Iperparatiroidismo Primario Normocalcemico: Vero o Falso ?

Bari,
7-10 novembre 2013

Definizione ed Epidemiologia

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Diagnosi di Iperparatiroidismo Primario *Ipercalcemico*

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- La diagnosi di iperparatiroidismo primario *ipercalcemico* è biochimica:

We recommend the concomitant determination of total serum calcium and PTH to confirm the diagnosis of PHPT. Correction for serum albumin is recommended.
We suggest using ionized calcium determination when a reliable assay is available.
We recommend evaluation of 25-OH-D status in all patients with PHPT, in order to provide supplementation if deficiency is found.

Si basa sul rilievo ripetuto e concomitante di:

1. Calcemia totale e corretta per albumina (o calcemia ionizzata) aumentata *

+

2. Livelli sierici di PTH aumentati od inappropriatamente normali

* Nel corso della malattia vi può essere sporadicamente il riscontro di normocalcemia

AME Position Statement on PHPT, 2012

Definizione di Iperparatiroidismo Primario *Normocalcemico*

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- L'iperparatiroidismo primario *normocalcemico* è una condizione patologica caratterizzata da un eccesso cronico di secrezione autonoma di PTH a fronte di valori di calcemia totale corretta per albuminemia e ionizzata nella norma.

Definizione di Iperparatiroidismo Primario *Normocalcemico*

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- La diagnosi di iperparatiroidismo primario *normocalcemico* è biochimica:
- Si basa sul rilievo ripetuto, concomitante e persistente di livelli sierici di calcio totale corretto per albuminemia e calcio ionizzato normali e di PTH aumentati
- Devono essere escluse/corrette cause concomitanti di iperparatiroidismo secondario:

Ipovitaminosi D	Livelli di 25 OH vitamina D ≥30 ng/ml
Insufficienza renale cronica	GFR≥60 ml/min
Farmaci (Sali di Litio, Tiazidici)	Sospendere per alcuni mesi
Ipercalciuria	Tiazidici
Malassorbimento Intestinale	Supplementi di calcio e vitamina D

Primary hyperparathyroidism: an evolving view

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Older Construct:

SUBCLINICAL	← CLINICAL →
PHASE 1	PHASE 2

Proposed Construct:

SUBCLINICAL	← CLINICAL →
PHASE 1: PTH High/ Calcium Normal	PHASE 2: PTH High/ Calcium High

SJ Silverberg & JP Bilezikian, J Clin Endocrinol Metab 88: 5348 –5352, 2003

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Un po' di storia…

Linea del tempo

1970

Prima era

- Iperparatiroidismo primario sintomatico: malattia relativamente rara e severa

1990

Seconda era

- Iperparatiroidismo primario asintomatico: malattia comune e lieve

2002

2008

2013

Terza era

- Iperparatiroidismo primario normocalcemico: riconoscimento ufficiale della nuova forma clinica

Incidence of Primary Hyperparathyroidism in Rochester, Minnesota, 1993–2001: An Update on the Changing Epidemiology of the Disease

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TABLE 2. INCIDENCE (PER 100,000 PERSON-YEARS) OF DEFINITE OR POSSIBLE PRIMARY HYPERPARATHYROIDISM AMONG ROCHESTER, MN, RESIDENTS IN 1965–2001

	Men		*Women*		*Both sexes*	
Age groups	*n*	*Incidence*	*n*	*Incidence*	*n*	*Incidence*
1965 to June 1974						
<45	11	6.6	9	4.8	20	5.6
45–54	4	19.4	8	34.0	12	27.2
55–64	1	6.5	15	70.4	16	43.6
65–74	2	20.4	9	53.5	11	41.3
>75	0	0.0	6	42.5	6	29.3
Total	18	9.0*	47	21.4*	65	15.8†
July 1975–1982						
<45	29	17.6	36	19.7	65	18.7
45–54	10	49.0	54	244.4	64	150.6
55–64	18	111.2	70	354.7	88	244.9
65–74	13	132.3	56	327.2	69	256.1
>75	3	44.8	34	198.5	37	155.3
Total	73	41.3*	250	118.6*	323	82.5†
1983–1992						
<45	24	10.4	23	9.5	47	10.0
45–54	8	26.5	30	93.5	38	61.0
55–64	8	36.1	34	135.1	42	88.7
65–74	5	33.2	18	82.7	23	62.5
>75	0	0.0	10	38.0	10	27.4
Total	45	16.1*	115	40.8*	160	29.1†
1993–2001						
<45	19	7.7	15	6.0	34	6.8
45–54	11	27.3	22	50.2	33	39.2
55–64	5	19.9	21	72.4	26	48.0
65–74	3	17.3	22	98.9	25	63.2
>75	4	29.2	14	47.7	18	41.8
Total	42	13.8*	94	28.4*	136	21.6†

RA Wermer et al., J Bone Miner Res 21:171–177, 2006

JOURNAL OF BONE AND MINERAL RESEARCH
Volume 17, Supplement 2, 2002
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Epidemiology of Primary Hyperparathyroidism in Europe

SILVANO ADAMI,[1] CLAUDIO MARCOCCI,[2] and DAVIDE GATTI[1]

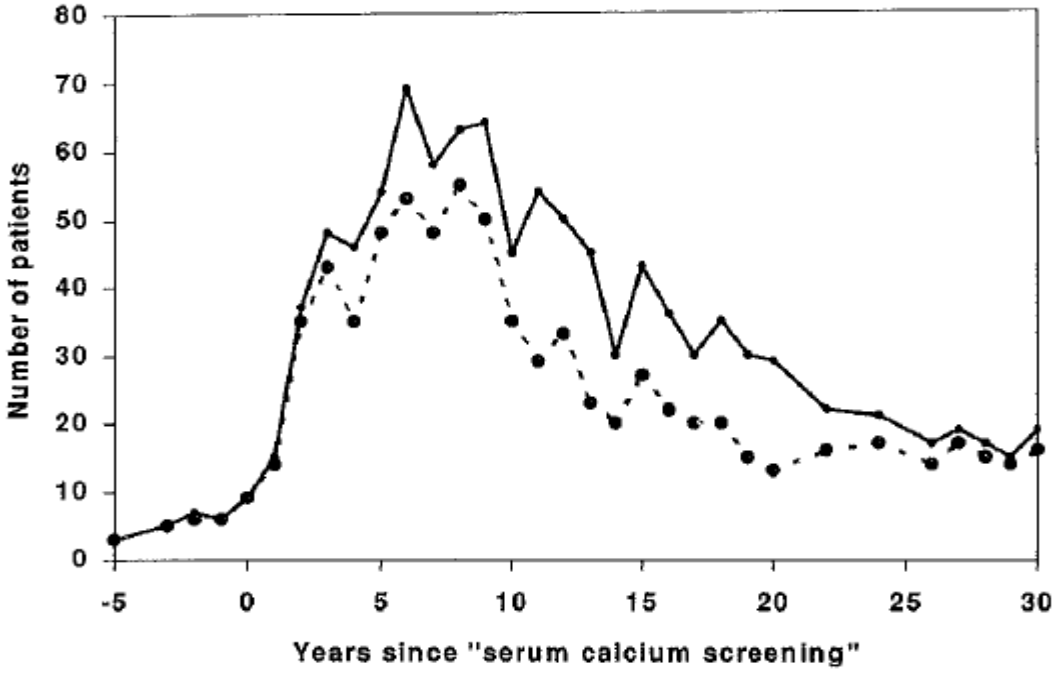

FIG. 3. Number of patients surgically treated for PHPT at the General Hospitals of Verona from 1966 to 2001. The time is reported in relation to the introduction in 1971 of serum calcium in the routine biochemical screening (SMA 12, Technicon, USA). The solid line indicates all patients, and the dotted line are the patients living in the health districts of the Verona region.

Prevalenza di Iperparatiroidismo Primario

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1.0 x1000

CE Boonstra & CE Jackson
Am J Clin Pathol. 55:523-526, 1971

4.3 x1000

T Christensson et al.
Acta Med Scand. 200:131-137, 1976

3.0 x1000 (età >75 aa)

R Jorde et al.,
J Clin Epidemiol. 53:1164-1169, 2000

21.0 x1000 (età >75 aa)

A Sorva et al.,
J Int Med. 231:309-312, 1992

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Population-based screening for primary hyperparathyroidism with serum calcium and parathyroid hormone values in menopausal women

Ewa Lundgren, MD, Jonas Rastad, MD, Erik Thurfjell, MD, Göran Åkerström, MD, *and* Sverker Ljunghall, MD, *Uppsala, Sweden*

N=5202 donne di età compresa tra 55 e 75 aa sottoposte a screening mammografico

Table I. Number of women with hyperparathyroidism and the mean (±SD) blood calcium (mmol/L) and PTH values (ng/L) according to the three applied criteria of biochemical recognition

Biochemical criteria	*Patient no.*	*Calcium*		*PTH*
		Total	*Ionized*	
Total calcium >2.60, PTH ≥25	37	2.72 ± 0.15	1.33 ± 0.08	86.1 ± 54.4
Total calcium 2.50-2.60, PTH ≥35	55	2.54 ± 0.03	1.26 ± 0.04	52.3 ± 15.0
Total calcium <2.50, PTH >55	17	2.42 ± 0.05	1.23 ± 0.04	69.5 ± 10.4
Total women	**109**			

Prevalenza di Iperparatiroidismo Primario=109/5202= 2.1%

Prevalenza di Iperparatiroidismo Primario Normocalcemico=28/5202=0.5%

E Lundgren et al. Surgery, 121:287-294, 1997

Coorti di Pazienti Affetti da Iperparatiroidismo Primario Normocalcemico

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Table 1
Summary of Cohorts With Normocalcemic Primary Hyperparathyroidism Described in the Literature

Study	Cohort size	Age (yr)	Female (%)	Osteoporosis (%)	Nephrolithiasis (%)	Comments
Symptomatic cohorts						
Lowe et al *(25)*	37	58 ± 12	95	57[a]	14	Ionized calcium not available for all
Tordjman et al *(26)*	32	61 ± 11	84	36	9	Six with hypercalciuria not responding to hydrochlorothiazide, 3 with vitamin D deficiency although hyperparathyroidism persisted despite vitamin D repletion
Amaral et al *(27)*	33	64 ± 14	79	15[b]	18	Ionized calcium not measured
Cakir et al *(28)*	18	50 ± 10	47	47	11	Ionized calcium not measured Aim of investigating glucose and lipid metabolism; no differences between patients and age-, sex-, and BMI-matched controls with respect to indicators of insulin resistance
Wade et al *(29)*	8	60	63	25[c]	25	Surgical cohort: Five subjects had single gland disease and 3 multiple glands
Asymptomatic cohort						
Garcia-Martin et al *(31)*	6	56 ± 3	100[d]	0	0	Ionized calcium not measured Population-based cohort

Note: Data are presented as mean ± SD.
Abbr: BMI, body mass index; SD, standard deviation.
[a]Approx 11% of subjects had fragility fracture.
[b]Only fracture history available.
[c]Approx 13% of subjects had fragility fracture.
[d]Study design.

NE Cusano et al., Journal of Clinical Densitometry: Assessment of Skeletal Health 16:33-39, 2013

Prevalenza di Iperparatiroidismo Primario *Normocalcemico*

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Table 2
Prevalence of Normocalcemic Primary Hyperparathyroidism in Various Populations

Study	Population	Prevalence (%)	Comments
Lundgren et al *(32)*	Postmenopausal women aged 55–75 yr, Sweden	0.5	Secondary etiologies of hyperparathyroidism not excluded
Misra et al *(33)*	Men and women older than 45 yr, United States (NHANES)	1	Excluding renal failure (GFR lower than 60 mL/min) and vitamin D deficiency (25-hydroxyvitamin D level lower than 30 ng/dL)
Berger et al *(34)*	Men and women aged 19–97 yr, Canada (CaMos)	16.7	Excluding vitamin D deficiency (25-hydroxyvitamin D level lower than 20 ng/dL)
Garcia-Martin et al *(31)*	Postmenopausal women, Spain	6	Excluding renal disease, vitamin D deficiency (25-hydroxyvitamin D level lower than 30 ng/dL), and malnutrition

Abbr: NHANES, National Health and Nutrition Examination Survey; GFR, *glomerular filtration rate;* CaMos, Canadian Multicentre Osteoporosis Study.

NE Cusano et al., Journal of Clinical Densitometry: Assessment of Skeletal Health 16:33-39, 2013

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7-10 novembre 2013

ORIGINAL ARTICLE

Endocrine Care

Normocalcemic Hyperparathyroidism and Hypoparathyroidism in Two Community-Based Nonreferral Populations

Natalie E. Cusano, Naim M. Maalouf, Patty Y. Wang, Chiyuan Zhang, Serge C. Cremers, Elizabeth M. Haney, Douglas C. Bauer, Eric S. Orwoll, and John P. Bilezikian

J Clin Endocrinol Metab
98: 2734–2741, 2013

Table 1. MrOS: Characteristics of Subjects With Normocalcemic Primary Hyperparathyroidism vs Normal PTH[a]

Parameter	Normocalcemic Primary Hyperparathyroidism (n = 9)	Normal PTH (n = 2224)	*P* Value
Age, y	70.0 ± 6	73.5 ± 6	.04
Height, cm	176.1 ± 11	174.3 ± 7	.90
Weight, kg	88.6 ± 20	83.4 ± 13	.50
BMI, kg/m^2	28.3 ± 3	27.4 ± 4	.49
White, %	8 (88.9)	2031 (91.3)	.56
Serum calcium adjusted for albumin, mg/dL	9.4 ± 0.6	9.3 ± 0.3	.75
Intact PTH, pg/mL[b]	**77.5 ± 13**	**32.5 ± 11**	**<.0001**
Serum phosphorus, mg/dL	3.0 ± 0.5	3.2 ± 0.4	.35
25-Hydroxyvitamin D, ng/mL[c]	25.2 ± 5	26.8 ± 9	.48
Creatinine, mg/dL	1.0 ± 0.1	1.0 ± 0.2	.76
Procollagen I N-terminal propeptide, ng/mL	31.6 ± 6	38.3 ± 25	.72
C-terminal telopeptide, ng/mL	0.4 ± 0.2	0.4 ± 0.2	.74
Tartrate-resistant acid phosphatase 5b, U/L	3.4 ± 0.6	3.2 ± 1.0	.48
SHBG, nmol/L	55.9 ± 22	49.2 ± 20	.42
Testosterone, ng/mL	526.8 ± 302	406.2 ± 171	.47
Free testosterone, ng/mL	9.4 ± 4	7.9 ± 3	.58
Estrogen, pg/mL	24.7 ± 11	22.5 ± 9	.92
Free Estrogen, pg/mL	0.5 ± 0.2	0.5 ± 0.2	.91
Lumbar spine BMD, g/cm^2	1.1 ± 0.1	1.2 ± 0.3	.99
Femoral neck BMD, g/cm^2	0.8 ± 0.1	0.8 ± 0.1	.97
Single-slice integral BMD, average L1L2, g/mL	0.24 ± 0.03	0.21 ± 0.04	.02
Single-slice trabecular BMD, average L1L2, g/mL	0.13 ± 0.02	0.11 ± 0.04	.08
Femoral neck, integral BMD, g/mL	0.28 ± 0.05	0.29 ± 0.06	.75
Femoral neck, trabecular BMD, g/mL	0.09 ± 0.05	0.07 ± 0.05	.46

[a] Results are shown as mean ± SD. Values in bold remain significant with Bonferroni correction.

[b] By definition, PTH was >66 pg/mL in the subjects with normocalcemic primary hyperparathyroidism.

[c] By definition, 25-hydroxyvitamin D was >20 pg/mL in the subjects with normocalcemic primary hyperparathyroidism.

MrOS: epidemiology

2364 men had full data for this analysis.

17 men had hypercalcemic primary hyperparathyroidism (excluded from further analysis) with a prevalence of 0.7%.

We identified among 87 men with elevated PTH and normal albumin-adjusted serum calcium after excluding all common secondary causes of hyperparathyroidism (renal insufficiency, 52 excluded, vitamin D deficiency ,24 excluded, and thiazide diuretic use, 2 excluded) **9 men in whom the presence of normocalcemic primary hyperparathyroidism was established as defined (prevalence 0.4%).**

ORIGINAL ARTICLE

Endocrine Care

J Clin Endocrinol Metab
98: 2734–2741, 2013

Normocalcemic Hyperparathyroidism and Hypoparathyroidism in Two Community-Based Nonreferral Populations

Natalie E. Cusano, Naim M. Maalouf, Patty Y. Wang, Chiyuan Zhang, Serge C. Cremers, Elizabeth M. Haney, Douglas C. Bauer, Eric S. Orwoll, and John P. Bilezikian

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Table 3. DHS: Characteristics of Subjects With Normocalcemic Primary Hyperparathyroidism vs Normal PTH[a]

Parameter	Normocalcemic Primary Hyperparathyroidism (n = 13)	Normal PTH (n = 2659)	*P* Value
Age, y	41.3 ± 12	43.2 ± 10	.37
Female, %	5 (38)	1435 (54)	.28
Height, cm	172.2 ± 9	167.8 ± 10	.12
Weight, kg	86.2 ± 22	84.6 ± 21	.89
BMI, kg/m^2	28.4 ± 8	29.0 ± 7	.48
Ethnicity, %			**.0016**
Black	8	48	
White	85	32	
Native American	8	18	
Asian	0	2	
Serum calcium adjusted for albumin, mg/dL	9.32 ± 0.6	9.37 ± 0.3	.58
Intact PTH, pg/mL[b]	**94.8 ± 46**	**34.3 ± 10**	**<.0001**
Serum phosphorus, mg/dL	3.12 ± 0.6	3.23 ± 0.6	.33
25-Hydroxyvitamin D, ng/mL[c]	**30.1 ± 11**	**19.8 ± 9**	**.0002**
Creatinine, mg/dL	0.93 ± 0.1	0.87 ± 0.2	.09
Osteoprotegerin	1216 ± 280	1305 ± 720	.81
C-terminal telopeptide, ng/mL	0.39 ± 0.2	0.36 ± 0.2	.47

[a] Results are shown as mean ± SD. Values in bold remain significant with Bonferroni correction.

[b] By definition, PTH was >55.0 pg/mL in the subjects with normocalcemic primary hyperparathyroidism.

[c] By definition, 25-hydroxyvitamin D was >20 pg/mL in the subjects with normocalcemic primary hyperparathyroidism.

DHS: epidemiology and natural history

Of the 3450 subjects remaining for this analysis, **20 subjects had hypercalcemic primary hyperparathyroidism (prevalence 0.6%)**.

108 subjects were classified provisionally with **normocalcemic primary hyperparathyroidism (prevalence 3.1%)** after excluding secondary causes of hyperparathyroidism .

Of the 108 subjects who were provisionally identified with normocalcemic primary hyperparathyroidism by their baseline values from the DHS study, 64 had follow-up laboratory data 8 years later.

Hypercalcemic primary hyperparathyroidism developed in 1 individual (1.6% of cohort), and **13** (20%) **continued to show evidence** of **normocalcemic primary hyperparathyroidism (prevalence 0.6% in the total cohort with follow-up data).** Of the remaining subjects 1 developed hypercalcemia in the setting of CKF and thiazide use, 20 maintained evidence of hyperparathyroidism in the setting of CKF, vitamin D deficiency or thiazide use and 29 subjects had normal PTH on follow-up.

Mortality In Mild Primary Hyperparathyroidism

Age and Gender-Adjusted Relative Risk of Death, by Diagnosis, among Rochester, Minnesota Residents with Primary Hyperparathyroidism, Compared with Expected Risk in White Minnesota Residents

Cause of Death	Relative Risk (95% Confidence Interval)
Cancer	0.58 (0.39–0.89)
Cardiovascular disease	0.60 (0.45–0.79)
Respiratory disease	0.97 (0.53–1.63)
Gastrointestinal disease	0.88 (0.29–2.06)
All other causes	1.00 (0.63–1.51)
All causes	0.69 (0.57–0.83)

RA Wermers et al. American Journal of Medicine 2, 115-122, 1998

Mortality In Mild Primary Hyperparathyroidism

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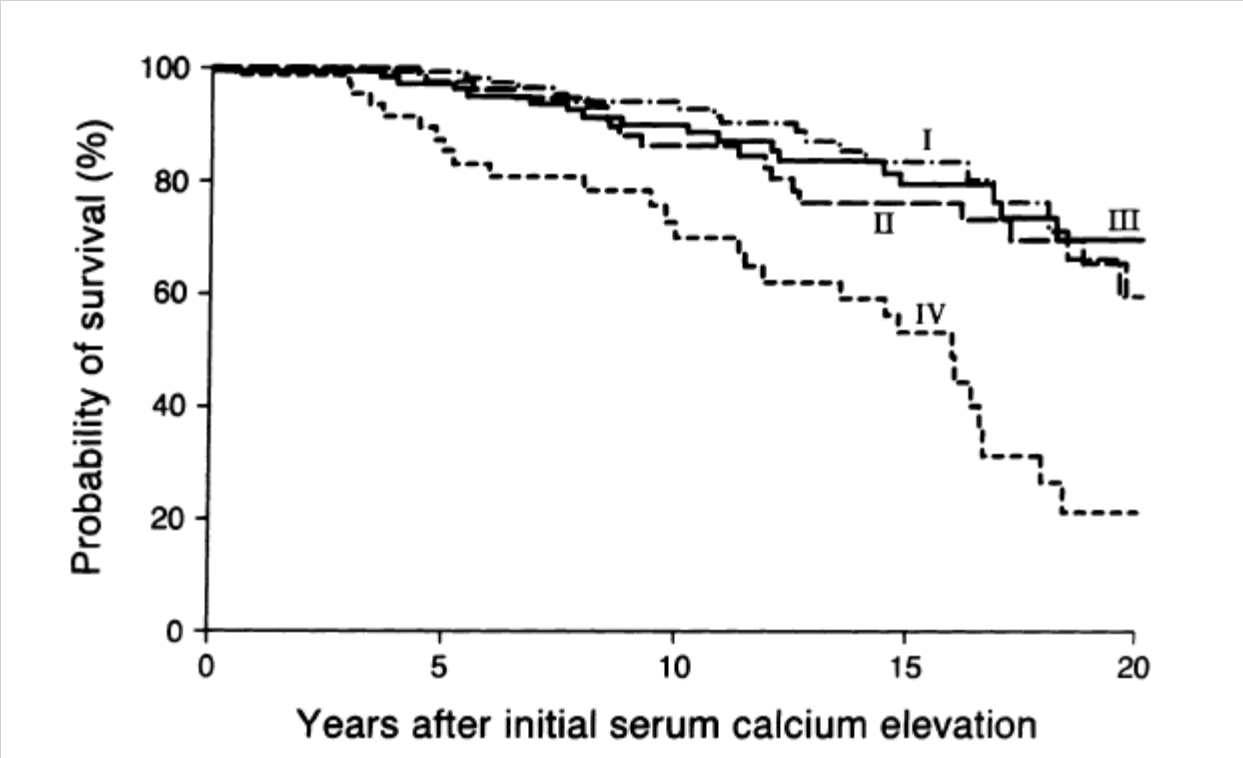

Survival as a function of quartile of serum calcium levels (I = 10.2 to 10.5 mg/dL; II = 10.6 to 10.7 mg/dL; III = 10.8 to 11.1 mg/dL; and IV = 11.2 to 16.0 mg/dL) among Rochester, Minnesota residents with primary hyperparathyroidism. Group IV had significantly reduced survival (*P* , 0.001) compared with the other 3 groups.

RA Wermers et al. American Journal of Medicine 2, 115-122, 1998

Increased mortality and morbidity in mild primary hyperparathyroid patients The Parathyroid Epidemiology and Audit Research Study (PEARS)

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Table 2 The baseline characteristics of mild PHPT patients in comparison with the total PHPT cohort

	Total PHPT	Mild PHPT
Count (%)	2 709 (100%)	1 683 (*62.1* %)
Mean age (SD)	67 (14)	69 (14)
Female (%)	1 918 (70.8%)	1 163 (69.1%)
Baseline Calcium (SD) (mmol/l)	2.63 (0.17)	2.58 (0.09)
PTH (SD) (pmol/l)*	12.5 (13.1)	10.9 (9.8)
Disease duration (SD) (month)+	57 (49)	41 (32)

* The mean of the maximum PTH measurements
+ The duration of the disease diagnosis (in months), measured by subtracting the event date (end of study 31.12.2006, date of death, or PTX date where applicable) from the date of entry (PHPT diagnosis date)

Table 3 Standardised mortality ratios (SMRs) adjusted for age and sex showing the observed and the expected numbers of deaths among mild PHPT patients between 1997 and 2006

Cause of death	Total event	Obs	Exp	SMR	95% CI
All cause	46 221	502	191.8	2.62	2.39-2.86
Cardiovascular	22 214	227	84.8	2.68	2.34-3.05
Cancer	12 390	137	46.4	2.95	2.48-3.49

+ Obs, observed number; ++ Exp, expected number.

N Yu et al. Clinical Endocrinology 73:30-34, 2010

Increased mortality and morbidity in mild primary hyperparathyroid patientsThe Parathyroid Epidemiology and Audit Research Study (PEARS)

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Table 4 Standardised all-cause mortality ratios (SMRs) among mild PHPT patients by diagnosis period (i.e. diagnosed between 1997-2001 and 2002-2006, respectively)

Period of diagnosis	Gender	Incident patients	Mean Calcium*	Obs*	Exp**	SMR	95% CI
1997-2001	Male	218	2.69	89	52.9	1.68	1.33-2.03
	Female	497	2.71	200	145.2	1.38	1.19-1.57
	Total	715	2.70	289	198.2	1.46	1.29-1.63
2002-2006	Male	302	2.67	66	40.0	1.66	1.26-2.07
	Female	666	2.70	147	81.0	1.81	1.52-2.11
	Total	968	2.69	213	120.7	1.76	1.53-2.00

* The mean of the maximum calcium concentration; Obs, observed number; Exp, expected number.

Table 5 Disease specific Standardised Morbidity Ratios (SMRs) adjusted for age and sex showing the observed and the expected number of events by condition.

Observed morbidity endpoints	Total events	Obs	Exp	SMR	95% CI
Cardiovascular disease	23 814	440	259.0	1.70	1.54-1.87
Cerebrovascular disease	9 716	191	118.4	1.61	1.39-1.86
Renal Failure	4 417	444	52.9	8.40	7.64-9.22
Renal Stones	2 278	33	11.9	2.77	1.91-3.90
Psychiatric disease	1 916	44	16.0	2.75	2.00-3.70
Hypertension	8 617	285	91.8	3.10	2.75-3.49
All fractures	15 530	200	149.5	1.34	1.16-1.54
Cancer	25 136	303	252.9	1.20	1.07-1.34
Diabetes	5 633	153	57.9	2.64	2.24-3.09
Glaucoma	957	14	11.6	1.20	0.66-2.02
Parkinson's Disease	2 444	39	28.8	1.35	0.96-1.85

* Obs, Observed number; ** Exp, expected number

N Yu et al. Clinical Endocrinology 73:30-34, 2010

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European Journal of Endocrinology (2006) **155** 33–39 ISSN 0804-4643

CLINICAL STUDY

Metabolic abnormalities in patients with normocalcemic hyperparathyroidism detected at a population-based screening

Emil Hagström[1], Ewa Lundgren[1], Jonas Rastad[1,2] and Per Hellman[1]

[1]Endocrine Unit, Department of Surgical Sciences, Uppsala University, University Hospital, SE-751 85 Uppsala, Sweden and [2]Clinical Science, AstraZeneca R&D, Södertälje, Sweden

Table 1 Baseline characteristics of normocalcemic pHPT cases (n=30) and controls (n=30) at study inclusion.

	pHPT		Controls		
Variable	Mean	s.d.	Mean	s.d.	P^a
Age (years)	66.4	5.6	66.7	5.7	ns
Total S-calcium (mmol/l)	2.50	0.05	2.36	0.07	<0.0001
P-ionized calcium (mmol/l)	1.25	0.03	1.17	0.03	<0.0001
Corrected u-calcium (mmol)	3.34	2.1	2.22	1.6	0.029
S-PTH (ng/l)	47.6	16	29.5	9.7	<0.0001
S-creatinine (μmol/l)	85.3	16	84.5	13	ns
BMI (kg/m^2)	28.5	4.8	26.1	4.3	0.009
S-glucose (mmol/l)	5.29	2.1	4.75	1.2	0.007
S-HbA1c (%)	4.87	1.1	4.73	0.70	ns
S-urate[b] (mmol/l)	338	90	251	60	0.004
S-total-cholesterol (mmol/l)	6.91	1.2	6.83	1.3	ns
S-LDL-cholesterol[b] (mmol/l)	4.82	1.1	5.0	1.0	ns
S-HDL-cholesterol (mmol/l)	1.31	0.31	1.40	0.36	0.013
S-VLDL-cholesterol (mmol/l)	0.62	0.63	0.528	0.46	0.032
S-LDL/HDL-cholesterol	3.92	1.3	3.64	1.2	0.035
S-total triglycerides (mmol/l)	1.93	1.1	1.72	0.88	0.007
S-LDL-triglycerides (mmol/l)	0.58	0.24	0.52	0.18	ns
S-HDL-triglycerides (mmol/l)	0.16	0.07	0.16	0.063	ns
S-VLDL-triglycerides (mmol/l)	1.22	0.96	1.09	0.81	0.007

ns, not significant.
[a]Normocalcemic cases vs matched controls, Wilcoxon's signed ranks test.
[b]Skewed variable, presented as median ± s.d.

European Journal of Endocrinology (2010) **162** 925–933 ISSN 0804-4643

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CLINICAL STUDY

Cardiovascular risk factors and arterial rigidity are similar in asymptomatic normocalcemic and hypercalcemic primary hyperparathyroidism

Karen M Tordjman, Marianna Yaron, Elena Izkhakov, Etty Osher, Galina Shenkerman, Yonit Marcus-Perlman and Naftali Stern

Table 2 Comparison of the frequency of metabolic and cardiovascular abnormalities accompanying a diagnosis of primary hyperparathyroidism (PHPT), and of the pattern of use of medications likely to affect calcium metabolism in both groups of subjects.

Condition	Normocalcemic *n* (%)	Hypercalcemic *n* (%)	*P*
Hypertension	20 (62.5)	50 (61.7)	NS
Hyperlipidemia	10 (31.3)	22 (27.2)	NS
Thyroid dysfunction			
Hypothyroid	4 (12.5)	7 (8.6)	NS
Hyperthyroid	1 (3.1)	3 (3.7)	NS
Diabetes or impaired fasting glucose	6 (19)	26 (32.1)	NS
CVA[a]	0	4 (4.9)	NS
IHD[b]	1 (3.1)	16 (19.8)	0.038
IHD and/or CVA	1 (3.1)	20 (24.7)[c]	0.007
Cardiac dysrhythmia	1 (3.1)	4 (4.9)	NS
Medications			
Thiazide diuretics	5 (15.6)	8 (9.9)	NS
Loop diuretics	0	6 (7.4)	NS
ACEi or/and ARB[d]	12 (37.5)	29 (35.8)	NS
Calcium channel blockers	12 (37.5)	32 (39.5)	NS
β-Blockers	5 (15.6)	20 (24.7)	NS
Calcium supplements	11 (34.4)	1 (1.2)	<0.0001
Vitamin D supplements	14 (43.8)	3 (3.7)	<0.0001

Note that patients received at times more than one medication for the treatment of hypertension or ischemic heart disease. Not detailed in the table, a few patients received α-blockers and spironolactone.
[a]CVA, cerebrovascular accident.
[b]IHD, ischemic heart disease.
[c]In the HC cohort, two patients had both IHD and CVA.
[d]ACEi, angiotensin-converting enzyme inhibitors; ARB, angiotensin receptor blockers.

Conclusioni

Bari,
7-10 novembre 2013

- La definizione di iperparatiroidismo primario normocalcemico (PHPNC) è operativa e si base sul rilievo ripetuto e persistente di valori di calcemia totale corretta per albuminemia e calcio ionizzato normali a fronte di livelli sierici di PTH aumentati dopo esclusione e correzione di eventuali cause di iperparatiroidismo secondario.

- L'epidemiologia di PHPNC è largamente ignota. Dai pochi studi emergono dati di prevalenza discordanti in rapporto a differenti criteri usati per la diagnosi biochimica e differenti campioni di popolazione o casistiche cliniche considerati.
In generale la prevalenza sembra simile a quella dell'iperparatiroidismo primario ipercalcemico. Sebbene non siano noti dati di morbilità e/o mortalità in PHPNC, alcuni studi suggeriscono la presenza di alterazioni metaboliche glicolipidiche in tale forma clinica.

- I pochi dati epidemiologici supportano la visione di PHPNC come una forma incipiente di malattia che può evolvere nella forma ipercalcemica.

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grazie per l'attenzione