



Università
degli Studi
di Ferrara

SERVIZIO SANITARIO REGIONALE
EMILIA-ROMAGNA
Azienda Ospedaliero - Universitaria di Ferrara
Azienda Unità Sanitaria Locale di Ferrara

Iperparatiroidismo Dal sospetto clinico alla terapia Percorso multidisciplinare

Le indicazioni chirurgiche

Dott. Andrea Daniele

Presentazione clinica

REVIEW

JBMR®

Evaluation and Management of Primary Hyperparathyroidism: Summary Statement and Guidelines from the Fifth International Workshop

John P. Bilezikian,¹ Aliya A. Khan,² Shonni J. Silverberg,¹ Ghada El-Hajj Fuleihan,³ Claudio Marcocci,⁴ Salvatore Minisola,⁵ Nancy Perrier,⁶ Antonio Sitges-Serra,⁷ Rajesh V. Thakker,⁸ Gordon Guyatt,⁹ Michael Mannstadt,¹⁰ John T. Potts,¹⁰ Bart L. Clarke,¹¹ and Maria Luisa Brandi,¹² On behalf of the International Workshop on Primary Hyperparathyroidism

2. What are the clinical phenotypes of PHPT?

- 2.1. Symptomatic PHPT: associated with overt skeletal and renal complications that may include osteitis fibrosa cystica and/or fractures, chronic kidney disease, nephrolithiasis and/or nephrocalcinosis
- 2.2. Asymptomatic PHPT: no overt symptoms or signs; typically discovered by biochemical screening. Two forms of asymptomatic PHPT are defined after evaluation:
 - 2.2.1. with target organ involvement
 - 2.2.2. without target organ involvement
- 2.3. Normocalcemic PHPT: Skeletal or renal complications may or may not exist in those whose presentation fits this definition.

Presentazione clinica

IPERPARATIROIDISMO SINTOMATICO



Osteite fibroso-cistica → Dolore osseo



Tumore bruno



Fratture

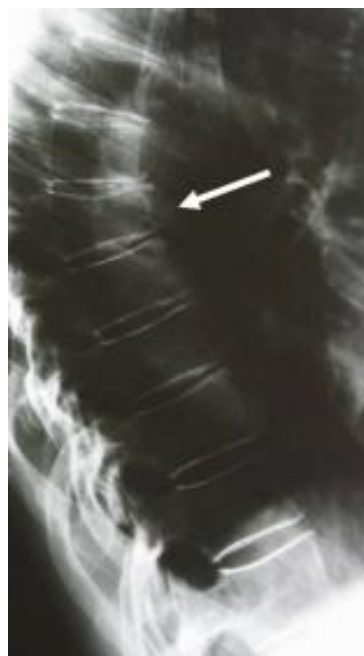


Osteoporosi

Emorragia spontanea
adenoma paratiroideo



Ematoma collo e mediastino



Litiasi renale



Colica renale

Nefrocalcinosi



IRC

Pancreatite

Crisi paratireotossica

Miopatia
prossimale

condrocalcinosi



Presentazione clinica

Neurobehavioural

- Altered mental status*
- Depression and anxiety
- Impaired cognition*
- Reduced quality of life

Renal

- Polyuria
- Nephrolithiasis, nephrocalcinosis
- Impaired renal function

Gastrointestinal

- Anorexia, nausea, vomiting and constipation
- Cholelithiasis
- Pancreatitis
- Peptic ulcer disease



Biochemical abnormalities

- Hypercalcemia
- Hypercalciuria
- Hyperchloremic acidosis
- Hyperuricemia
- Hypophosphatemia

Cardiovascular

- Atherosclerosis
- Cardiac arrhythmias
- CV risk factors (insulin resistance, cholesterol, etc.)
- Hypertension
- Left ventricular hypertrophy
- Vascular stiffness

Skeletal

- Bone pain
- Osteitis fibrosa cystica/brown tumours
- Osteoporosis (fractures)
- Pseudogout

Neuromuscular

- Myopathy
- Impaired neuromuscular function

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A summary of panel recommendations for evaluation

Biochemical:

1. Measure adjusted total serum calcium (ionized if NPHPT is a consideration), phosphorus, intact PTH, 25OHD, creatinine

Skeletal:

2. Three-site DXA (lumbar spine, hip, distal 1/3 radius); imaging for vertebral fractures (VFA or vertebral X-rays). As an adjunctive test, the TBS can be helpful if available.

Renal:

3. eGFR or, preferably, creatinine clearance, full 24-hour urinary calcium. Imaging for nephrolithiasis/nephrocalcinosis. In those with hypercalciuria, a stone risk profile is recommended. In those with stones (an indication for surgery) a stone risk profile is recommended whether or not the patient has hypercalciuria.

A summary of panel recommendations

1. Neurocognitive or neuropsychiatric testing should not be routinely conducted in PHPT.
2. Neurocognitive or neuropsychiatric manifestations, if present, should not be used, by themselves, to recommend parathyroid surgery.
3. More research is needed including further development of a disease-specific quality of life tool.

A summary of panel recommendations

1. Cardiovascular or metabolic evaluations in PHPT are not recommended.
2. Cardiovascular or metabolic abnormalities, if present, are not clearly related to PHPT.
3. Cardiovascular or metabolic abnormalities, if present, should not be used as criteria for decision making vis-à-vis PTX.

A summary of panel recommendations

1. There is no indication for a gastrointestinal evaluation in PHPT
2. If gastrointestinal manifestations are present, they are not clearly linked to PHPT, unless the patient has the symptomatic form of the disease, or MEN with Zollinger Ellison syndrome.

Indicazioni chirurgiche

IPERPARATIROIDISMO SINTOMATICO

JAMA Surgery | Special Communication

The American Association of Endocrine Surgeons Guidelines for Definitive Management of Primary Hyperparathyroidism

Scott M. Wilhelm, MD; Tracy S. Wang, MD, MPH; Daniel T. Ruan, MD; James A. Lee, MD; Sylvia L. Asa, MD, PhD; Quan-Yang Duh, MD; Gerard M. Doherty, MD; Miguel F. Herrera, MD, PhD; Janice L. Pasieka, MD; Nancy D. Perrier, MD; Shonni J. Silverberg, MD; Carmen C. Solórzano, MD; Cord Sturgeon, MD; Mitchell E. Tublin, MD; Robert Udelsman, MD, MBA; Sally E. Carty, MD

- **Recommendation 3-1:** Parathyroidectomy is indicated, and is the preferred treatment, for all patients with symptomatic pHPT (strong recommendation; high-quality evidence).

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ORIGINAL ARTICLE



A summary of panel recommendations for surgical management of PHPT

1. Symptomatic PHPT: all symptomatic patients should be offered parathyroid surgery unless medically contraindicated.

Management of surgical diseases of Primary Hyperparathyroidism: indications of the United Italian Society of Endocrine Surgery (SIUEC)

Paolo Del Rio^{1,12} · Marco Boniardi^{12,2} · Loredana De Pasquale^{12,3} · Giovanni Docimo^{12,4} · Maurizio Iacobone^{12,5} · Gabriele Materazzi^{12,6} · Fabio Medas^{12,7} · Michele Minuto^{12,8} · Barbara Mullineris^{12,9} · Andrea Polistena^{10,12} · Marco Raffaelli^{11,12} · Pietro Giorgio Calò^{12,7}

– Indications for parathyroidectomy (PTx):

- symptomatic primary hyperparathyroidism;

AAES 2016

FIW2022

SIUEC 2024

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Dopo PTX

- aumenta BMD correlato a età, severità IP e funzione renale
- riduzione incidenza nefrolitiasi e coliche renali
- riduzione declino eGFR
- riduzione insulino-resistenza e glicemia
- riduzione pressione arteriosa, reversibilità disfunzione diastolica
- riduzione disturbi aritmici e normalizzazione QT
- miglioramento di alcuni aspetti cognitivi, ansia, depressione
- miglioramento di alcuni domini QoL

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- Guarigione 97.8%
- aumento significativo BMD
- nessuna conclusione su riduzione rischio fratturativo, miglioramento QoL, riduzione incidenza calcoli renali e miglioramento funzionalità renale

Dopo PTX

Table 1. Trials Included in Systematic Review of Parathyroid Surgery⁽⁷⁾

Categories of subjects	[Calcium] (mg/dL)	[PTH] (pg/mL)	Urinary Ca (mg/day)	Conclusions of all systematic reviews (both rows)	References
No surgical criteria	10.3 ± 0.46	105 ± 38	239 ± 104	Surgery results in biochemical cure; patients are not cured if they do not undergo surgery.	Ambrogini and colleagues ⁽¹⁵³⁾ ; Morris and colleagues ⁽¹⁵⁸⁾ ; Perrier and colleagues ⁽¹⁴⁵⁾ ; Rao and colleagues ⁽¹⁵²⁾
Asymptomatic with or without surgical criteria	10.9 ± 0.38	92 ± 31	264 ± 121	Surgery increases BMD See text and systematic review ⁽⁷⁾ for more details	Almqvist and colleagues ^(155,156) ; Ejlsmark-Svensson and colleagues ⁽¹⁵⁷⁾ ; Lundstam and colleagues ⁽¹⁰³⁾ ; Pretorius and colleagues ⁽¹⁴⁵⁾ ; Persson and colleagues ⁽¹⁵¹⁾ ; Ambrogini and colleagues ⁽¹⁵³⁾ ; Bollerslev and colleagues ⁽²²⁰⁾ ; Lundstam and colleagues ⁽¹⁵⁹⁾ .

The Efficacy and Safety of Medical and Surgical Therapy in Patients With Primary Hyperparathyroidism: A Systematic Review and Meta-Analysis of Randomized Controlled Trials

Zhikang Ye,¹ Shonni J. Silverberg,² Ashwini Sreekanta,¹ Kyle Tong,³ Ying Wang,¹ Yaping Chang,¹ Mengmeng Zhang,¹ Gordon Guyatt,¹ Wimonchat Tangamornsuksun,^{1,4} Yi Zhang,^{5,6} Veena Manja,⁷ Layla Bakaa,⁸ Rachel J. Couban,⁹ Maria Luisa Brandi,¹⁰ Bart Clarke,¹¹ Aliya A. Khan,¹² Michael Mannstadt,¹³ and John P. Bilezikian²

- Cura biochimica 96.1%
- Aumento significativo della BMD

Dopo PTX

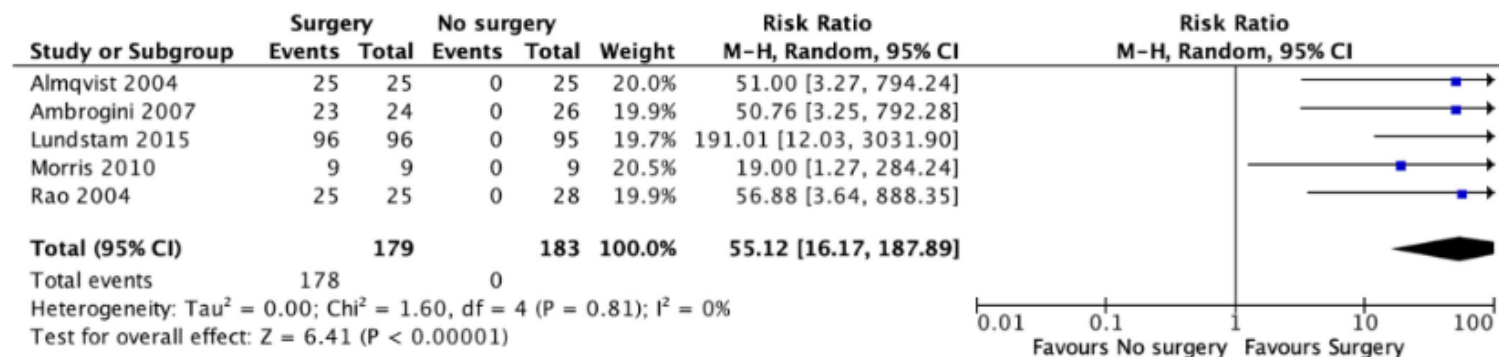


Fig. 9. Effects of surgery on biochemical cure in asymptomatic patients with asymptomatic primary hyperparathyroidism patients.

Table 10. Effect of Surgery on Bone Mineral Density by DXA in Primary Hyperparathyroidism

Site	Lumbar spine	Femoral neck	Total hip	1/3 radius
Mean difference	4.82 (2.55 to 7.09) ^a	3.18 (−0.95 to 7.31) ^a	4.41 (2.62 to 6.20) ^a	0.28 (−1.25 to 9.58) ^b −1.47 (−10.13 to 7.19) ^c
Trial ^c	4	3	2	2 ^b ; 1 ^c
Patient ^c	258	208	103	136 ^b ; 53 ^c

Data presented as MDs with 95% CIs.
 DXA = dual-energy X-ray absorptiometry.
^aAt 2–5 years.
^bAt 1–5 years.
^cAt 2 years.

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Dopo PTX

Nessuna evidenza convincente che supporti l'effetto della chirurgia su fratture, QoL, sviluppo di calcoli renali e funzionalità renale

Outcomes (duration of follow-up in studies)	Relative effects and/or MD (95% CI); number of patients and trials	Absolute effect estimates (10 years)		Quality of evidence	Plain language summary
		Baseline risk for control group	Difference (95% CI)		
Biochemical cure (0.5 to 5 years)	316 patients in five trials	0	96.1% (92.1% to 98.4%)	High	Surgery results in a very high rate of biochemical cure; cure does not occur in patients who do not undergo surgery
Vertebral fracture (1 to 5 years)	RR 0.18 (0.02 to 1.48); 156 patients in two trials	Not applicable	−7% (−13% to −1%)*	Very low (serious risk of bias and very serious imprecision)	We are very uncertain of the effect of surgery on vertebral fracture
Nonvertebral fracture (2 to 5 years)	RR 0.81 (0.19 to 3.44); 159 patients in two trials	Not applicable	−1% (−6% to 5%)*	Very low (serious risk of bias and very serious imprecision)	We are very uncertain of the effect of surgery on non-vertebral fracture
Quality of life (1 to 10 years)	225 patients in three trials	Not applicable	Social functioning CI excluded no effect, other seven domains CI included both benefit and harm	All domains rated down for risk of bias and imprecision, some domains rated down twice for imprecision	We are very uncertain of the effect of surgery on Quality of Life.
Kidney stone (1 to 5 years)	RR 0.55 (0.10 to 3.10); 248 patients in three trials		−1% (−4% to 3%)*	Very low (serious risk of bias and very serious imprecision)	We are very uncertain of the effect of surgery on kidney stones
Renal failure (2 years)	RR not estimable; 53 patients in one trial	0	0 (−7%, 7%)*	Low (very serious imprecision)	Surgery may have a small or no effect on renal failure
Surgical complications (1 year)	RR not estimable; 50 patients in one trial	0	0 (−7%, 7%)*	Low (very serious imprecision)	Surgical complications may be very rare

GRADE = Grading of Recommendations, Assessment, Development, and Evaluation; MD = mean difference; RR = risk ratio.

*We calculated the risk difference directly in Revman.

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Indicazioni chirurgiche IPERPARATIROIDISMO ASINTOMATICO

A summary of panel recommendations for surgical management of PHPT

1. Symptomatic PHPT: all symptomatic patients should be offered parathyroid surgery unless medically contraindicated.
2. Asymptomatic PHPT
 - A. Serum calcium >1 mg/dL (0.25 mmol/L) above the upper limit of normal
 - B. Skeletal involvement:
 - a. A fracture by VFA or vertebral X-ray or
 - b. BMD by T-score ≤ -2.5 at any site or
 - C. Renal involvement:
 - a. eGFR or creatinine clearance <60 mL/min or
 - b. Nephrocalcinosis or nephrolithiasis by X-ray, ultrasound, or other imaging modality or
 - c. Urinary calcium excretion: hypercalciuria (eg, >250 mg/day in women; >300 mg/day in men).

- D. Age <50 years (no other indications are necessary; age <50 years is a sufficient indication)
- E. If no aforementioned guidelines are met, PTX is still an option with concurrence of the patient and physician and if there are no contraindications

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Indicazioni chirurgiche

IPERPARATIROIDISMO ASINTOMATICO

Parameter	1990	2002	2008	2013	2022
Serum Calcium (>upper limit of normal)	1–1.6 mg/dL (0.25–0.4 mmol/L)	1.0 mg/dL (0.25 mmol/L)	1.0 mg/dL (0.25 mmol/L)	1.0 mg/dL (0.25 mmol/L)	1.0 mg/dL (0.25 mmol/L)
Skeletal	BMD by DXA: Z-score < –2.0 (site unspecified)	BMD by DXA: T-score < –2.5 at any site	BMD by DXA: T-score < –2.5 at any site Previous fragility fracture	a. BMD by DXA: T-score < –2.5 at lumbar spine, total hip, femoral neck or distal 1/3 radius b. Vertebral fracture by X-ray, CT, MRI, or VFA	a. BMD by DXA: T-score < –2.5 at lumbar spine, total hip, femoral neck or distal 1/3 radius* b. Vertebral fracture by X-ray, CT, MRI or VFA
Renal	a. eGFR reduced by >30% from expected. b. 24-Hour urine for calcium >400 mg/day (>10 mmol/day)	a. eGFR reduced by >30% from expected b. 24-Hour urine for calcium >400 mg/day (>10 mmol/day)	a. eGFR <60 cc/min b. 24-Hour urine for calcium not recommended	a. eGFR <60 cc/min b. 24-hour urine for calcium >400 mg/day (>10 mmol/day) and increased stone risk by biochemical stone risk analysis c. Presence of nephrolithiasis or nephrocalcinosis by X-ray, ultrasound, or CT	a. eGFR <60 cc/min** b. Complete 24-hour urine for calcium >250 mg/day in women (>6.25 mmol/day) or > 300 mg/day in men (>7.5 mmol/day) c. Presence of nephrolithiasis or nephrocalcinosis by X-ray, ultrasound, or CT
Age	<50 years	<50 years	<50 years	<50 years	<50 years

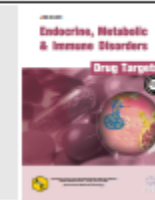


Indicazioni chirurgiche



GUIDELINES

Italian Guidelines for the Management of Sporadic Primary Hyperparathyroidism



Qualità delle prove	Raccomandazione 1	Forza della raccomandazione
Bassa	Nel soggetto adulto/anziano (escluse donne in gravidanza), con diagnosi di iperparatiroidismo primario sporadico sintomatico oppure nel paziente con almeno uno dei seguenti criteri: • calcemia > 1 mg/dL rispetto ai limiti superiori della norma del laboratorio, • escrezione urinaria di calcio > 4 mg/kg/die, • osteoporosi rilevata con densitometria eseguita in uno qualunque dei tre siti abitualmente indagati (rachide lombare, femore e radio) e/o frattura da fragilità, • riduzione della funzione renale ($GFR < 60$ mL/min), • nefrolitiasi clinica o silente, • età ≤ 50 anni, il panel raccomanda l'intervento di paratiroidectomia rispetto a una strategia di sorveglianza o alla terapia farmacologica. Nota. Nei soggetti in cui non sono soddisfatti i criteri per la chirurgia o che per qualsiasi altro motivo non sono stati sottoposti a paratiroidectomia, il panel suggerisce il monitoraggio e trattamento delle eventuali comorbidità/complicanze (ossee, renali, cardio-vascolari, ecc) con provvedimenti <i>ad hoc</i>.	Forte a favore dell'intervento (paratiroidectomia)

8. La paratiroidectomia è sempre appropriata in assenza di controindicazioni, tenendo conto delle comorbidità e dell'aspettativa di vita del paziente.

Indicazioni chirurgiche

IUPERPARATIROIDISMO ASINTOMATICO

AAES 2016

- **Recommendation 3-2:** Parathyroidectomy is indicated when the serum calcium level is greater than 1 mg/dL above normal, regardless of whether objective symptoms are present or absent (strong recommendation; low-quality evidence).
- **Recommendation 3-3:** Parathyroidectomy is indicated for objective evidence of renal involvement, including silent nephrolithiasis on renal imaging, nephrocalcinosis, hypercalciuria (24-hour urine calcium level >400 mg/dL) with increased stone risk, or impaired renal function (glomerular filtration rate <60 mL/min) (weak recommendation; low-quality evidence).
- **Recommendation 3-4:** Parathyroidectomy is indicated in patients with pHPT and osteoporosis, fragility fracture, or evidence of vertebral compression fracture on spine imaging (strong recommendation; high-quality evidence).
- **Recommendation 3-5:** Parathyroidectomy is indicated when pHPT is diagnosed at 50 years or younger regardless of whether objective or subjective features are present or absent (strong recommendation; moderate-quality evidence).
- **Recommendation 3-6:** Parathyroidectomy is indicated when the clinical or biochemical evidence is consistent with PCA (strong recommendation; high-quality evidence).
- **Recommendation 3-7:** Parathyroidectomy is the preferred treatment for patients who are unable or unwilling to comply with observation protocols (strong recommendation; low-quality evidence).
- **Recommendation 3-8:** Parathyroidectomy is recommended for patients with neurocognitive and/or neuropsychiatric symptoms that are attributable to pHPT (strong recommendation; low-quality evidence).
- **Recommendation 3-9:** Parathyroidectomy may be offered to surgical candidates with cardiovascular disease who might benefit from mitigation of potential cardiovascular sequelae other than hypertension (weak recommendation; low-quality evidence).

Indicazioni chirurgiche

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In selected cases of asymptomatic HPT I (with difficult follow-up, when the patient appears to be willing to solve the problem even though the criteria are not met), PTx may be considered even in the absence of at least one of the aforementioned criteria, if only one parathyroid gland is suspected to be affected based on preoperative localization studies (ultrasound or scintigraphy) [5].

Surgical indications for pHPT

– Indications for parathyroidectomy (PTx):

- symptomatic primary hyperparathyroidism;
- asymptomatic primary hyperparathyroidism with at least one of the following conditions [3, 25]:
 - serum calcium levels: 1.0 mg/dL above the upper limit of normal;
 - creatinine clearance < 60 cc/min;
 - bone mineral density: T score < -2.5 at the 3 measurement sites (lumbar spine, femur, and 1/3 distal radius)/prior fragility fracture;
 - age < 50 years.



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Quale chirurgia?

Singola paratiroide patologica

- Chirurgia mini-invasiva (quando c'è localizzazione preoperatoria e concordanza tra ecografia e imaging mediconucleare):
 - Open (Open Minimally Invasive Parathyroidectomy) con dosaggio PTH intraoperatorio
 - Radioguidata (Minimally Invasive Radio-guided Parathyroidectomy)
 - Video-assistita (Minimally Invasive Video-Assisted Parathyroidectomy) con dosaggio PTH intraoperatorio
 - Endoscopica con approccio mediano o laterale e dosaggio del PTH intraoperatorio
- Chirurgia tradizionale con esplorazione di tutte e 4 le paratiroidi
- RAP (remote access parathyroidectomy) con possibile approccio endoscopico o robotico transascellare, toracico anteriore, transorale o retroauricolare o una combinazione di questi.

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- **Recommendation 7-1:** Defined as a focused dissection, MIP is ideally used in patients who appear clinically and by imaging to have a single parathyroid adenoma. It is not routinely recommended in patients with known or suspected high risk of MGD (strong recommendation; high-quality evidence).



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Quale chirurgia? Patologia multighiandolare

Esplorazione di tutte e 4 le paratiroidi con tecnica convenzionale o videoassistita in mani esperte

JAMA Surgery | Special Communication

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Recommendation 8-2: Planned BE is the preferred operative strategy in situations of discordant or nonlocalizing preoperative imaging, when there is a high suspicion of MGD, when IPM is not available, or at the discretion of the surgeon (strong recommendation; moderate-quality evidence).

Ausili Chirurgici

Dosaggio PTH
intraoperatorio

Parathyroid Fluorescence Indocyanine
green (ICG) fluorescence and near-infrared
autofluorescence

Carcinoma paratiroideo

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ORIGINAL ARTICLE



Management of surgical diseases of Primary Hyperparathyroidism: indications of the United Italian Society of Endocrine Surgery (SIUEC)

Paolo Del Rio^{1,12} · Marco Boniardi^{12,2} · Loredana De Pasquale^{12,3} · Giovanni Docimo^{12,4} · Maurizio Iacobone^{12,5} · Gabriele Materazzi^{12,6} · Fabio Medas^{12,7} · Michele Minuto^{12,8} · Barbara Mullineris^{12,9} · Andrea Polistena^{10,12} · Marco Raffaelli^{11,12} · Pietro Giorgio Calò^{12,7}

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The American Association of Endocrine Surgeons Guidelines for Definitive Management of Primary Hyperparathyroidism

Scott M. Wilhelm, MD; Tracy S. Wang, MD, MPH; Daniel T. Ruan, MD; James A. Lee, MD; Sylvia L. Asa, MD, PhD; Quan-Yang Duh, MD; Gerard M. Doherty, MD; Miguel F. Herrera, MD, PhD; Janice L. Pasieka, MD; Nancy D. Perrier, MD; Shonni J. Silverberg, MD; Carmen C. Solórzano, MD; Cord Sturgeon, MD; Mitchell E. Tublin, MD; Robert Udelsman, MD, MBA; Sally E. Carty, MD

Parathyroid carcinoma Parathyroid carcinoma is a rare disease that should be suspected in the presence of substantially increased serum calcium and PTH levels. It must be treated surgically, with removal of the tumour and the surrounding structures: thyroid lobe, ipsilateral parathyroid gland, and ipsilateral central compartment lymph node dissection [42], despite recent findings have somehow questioned the utility of lymph node dissection in every case [43, 44].

- **Recommendation 12-2:** With intraoperative suspicion of parathyroid carcinoma, complete resection avoiding capsular disruption improves the likelihood of cure and may require en bloc resection of adherent tissues (strong recommendation; low-quality evidence).
- **Recommendation 12-3:** Prophylactic central or lateral neck dissection should not be performed for parathyroid carcinoma (insufficient evidence).

Evaluation and Management of Primary Hyperparathyroidism: Summary Statement and Guidelines from the Fifth International Workshop

John P. Bilezikian,¹ Aliya A. Khan,² Shonni J. Silverberg,¹ Ghada El-Hajj Fuleihan,³ Claudio Marcocci,⁴ Salvatore Minisola,⁵ Nancy Perrier,⁶ Antonio Sitges-Serra,⁷ Rajesh V. Thakker,⁸ Gordon Guyatt,⁹ Michael Mannstadt,¹⁰ John T. Potts,¹⁰ Bart L. Clarke,¹¹ and Maria Luisa Brandi,¹² On behalf of the International Workshop on Primary Hyperparathyroidism

Forme genetiche

- 1. If the diagnosis is the hyperparathyroidism jaw tumor (HPT-JT) syndrome, early parathyroidectomy (bilateral exploration) is indicated because of the increased risk of parathyroid carcinoma.
- 2. If the diagnosis is multiple endocrine neoplasia type 1 (MEN1) or MEN2, a bilateral neck exploration is needed. Selective parathyroidectomy is contraindicated because of the presence of multiglandular disease in these patients.
- 3. In patients whose genetic testing reveals hypocalciuric hypercalcemia (FHH), surgery is contraindicated in most cases.
- 4. Genetic testing helps to identify family members who may or may not be at risk. Genetic counseling and evaluation, thus, should be considered for patients <30 years with PHPT, those with multigland disease by history or imaging, those with a family history of hypercalcemia or syndromic diseases such as MEN1, MEN2A, MEN4, or HPT-JT syndrome,^(3,71) and in patients with atypical parathyroid adenoma and parathyroid carcinoma.^(58,59)

MEN1	Autosomal dominant	<i>MEN1</i>	PHPT (95%); pancreatic islet tumors (40%); anterior pituitary adenomas (30%); additional features: adrenocorticoid or carcinoid tumors, lipomas, cutaneous angiofibromas and collagenomas
MEN2a (or MEN2)	Autosomal dominant	<i>RET</i>	PHPT (20%); Medullary thyroid carcinomas (99%); pheochromocytomas (50%).
MEN4	Autosomal dominant	<i>CDKN1B</i>	PHPT (~80%), anterior pituitary tumors (~40%), pancreatic neuroendocrine tumors; other features: adrenal, thyroid, gonadal and renal tumors
HPT-JT	Autosomal dominant	<i>CDC73</i>	PHPT with a high prevalence of parathyroid carcinomas (15%); ossifying fibromas of the mandible and maxilla; renal and uterine tumors.
FIHP	Autosomal dominant	<i>MEN1, CDC73, CASR, GCM2, CDKN1B</i>	Isolated PHPT
NSHPT	Autosomal recessive or dominant	<i>CASR</i>	Severe neonatal PHPT
FHH	Autosomal dominant	<i>CASR, GNA11, AP2S1</i>	Mild PTH-dependent hypercalcemia, associated with low concentration of urinary calcium

Forme genetiche

SIUEC 2024

MEN1

1° scelta: Paratiroidectomia subtotale

2° scelta: paratiroidectomia totale con autotrapianto e criopreservazione.

Il legamento tireotimico e residui timici devono essere rimossi per il rischio di paratiroidi soprannumerarie

MEN2A

Esplorazione di tutte le paratiroidi con asportazione limitata a quelle patologiche/ingrandite

MEN4

Come MEN 1

HPT-JT

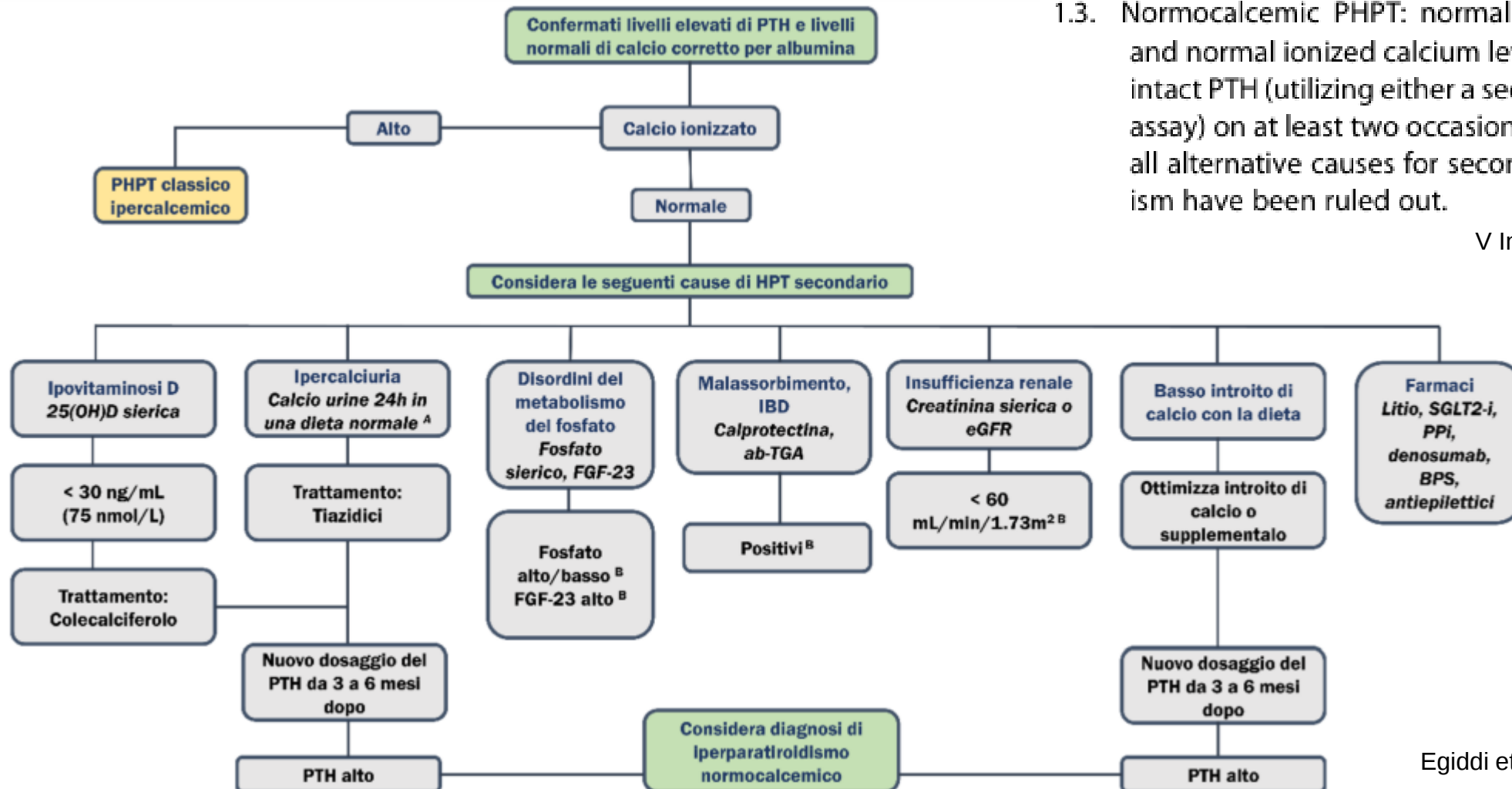
Approccio chirurgico dibattuto.

Inizialmente proposta paratiroidectomia totale o subtotale

Attualmente chirurgia selettiva della paratiroide patologica

Se sospetto di Carcinoma seguire indicazioni specifiche

Iperparatiroidismo primario normocalcémico



1.3. Normocalcemic PHPT: normal adjusted total calcium and normal ionized calcium levels along with elevated intact PTH (utilizing either a second or third generation assay) on at least two occasions over 3–6 months after all alternative causes for secondary hyperparathyroidism have been ruled out.

V International Workshop 2022

Iperparatiroidismo primario normocalcemico

Tabella 1 Frequenza delle complicanze classiche nelle maggiori coorti di riferimento con NHPT

STUDIO	Dimensioni coorte, n	Età, anni (media $\pm$ DS)	Femmine, %	Osteoporosi, %	Nefrolitiasi, %
Palermo et al. [11]	47	63,8 (9,3)	91	–	13
Silverberg et al. [12]	22	57 (10)	91	45	14
Amaral et al. [13]	70	63,67 (13,83)	78,8	–	18,2
Cakir et al. [14]	18	49,9 (2,4)	88,8	47	11,1
Siprova et al. [15]	187	61,1	80,7	–	4
Marques et al. [16]	14	60,6 (14,8)	100	35,7	28,6
Tordjman et al. [17]	32	60,5 (10,5)	84	46	9,3
Lowe et al. [18]	37	58 (2)	94,6	57	14
Koumakis et al. [19]	60	64 (10)	95	86,7	13,3
Maruani et al. [20]	21	52 (10)	71,4	–	35
Wade et al. [21]	93	60	63	25	25

Tabella 2 Riassunto delle evidenze principali emerse dagli studi che hanno valutato le complicanze non classiche dell'NHPT. Adattata da [4]

Complicanze non classiche NHPT	Possibile spiegazione
Iperensione arteriosa	Il recettore 1 del PTH espresso sulle cellule dei vasi potrebbe aumentare il tono vascolare e, quindi, la resistenza vascolare portando a un aumento della pressione arteriosa
Iperaldosteronismo	C'è una correlazione diretta tra i livelli PTH quelli di aldosterone, per una diretta stimolazione delle ghiandole surrenali da parte del PTH
Patologie cardiovascolari	Alti livelli di PTH sono stati associati con complicanze cardiovascolari ma la paratiroidectomia non ha ancora dimostrato di ridurre la comorbidità cardiovascolare
Controllo glicemico	Aumentati livelli di PTH sono stati associati con insulino-resistenza e iperglicemia [22]. La paratiroidectomia è associata a un miglioramento della HbA1c ma sembra migliorare i livelli ematici di glucosio
Qualità della vita	La qualità della vita potrebbe essere ridotta nel NHPT sebbene le evidenze (più forti) in PHPT lasciano pensare che la riduzione di qualità di vita sia in parte dovuta all'alterazione dei livelli di calcio
Funzione muscolare	La forza e la lunghezza muscolare sono ridotti nei pazienti con NHPT rispetto a controlli sani

- Assenza di chiaro coinvolgimento scheletrico
- Aumentato rischio di litiasi renale
- associazione tra eccesso di PTH e ipertensione, morbidità cardiovascolare, omeostasi glucidica e qualità della vita

Iperparatiroidismo primario normocalcemico

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How should normocalcemic PHPT be managed? Panel recommendations

8.1. Because of limited data, we cannot recommend guidelines for surgery in normocalcemic PHPT at this time.

- Più alta prevalenza di patologia multighiandolare
- Paratiroidi di piccole dimensioni
- Più difficili da localizzare
- Maggior rischio di persistenza dopo paratiroidectomia
- Necessità di esplorazione bilaterale del collo
- Pochi studi a lungo termine per valutare efficacia paratiroidectomia su complicanze
- Paratiroidectomia dovrebbe raramente essere proposta
- Approccio caso per caso.

In gravidanza....

COMPLICANZE MATERNE

Nefrolitiasi

Fratture da fragilità

Pancreatite

Infezioni urinarie

Preeclampsia

Crisi paratireotossica

COMPLICANZE FETALI

Ipocalcemia

Prematurità

Ritardo di crescita intrauterina

Basso peso alla nascita

Aborto e natimortalità



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Panel recommendations for management of PHPT during pregnancy (unGRADEd)

1. Mild cases should be managed with hydration and monitoring of calcium levels
2. Bisphosphonates and denosumab should not be used
3. Data are very limited on use of cinacalcet
4. Consider surgery in the second trimester for patients with serum calcium >1 mg/dL (>0.25 mmol/L) above the upper limits of normal and for whom surgery is not contraindicated
5. Preoperative imaging should be limited to ultrasound
6. If surgery is deferred, the neonate should be closely monitored for hypocalcemia
7. If surgery is deferred, PTX should be done after delivery, and before a subsequent pregnancy

In gravidanza....



Sospetto carcinoma

Volontà del paziente

Comorbidità

Persistenza dopo paratiroidectomia

Scarsa compliance del
paziente al follow up

Singola paratiroide patologica

ENDOCRINOLOGO

MEDICO NUCLEARE

Discussione multidisciplinare

CHIRURGO

Patologia
multighiandolare

RADIOLOGO

Età

Mancata localizzazione

Criteri chirurgici

Genetica

Iperparatiroidismo
normocalcemico



**GRAZIE
PER
L'ATTENZIONE**