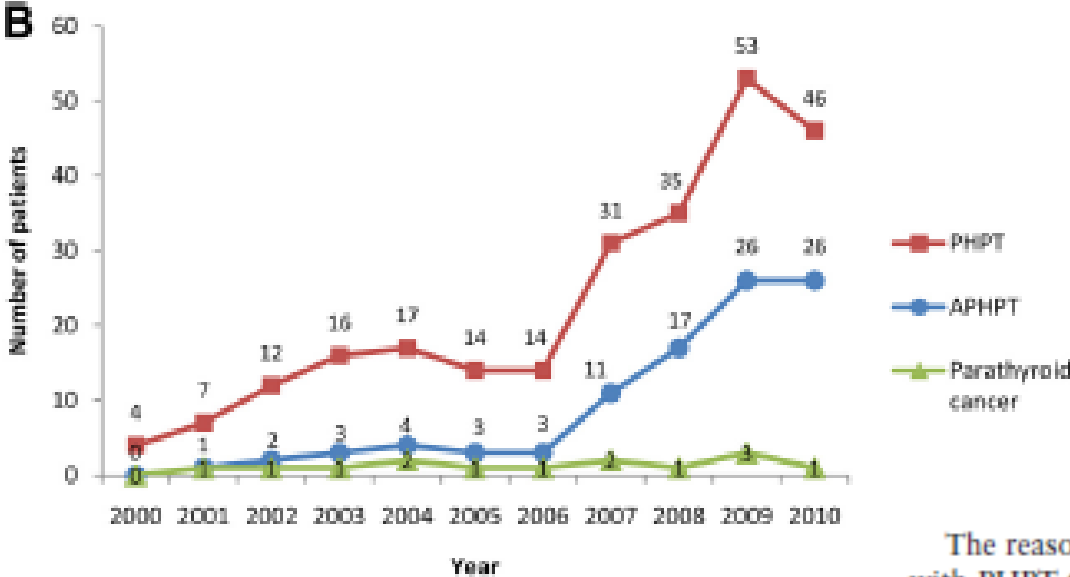
Livelli circolanti di calcio e PTH < ai restanti asintomatici

Come si spiega questa differenza quantitativa dei mild PHPT?



- Diversi criteri chirurgici secondo LG
- Come viene cercato il PHPT
- Come viene studiato il PHPT diagnosticato

The Changing Clinical Patterns of Primary Hyperparathyroidism in Chinese Patients: Data from 2000 to 2010 in a Single Clinical Center



249 pazienti

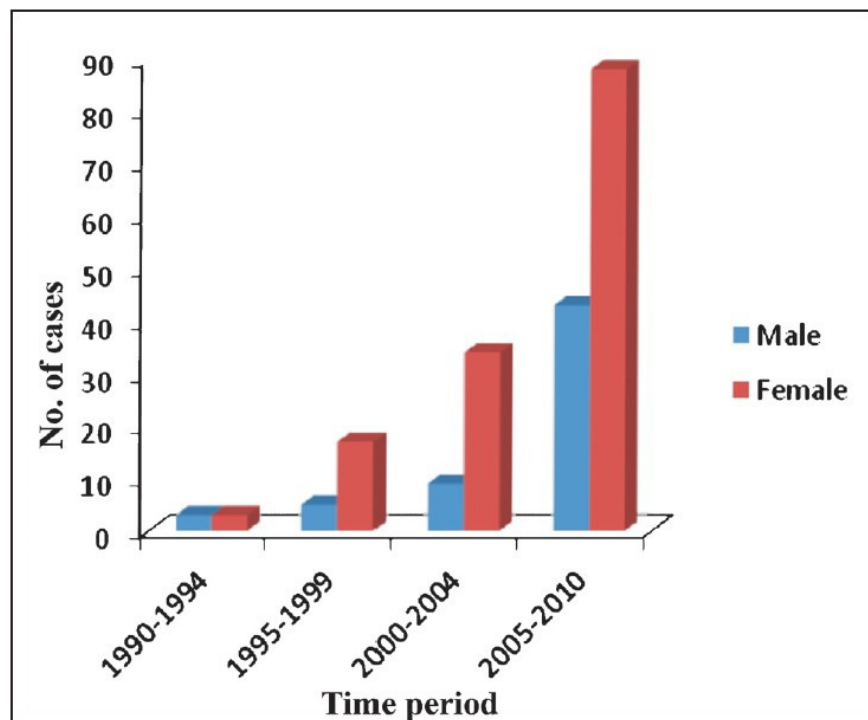
The reasons for referral of the asymptomatic patients with PHPT to our center were explored. Reviewing our source documents, we found no relevant records for 4 patients between 2000 and 2006. It was revealed that the 2 most common reasons for the 96 asymptomatic patients to seek medical consultation in our center were elevation of serum calcium levels (48.9% [47 of 96]) and parathyroid nodule(s) that were incidentally discovered by thyroid ultrasonography (46.9% [45 of 96]) during routine examinations.

Changes in clinical & biochemical presentations of primary hyperparathyroidism in India over a period of 20 years.

Shah VN, Bhadada S¹, Bhansali A, Behera A, Mittal BR.



Fig



Number of cases and gender-wise distribution of PHPT patients according to different time period (n=202).

INTERPRETATION & CONCLUSIONS: The findings of this retrospective analysis show that the PHPT still remains symptomatic disease with increasing awareness over the last two decades in our center. There was not much change in the clinical presentation, in the past two decades.

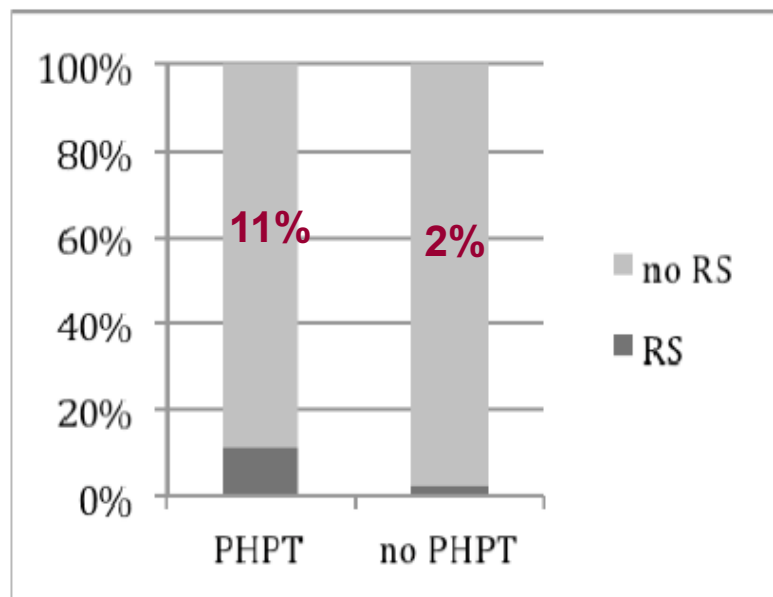


SILENT RENAL STONES IN PRIMARY HYPERPARATHYROIDISM: PREVALENCE AND CLINICAL FEATURES

Sara Cassibba, MD¹; Micaela Pellegrino, MD¹; Laura Gianotti, MD, PhD¹;
Claudia Baffoni, MD, PhD¹; Enrico Baralis, MD²; Roberto Attanasio, MD, PhD³;
Andrea Guarnieri, MD⁴; Giorgio Borretta, MD¹; Francesco Tassone, MD, PhD¹



141 patients



% of renal stones in PHPT and controls
 $P < 0.003$

NEPHROLITHIASIS IN PRIMARY HYPERPARATHYROIDISM: A COMPARISON BETWEEN SILENT AND SYMPTOMATIC PATIENTS

Elena Castellano, MD¹; Roberto Attanasio, MD, PhD²; Adele Latina, MD, PhD¹;
Gian L. Visconti, MD, PhD³; Sara Cassibba, MD⁴; Giorgio Borretta, MD¹

Table 2
Comparison Between Patients with Symptomatic and Silent Renal Stones

	Symptomatic (n = 93)	Silent (n = 16)	P value
BMI (kg/m ²)	24.8 ± 4.9	24.5 ± 4.9	n.s.
Age (years)	54.4 ± 12.9	57.6 ± 15.4	n.s.
Sex (F/M, %)	68.7/31.3	75/25	n.s.
PTH (ng/L)	146.5 [112]	207 [241]	.016
Serum calcium (mg/dL)	11.1 ± 0.9	12 ±	
Serum ionized calcium (mmol/L)	1.5 ± 0.1	1.6 ±	
25-hydroxyvitamin D (ng/mL)	28 [27]	18 [2]	
Serum creatinine (mg/dL)	0.8 ± 0.2	0.9 ±	
eGFR (mL/min/1.73 m ²)	83.9 ± 18.5	77.4 ±	
Serum phosphate (mg/dL)	2.47 ± 0.5	2.41 ±	
Urinary phosphate (mg/24 hours)	596.3 ± 380.4	459 ±	
Urinary calcium (mg/24 hours)	281.5 ± 160.6	267.4 ± 178	n.s.
HOMA-IR	1.91 ± 1.35	2.07 ± 1.46	n.s.
Insulin resistance (%)	20.8	37.5	n.s.
History of diabetes mellitus (%)	6.2	12.5	.0002
History of arterial hypertension (%)	39.8	37.5	n.s.
T-score at lumbar spine	-2.4 ± 1.5	-2.5 ± 1.1	n.s.
T-score at forearm	-2.0 ± 1.5	-2.3 ± 1.6	n.s.
T-score at hip	-1.9 ± 1.4	-2 ± 1	n.s.
Urine pH	6.16 ± 0.67	6.1 ± 0.516	n.s.
Urine concentration	1.014 ± 0.006	1.015 ± 0.006	n.s.
Mono/bilateral renal involvement (%)	55/45	44/56	n.s.
Micro/macro stone size (%)	15/85	87/13	.00001

Abbreviations: BMI = body mass index; eGFR = estimated glomerular filtration rate; HOMA-IR = Homeostasis Model Assessment-Insulin Resistance; IQR = interquartile range; PHPT = primary hyperparathyroidism; PTH = parathyroid hormone.

associated with higher urinary calcium levels. Our study also underlines some distinctive features of patients with silent nephrolithiasis in comparison to those with overt renal stones. The most intriguing peculiarity is that most patients of the silent group had **microlithiasis**, while this



“Silent” kidney stones in “asymptomatic” primary hyperparathyroidism—a comparison of multidetector computed tomography and ultrasound

Andreas Selberherr¹ · Marcus Hörmann² · Gerhard Prager¹ · Philipp Riss¹ · Christian Scheuba¹ · Bruno Niederle¹

Table 2 Kidney stones detected by ultrasound (US) and multidetector computed tomography (MDCT)

Results		US				Total <i>n</i>
		Positive		Negative		
		<i>n</i>	%	<i>n</i>	%	
MDCT	Positive	3	7.5	12	30.0	15
	Negative	1	4.0	24	60.0	25
	Total	4	10.0	36	90.0	40

n = patients; 40 patients were evaluated prospectively

The superiority of MDCT in determining the size, number, and the position of kidney stones was convincing in this study, and the possibility of low-dose protocols seems to justify the use of ionizing radiation. As shown, there was a larger number of patients with clinically “silent” kidney stones detected by MDCT compared to US [6, 16], demonstrating the superiority of MDCT and the necessity of an adaption of the current consensus [1].

Morphometric Vertebral Fractures in Postmenopausal Women with Primary Hyperparathyroidism

Edda Vignali,* Giuseppe Viccica,* Daniele Diacinti, Filomena Cetani, Luisella Cianferotti, Elena Ambrogini, Chiara Banti, Romano Del Fiacco, John P. Bilezikian, Aldo Pinchera, and Claudio Marcocci

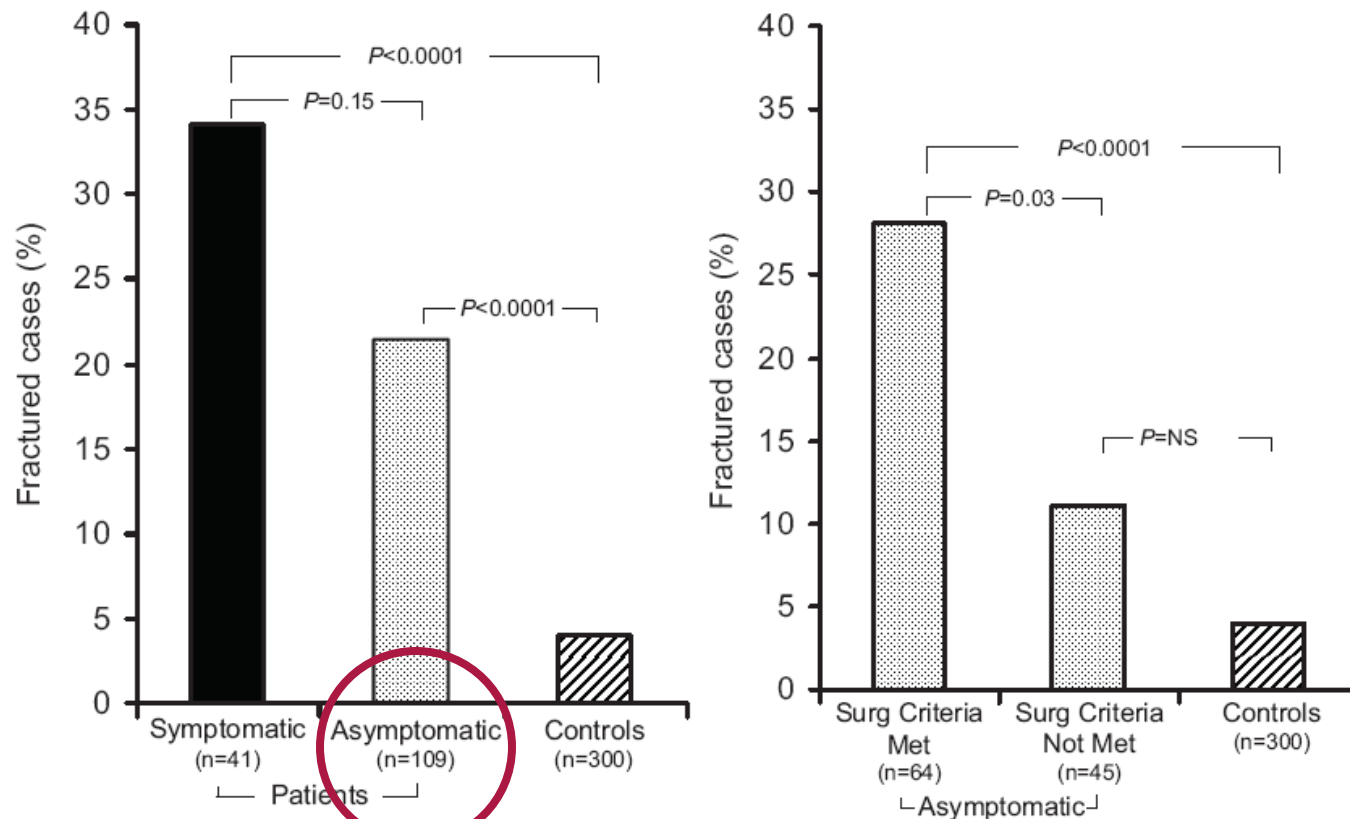
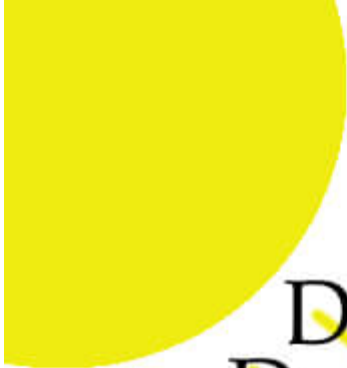


FIG. 3. Rate of VF in patients and controls. *Left*, Symptomatic and asymptomatic patients and controls. *Right*, Asymptomatic patients, grouped according to whether they met or did not meet the criteria for surgery established by the 2002 Workshop on Asymptomatic PHPT (17), and controls. *P* value refers to OR between different groups.

Prevalence of Kidney Stones and Vertebral Fractures in Primary Hyperparathyroidism Using Imaging Technology

Characteristics	Symptomatic	Asymptomatic	P
n	64	76	
Age, y	62.2 ± 11	63.9 ± 12	NS
Weight, kg	68.2 ± 12	64.2 ± 10	<.05 ^a
Height, cm	162.7 ± 9	159.6 ± 7	<.05 ^a
BMI, kg/m ²	25.8 ± 4	25.2 ± 4	NS
Time since menopause, y	17.4 ± 11	16.5 ± 10	NS
sCa, mg/dL	11.3 ± 0.9	11 ± 0.8	NS
Ca ²⁺ , mmol/L	1.47 ± 0.13	1.43 ± 0.12	NS
P, mg/dL	2.8 ± 0.5	2.9 ± 0.6	NS
Cr, mg/dL	0.8 ± 0.2	0.8 ± 0.3	NS
PTH, pg/mL	115 ± 88	106 ± 100	NS
25(OH)D, ng/mL	26.6 ± 16	29.5 ± 15	NS
uCa, mg/24 h	294.5 ± 138	288.3 ± 157	NS
L1-L4 BMD, g/cm ²	0.844 ± 0.146	0.826 ± 0.153	NS
T-score	-1.9 ± 1.3	-2 ± 1.3	
FN BMD, g/cm ²	0.642 ± 0.114	0.648 ± 0.103	NS
T-score	-1.9 ± 0.9	-1.9 ± 0.7	
TH BMD, g/cm ²	0.757 ± 0.133	0.766 ± 0.147	NS
T-score	-1.6 ± 1.4	-1.4 ± 0.9	
Rad BMD, g/cm ²	0.589 ± 0.096	0.557 ± 0.117	NS
T-score	-1.9 ± 1.5	-2.3 ± 1.3	
Osteoporosis, % ^c	59.4	65.8	NS
KS, %	78.1	35.5	<.0001 ^b
VFs, %	34.4	34.7	NS

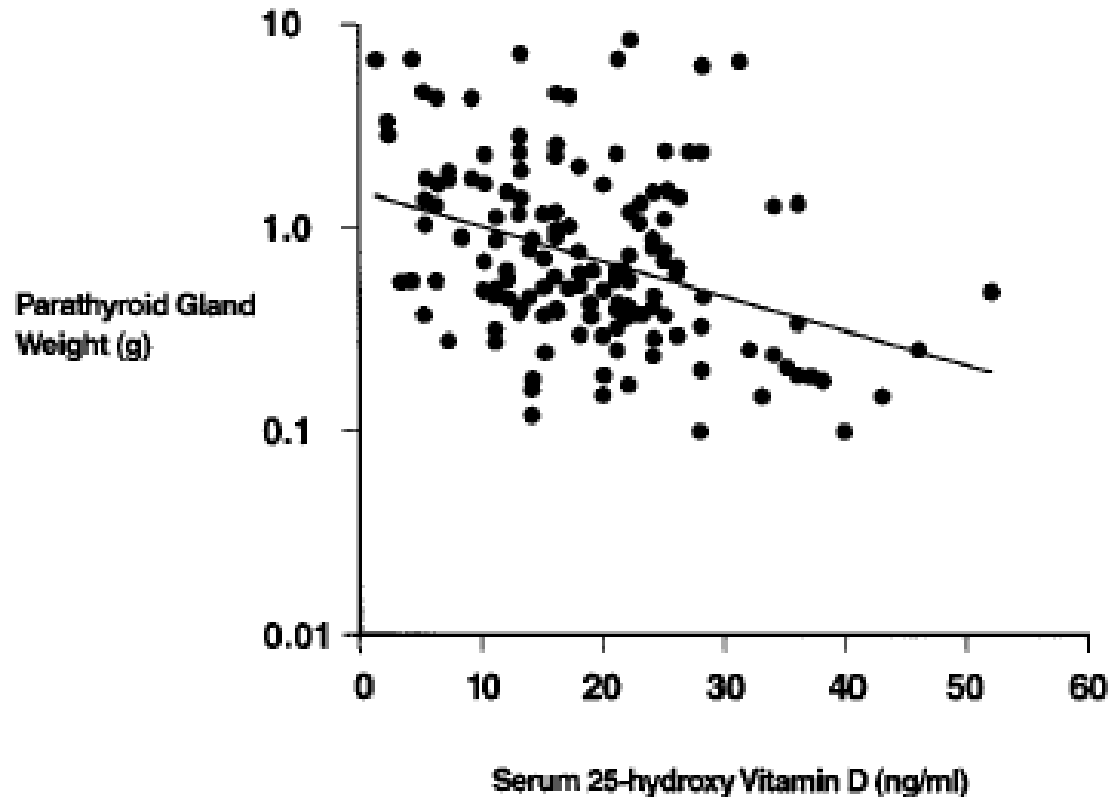
**140 pazienti consecutivi
2009-2013**
Calcoli renali: 55%
Fratture vert.: 35%



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Effect of Vitamin D Nutrition on Parathyroid Adenoma Weight: Pathogenetic and Clinical Implications*



148 pazienti PHPT

Vitamin D status in primary hyperparathyroidism in India.

Harinarayan CV, Gupta N, Kochupillai N



20 pazienti consecutivi con PHPT

- Osteite fibrosocistica nel 90% (60% con tumori bruni)
- Nefrolitiasi/calcinosi: 50%
- Peso medio dell' adenoma: 4.6 g (range 0.125-25 g)
- Livello medio di 25OHD3: 8.4 $\mu\text{g/L} \pm 2.5$

Vitamin D in Primary Hyperparathyroidism: Effects on Clinical, Biochemical and Densitometric Presentation

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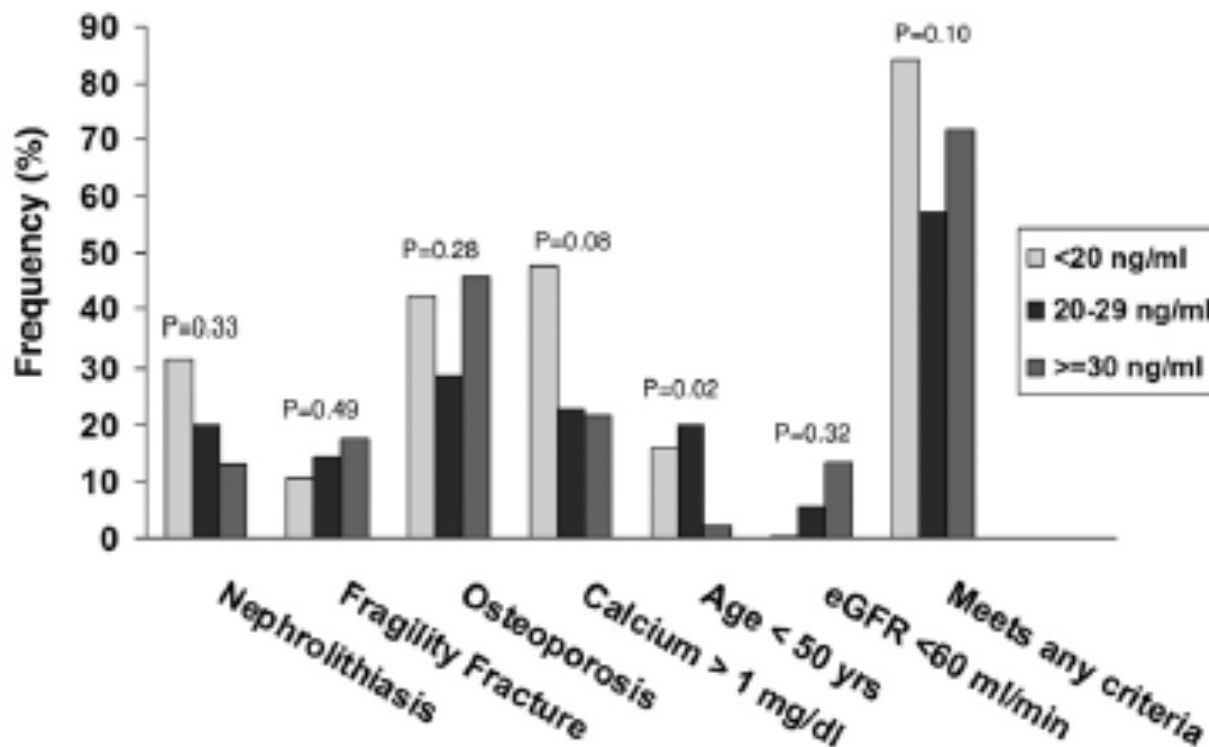


Figure 2. Frequency of symptoms and meeting surgical criteria in patients with PHPT using different 25OHD thresholds: <20 (light gray), 20–29 (dark gray) and ≥ 30 (medium gray) ng/ml.

D	p- value
ml	
.7	N/A
.6	0.06
.1	0.32
	<0.0001
a,d	0.0004
1	0.99
	0.11
2	0.25
.9	0.28
lter)	
C-telopeptide (ng/ml)	
0.142–1.351	
0.738 ± 0.08	
0.631 ± 0.06	
0.604 ± 0.05	
	0.39

However, in this cohort with few profoundly vitamin D deficient patients, vitamin D status did not appear to significantly impact clinical presentation or bone density.

Impact of vitamin D deficiency on the clinical and biochemical phenotype in women with sporadic primary hyperparathyroidism

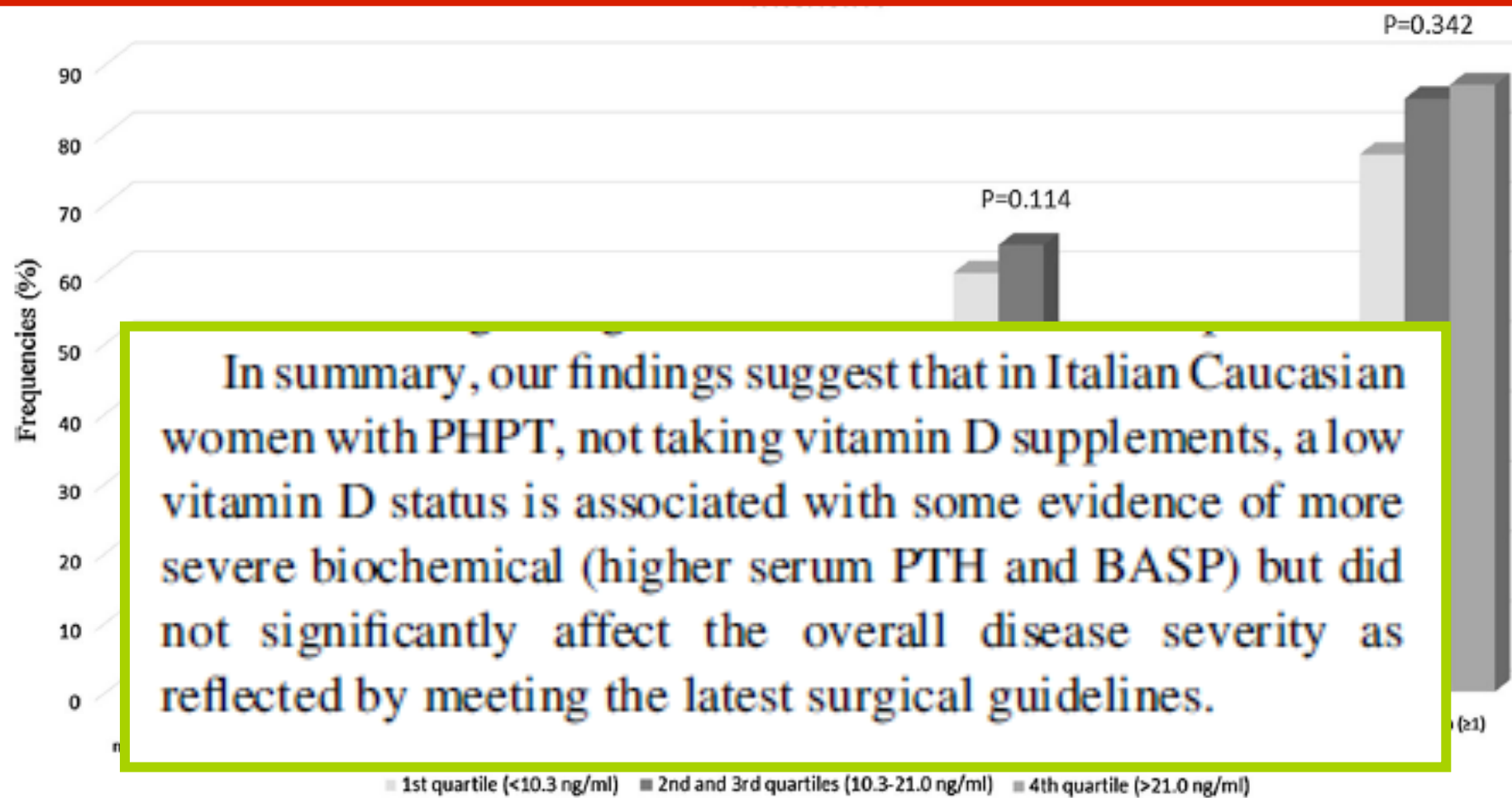
Clinical and biochemical features

Overall
(n = 215)

Normal
range

Quartiles

P value



Clinical and biochemical features	Overall (n = 215)	Normal range	1st quartile (<10.3 ng/ml)	2nd and 3rd quartiles (10.3-21.0 ng/ml)	4th quartile (>21.0 ng/ml)	P value
Fracture	70 (32 %)	-	21 (40 %)	29 (27 %)	20 (38 %)	0.164
Nephrolithiasis	51 (24 %)	-	14 (26 %)	20 (18 %)	17 (32 %)	0.136

VITAMIN D DEFICIENCY DOES NOT AFFECT THE LIKELIHOOD OF PRESURGICAL LOCALIZATION IN ASYMPTOMATIC PRIMARY HYPERPARATHYROIDISM

Francesco Tassone MD, PhD¹, Elena Castellano MD¹, Laura Gianotti MD, PhD¹, Franco Acchiardi MD², Ignazio Emmolo MD³, Roberto Attanasio MD⁴, Giorgio Borretta MD¹

Table 2: Positive localization (imaging) studies between aPHPT patients with and without VDD.

	VDD, n (%)	w/o VDD, n (%)	p
US +	19 (52.3%)	34 (55.7%)	1.0
MIBI +	15 (42.9%)	32 (52.4%)	0.40
US + or MIBI+	26 (74.3%)	44 (72.1%)	1.0



Clinical profile of juvenile primary hyperparathyroidism: a prospective study

154 casi: 116 sporadici + 42 familiari

	Whole group (n = 154)	Normal range	Sporadic (n = 112)	Familial (n = 42)	P
Sex (F:M)	2.8:1	–	3.6:1	1.6:1	P = 0.036
Age at diagnosis (years)	32 ± 7	–	33.3 ± 7	29 ± 8	0.001
Serum calcium (mg/dL)	10.9 ± 1	8.6–10.2	11 ± 0.9	10.9 ± 1.1	0.3
Serum albumin adjusted calcium (mg/dL)	10.6 ± 1	8.6–10.2	10.6 ± 1.1	10.6 ± 1.2	0.7
Ionized serum calcium (mmol/L)	1.50 ± 0.1	1.13–1.32	1.49 ± 0.13	1.50 ± 0.16	0.8
Serum phosphate (mg/dL)	2.4 ± 0.56	2.7–4.5	2.4 ± 0.54	2.5 ± 0.61	0.3
Plasma intact PTH (pg/mL)	111 (78–171)	15–75	118 (80–174)	97 (71–161)	0.05
Serum 25OHD (ng/mL)	19.6 ± 10	30–100	17.7 ± 9.8	21.7 ± 12.4	0.2
Serum osteocalcin (ng/mL)	32.5 ± 25.2	6.8–34	33.2 ± 27.5	30.9 ± 19.1	0.9
Serum BSAP (µg/L)	23.2 ± 15.8	2–20	23.8 ± 16.2	21.9 ± 14.9	0.2
24-h Urinary calcium (mg/24 h)	376.7 ± 154	<300	372.2 ± 156.4	401.3 ± 230	0.2
Lumbar spine		–			
BMD (g/cm ²)	0.93 ± 0.18		0.93 ± 0.18	0.94 ± .17	0.4
z-score	–1.08 ± 1.16		–1.06 ± 1.16 ^a	–0.85 ± 1.26 ^a	0.4
Femoral neck		–			
BMD (g/cm ²)	0.74 ± 0.12		0.73 ± 0.17	0.78 ± 0.13	0.5
z-score	–0.98 ± 0.95		–1.02 ± 0.96	–0.87 ± 0.93	0.4
One-third distal radius		–			
BMD (g/cm ²)	0.66 ± 0.19		0.67 ± 0.14	0.62 ± 0.23	0.6
z-score	–0.84 ± 1.31		–0.71 ± 1.34	–1.18 ± 1.27	0.07
→ Nephrolithiasis n (%)	77 (50%)	–	62 (55%)	15 (35.7%)	0.005
→ Clinical fractures n (%)	7 (4.5%)	–	4 (3.5%)	3 (2.6%)	0.5
→ Neuropsychiatric symptoms n (%)	49 (31.8%)	–	41 (36.6%)	8 (19%)	0.04
Low BMD (%)	27 (17.5%)	–	21 (18.7%)	6 (14.2%)	0.5



GENDER DIFFERENCE IN THE CLINICAL PRESENTATION OF PRIMARY HYPERPARATHYROIDISM: INFLUENCE OF MENOPAUSAL STATUS

Elena Castellano, Roberto Attanasio, Alberto Boriano, Micaela Pellegrino, Francesca Garino, Laura Gianotti, and Giorgio Borretta

Table 1. Demographics, biochemical and clinical characteristics of patients

	Whole series (n = 417)	Males (n = 93)	Females (n = 324)	p
Age (years)	61.0 ± 13.2	58.6 ± 14.5	61.7 ± 12.8	0.046
BMI (kg/m ²)	25.3 ± 5	25.7 ± 4.5	25.1 ± 5.2	0.31
Symptomatic (n, %)	210 (50.4%)	58 (62.3%)	152 (47%)	0.016
PTH (ng/L)	135.9 [134.5]	121 [148]	138 [130]	0.783
Total serum calcium (mg/dL)	11.2 ± 1.1	11.2 ± 1.2	11.2 ± 1.1	0.654
Ionized calcium (mmol/L)	1.45 ± 0.2	1.5 ± 0.2	1.4 ± 0.2	0.337
25OH vitamin D (µg/L)	28.5 ± 19.4	27.9 ± 14.3	28.6 ± 20.5	0.758
Vitamin D deficiency (%)	36	29.8	37.5	0.53
Urinary calcium (mg/24h)	257.4 ± 171.1	278.2 ± 195.3	250.3 ± 163.9	0.167
Serum Phosphate (mg/dL)	2.61 ± 0.6	2.37 ± 0.5	2.68 ± 0.6	0.0001
eGFR (mL/min/1.73 m ²)	79.7 ± 22.2	82.9 ± 23.9	78.6 ± 21.6	0.099
Presence of kidney stones (n, %)	155 (37%)	47 (50.5%)	108 (33.3%)	0.003
Presence of osteitis fibrosa cystica (n, %)	87 (20.9%)	20 (21.5%)	67 (20.7%)	0.977
Distal third radius T score	-2.3 ± 1.6	-1.9 ± 1.4	-2.4 ± 1.7	0.001
Lumbar spine T score	-2.4 ± 1.5	-1.7 ± 1.5	-2.6 ± 1.4	0.001
Femoral neck T score	-2.0 ± 1.2	-1.8 ± 1.3	-2.1 ± 1.2	0.013
Osteoporosis at any site (n, %)	202 (48.4%)	33 (35.5%)	169 (52.2%)	0.0066
Positive pre-surgical localization (n, %)	298 (71.5%)	66 (71%)	232 (71.6%)	0.992

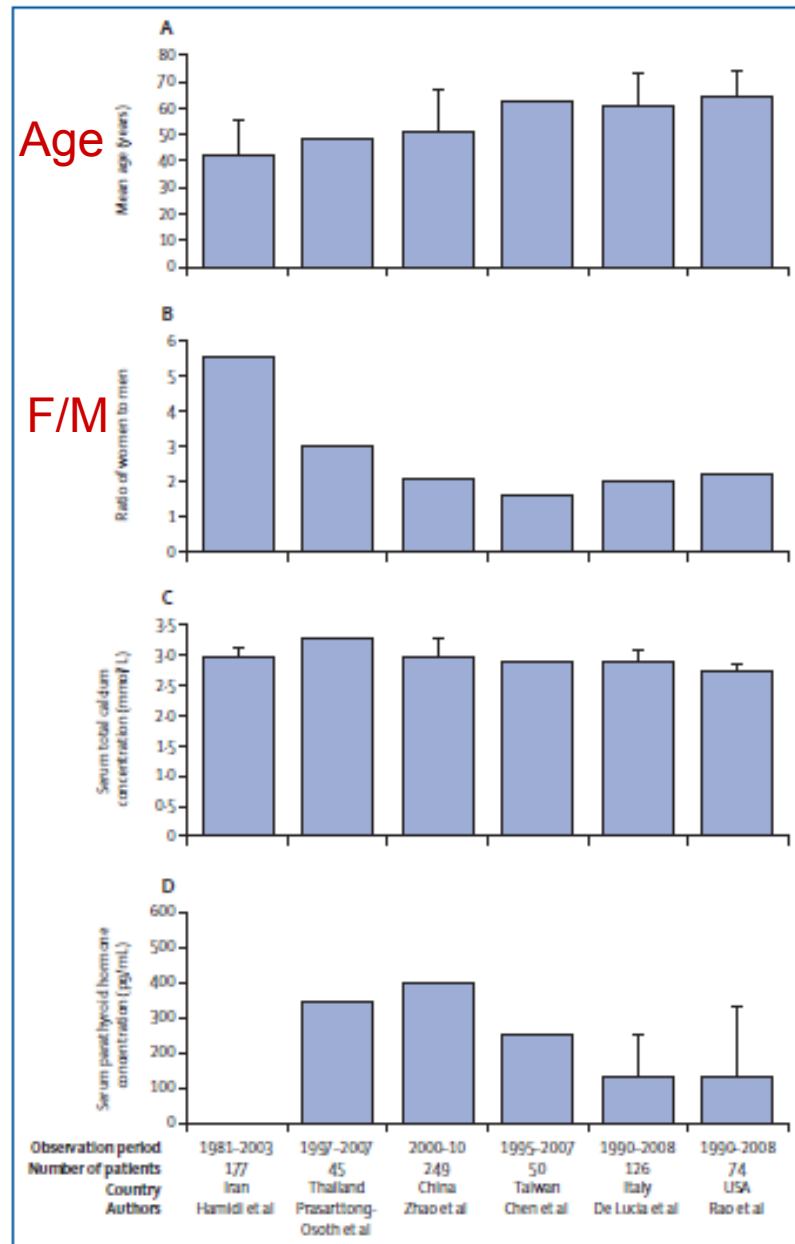
GENDER DIFFERENCE IN THE CLINICAL PRESENTATION OF PRIMARY HYPERPARATHYROIDISM: INFLUENCE OF MENOPAUSAL STATUS

Elena Castellano, Roberto Attanasio, Alberto Boriani, Micaela Pellegrino, Francesca Garino, Laura Gianotti, and Giorgio Borretta

Table 2. Comparison between men and women (according to menopausal state)

	Males (n = 93)	F-pre (n = 54)	F-post (n = 270)	p
Age (years)	58.6 ± 14.5° *	40.5 ± 8*	65.9 ± 8.7	0.001
BMI (kg/m ²)	25.7 ± 4.5°	22.6 ± 5.7*	25.7 ± 4.9	0.0001
Symptomatic (n, %) →	58 (62.3%)*	35 (64.8%)*	117 (43.3%)	0.0005
PTH (ng/L)	121 [148]	126.5 [96.8]	139 [137]	0.955
Total serum calcium (mg/dL)	11.2 ± 1.2	11.2 ± 1	11.2 ± 1.2	0.985
Ionized calcium (mmol/L)	1.5 ± 0.2	1.5 ± 0.2	1.4 ± 0.2	0.639
25OH vitamin D (µg/L)	27.9 ± 14.3	31.8 ± 21.6	28.1 ± 20.3	0.560
Vitamin D deficiency (%)	29.8	30.5	38.9	0.27
Urinary calcium (mg/24h)	278.2 ± 195.3	296 ± 175.4	241.3 ± 160.5	0.080
Serum Phosphate (mg/dL)	2.37 ± 0.5*	2.54 ± 0.6*	2.71 ± 0.6	0.0001
eGFR (mL/min/1.73 m ²)	82.9 ± 23.9*	90.9 ± 22.7*	76.1 ± 20.5	0.0001
Presence of kidney stones (n, %) →	47 (50.5%)*	32 (59.2%)*	76 (28.1%)	0.0001
Presence of osteitis fibrosa cystica (n, %)	20 (21.5%)	7 (12.9%)	60 (22.2%)	0.308
Distal third radius T score	-1.9 ± 1.4° *	-1.1 ± 1.2*	-2.7 ± 1.6	0.0001
Lumbar spine T score	-1.7 ± 1.5*	-1.7 ± 1.3*	-2.7 ± 1.4	0.0001
Femoral neck T score	-1.8 ± 1.3*	-1.5 ± 1.2*	-2.2 ± 1.1	0.0001
Osteoporosis at any site (n, %) →	33 (35.5%)° *	10 (18.5%)*	159 (58.9%)	0.0004
Positive pre-surgical localization (n, %)	66 (71%)	42 (77.7%)	190 (70.4%)	0.544

Explaining geographical variation in the presentation of primary hyperparathyroidism



- **Non modificabili:**
 - Età
 - Fattore geografico
 - Fattore razziale
 - Fattore genetico: polimorfismo CaSR, forme sindromiche
 - Genere
- **Modificabili:**
 - BMI
 - Stile di vita
 - Stato vitaminico D
 - Utilizzo di farmaci (furosemide, litio)
 - SSN

Questioni aperte

- Le manifestazioni aspecifiche o non classiche di malattia (cardiovascolari, metaboliche, neuropsichiatriche)
- PHPT normocalcemico: diversa incidenza dei sintomi classici
- Impatto della terapia chirurgica e farmacologica sulla prognosi delle manifestazioni cliniche di malattia



obrigado

Dank U

Merci

mahalo

Köszö

спасибо

Grazie

Thank
you

mausuru

Takk

Gracias

Dziękuję

Děkuju

danke

Kiitos