

Donna di 37 anni, XIV settimana di gravidanza, con riscontro di TSH= 2.8 mIU/L e nodulo tiroideo di 7 mm, ipoecogeno.

Consigliereste:

- 1. Terapia con l-tiroxina ed agoaspirato tiroideo**
- 2. Rivalutazione della funzionalità tiroidea (compresi ATG ed ATPO) ed agoaspirato tiroideo**
- 3. Rivalutazione dopo il parto**
- 4. Supplementazione iodica e follow-up ecografico**

Linee guida AACE/ATA

In donne gravide con ipotiroidismo la terapia con l-tiroxina dovrebbe essere modificata secondo i range di riferimento trimestre-specifici del TSH

Se i range locali non sono disponibili bisognerebbe mirare ad ottenere livelli di TSH

- < 2.5 mU/L per il primo trimestre
- < 3 mU/L per il secondo trimestre
- < 3.5 mU/L per il terzo trimestre

Nodulo tiroideo in paziente gravida

Il carcinoma tiroideo differenziato è la neoplasia endocrina maligna più frequente (2/3 donne; 1/3 uomini)

Smith et al.

→ 14 casi su 100.000 (dati della California)

25% prima del parto

2% al parto

75% nel postpartum

Smith et al. Am J Obst Gynecol 2003; 189: 1128–1135

Nel 15% delle donne gravide si riscontrano noduli "de novo"

Glinoeer et al. J Clin Endocrinol Metab 1991; 73: 421–427

Kung et al. J Clin Endocrinol Metabolism 2002; 87: 1010–1014

In Cina è stata riscontrata la comparsa di nuovi noduli tiroidei nel 11.3% di 221 gravide sane

21 donne hanno eseguito FNAB → nessuna lesione maligna

Kung et al. J Clin Endocrinol Metabolism 2002; 87: 1010–1014

**LA COMPARSA DI UNA LESIONE TIROIDEA MALIGNA IN GRAVIDANZA E' RARA
MA LA PREVALENZA DEI NODULI TIROIDEI E' ELEVATA**

Nodulo tiroideo in paziente gravida

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ORIGINAL STUDIES, REVIEWS,
AND SCHOLARLY DIALOG

THYROID CANCER AND NODULES

Revised American Thyroid Association Management
Guidelines for Patients with Thyroid Nodules
and Differentiated Thyroid Cancer

The American Thyroid Association (ATA) Guidelines Taskforce
on Thyroid Nodules and Differentiated Thyroid Cancer

[A18] How should thyroid nodules in pregnant women be managed? It is uncertain if thyroid nodules discovered in pregnant women are more likely to be malignant than those found in nonpregnant women (103), since there are no population-based studies on this question. The evaluation is the same as for a nonpregnant patient, with the exception that a radio-nuclide scan is contraindicated. In addition, for patients with nodules diagnosed as DTC by FNA during pregnancy, delaying surgery until after delivery does not affect outcome (104).

103. Tan GH, Gharib H, Goellner JR, van Heerden JA, Bahn RS 1996 Management of thyroid nodules in pregnancy. *Arch Intern Med* 156:2317–2320.
104. Moosa M, Mazzaferri EL 1997 Outcome of differentiated thyroid cancer diagnosed in pregnant women. *J Clin Endocrinol Metab* 82:2862–2866.



Nodulo tiroideo in paziente gravida

■ RECOMMENDATION 19

For euthyroid and hypothyroid pregnant women with thyroid nodules, FNA should be performed. For women with suppressed serum TSH levels that persist after the first trimester, FNA may be deferred until after pregnancy and cessation of lactation, when a radionuclide scan can be performed to evaluate nodule function. Recommendation rating: A

If the FNA cytology is consistent with PTC, surgery is recommended. However, there is no consensus about whether surgery should be performed during pregnancy or after delivery. To minimize the risk of miscarriage, surgery during pregnancy should be done in the second trimester before 24 weeks gestation (105). However, PTC discovered during pregnancy does not behave more aggressively than that diagnosed in a similar-aged group of nonpregnant women (104,106). A retrospective study of pregnant women with DTC found there to be no difference in either recurrence, or survival rates, between women operated on during or after their pregnancy (104). Further, retrospective data suggest that treatment delays of less than 1 year from the time of thyroid cancer discovery do not adversely affect patient outcome (107). Finally, a recent study reported a higher rate of complications in pregnant women undergoing thyroid surgery compared with nonpregnant women (108). Some experts recommend thyroid hormone suppression therapy for pregnant women with FNA suspicious for or diagnostic of PTC, if surgery is deferred until the postpartum period (109).

Nodulo tiroideo in paziente gravida

■ RECOMMENDATION 20

- (a) A nodule with cytology indicating PTC discovered early in pregnancy should be monitored sonographically and if it grows substantially (as defined above) by 24 weeks gestation, surgery should be performed at that point. However, if it remains stable by midgestation or if it is diagnosed in the second half of pregnancy, surgery may be performed after delivery. In patients with more advanced disease, surgery in the second trimester is reasonable. Recommendation rating: C
- (b) In pregnant women with FNA that is suspicious for or diagnostic of PTC, consideration could be given to administration of LT_4 therapy to keep the TSH in the range of 0.1–1 mU/L. Recommendation rating: C

Donna di 51 anni, con nodulo solido disomogeneo di 28 mm al lobo tiroideo destro, citologia Thy 3, TSH 2.2 μ U/ml. Come classifichereste questo reperto citologico e cosa suggerireste in questa paziente ?

- 1) Citologia “indeterminata”
 - chirurgia per elevato rischio di malignità
- 2) Citologia “indeterminata”
 - chirurgia per rischio di malignità basso
- 3) Citologia sospetta
 - chirurgia
- 4) Citologia non dirimente
 - necessari altri accertamenti

Summary of Current Classification Schemes for Cytologic Diagnosis on the Basis of Thyroid Fine-Needle Aspiration Biopsy^a

AACE-AME, 2010	ATA, 2006	SIAPEC/BTA, 2007	NCI, 2008
1. Nondiagnostic	Nondiagnostic/inadequate	Nondiagnostic	Unsatisfactory
2. Benign	Non-neoplastic	Benign	Benign
3. Follicular lesion	Indeterminate	Follicular lesion	Follicular lesion Follicular neoplasm
4. Suspicious		Suspicious	Suspicious
5. Malignant	Malignant	Malignant	Malignant

The British system (Thy1-5), the Italian Society of Anatomic Pathology and Cytology classification (SIAPEC) and the Bethesda system for reporting thyroid cytopathology (BSRTC) represent the most important international classifications for thyroid cytopathology.

Irrespective of the system used, the 'indeterminate' categories are still debated among cytopathologists, particularly with regard to diagnostic criteria, clinical impact of subclassification and role of molecular techniques.

SIAPEC-SIE (2007)

- Tir 1. Non diagnostico
- Tir 2. Negativo per cellule maligne
- Tir 3. Indeterminato (Proliferazione follicolare)

BTA (2002/7)

- Thy 1. Non diagnostico
- Thy 2. Non neoplastico
- Thy 3. Follicular lesion

Tir 3/Thy 3

Including:

- *Adenomatoid hyperplasia,*
- *Follicular adenoma,*
- *Follicular carcinoma,*
- *hurtle cell neoplasm,*
- *Follicular variant of papillary carcinoma,*
- *Worrisome follicular alterations that cannot be placed in Tir 2 but are not sufficient for a Tir 4 categorization.*

The Bethesda System for Reporting Thyroid Cytopathology

Edmund S. Cibas, MD,¹ and Syed Z. Ali, MD²

The Bethesda System for Reporting Thyroid Cytopathology: Implied Risk of Malignancy and Recommended Clinical Management

Diagnostic Category	Risk of Malignancy (%)	Usual Management [†]
Nondiagnostic or Unsatisfactory	1-4	Repeat FNA with ultrasound guidance
Benign	0-3	Clinical follow-up
Atypia of Undetermined Significance or Follicular Lesion of Undetermined Significance	~5-15 [‡]	Repeat FNA
Follicular Neoplasm or Suspicious for a Follicular Neoplasm	15-30	Surgical lobectomy
Suspicious for Malignancy	60-75	Near-total thyroidectomy or surgical lobectomy [§]
Malignant	97-99	Near-total thyroidectomy [§]

FNA, fine-needle aspiration.



* Adapted with permission from Ali and Cibas.³

[†] Actual management may depend on other factors (eg, clinical, sonographic) besides the FNA interpretation.

[‡] Estimate extrapolated from histopathologic data from patients with “repeated atypicals.”

[§] In the case of “Suspicious for metastatic tumor” or a “Malignant” interpretation indicating metastatic tumor rather than a primary thyroid malignancy, surgery may not be

**2009-RCPATH modified BTA nomenclature to compare with the BSRTC
2013 Italian Consensus for New Classification and Reporting of Thyroid Cytology**

 UK RCPATH Diagnostic category	SIAPEC-AIT 2013	 USA BETHESDA <small>Roma, 9-11 novembre 2013</small> Terminology
Thy1/Thy1c Non-diagnostic for cytological diagnosis Unsatisfactory, consistent with cyst	TIR 1 TIR 1c (cystic)	I. Non-diagnostic Cystic fluid only
Thy2/Thy2c Non-neoplastic	TIR 2	II. Benign
Thy 3a Neoplasm possible – atypia/non-diagnostic	TIR 3A	III. Atypia of undetermined significance or follicular lesion u.s. AUS/FLUS
Thy 3f Neoplasm possible - suggesting follicular neoplasm	TIR 3B	IV. Follicular neoplasm or suspicious for a follicular neoplasm
Thy 4 Suspicious of malignancy	TIR 4	V. Suspicious of malignancy
Thy5 Malignant	TIR 5	VI. Malignant



Follicular neoplasms: histological correlations

	Rago et al., 2007	Yang et al., 2007
Thyroiditis	4 (0.8%)	11 (3.4%)
Goiter	52 (10.3%)	53 (16.3%)
Follicular /Hürtle cell Adenoma	290 (57.4%)	157 (48.2%)
PTC	138 (27.3%)	71 (21.8%)
Follicular /Hürtle cell Carcinoma	21 (4.1%)	29 (8.9%)
Total	505	326

Indeterminate cytology:

15-20 % of FNA specimens (Hegedus L, Clinical Practise, Engl J Med, 2004)

Risk of malignancy: 20-30% for follicular neoplasm or Hurtle cell neoplasm

5-10% for follicular lesions of indeterminate significance

(Baloch ZW, LiVolsi VA, 2008)

Clinical features as male sex, large tumors (> 4 cm), marked atypia on biopsy, family history of thyroid carcinoma or radiation exposure, improve the diagnostic accuracy for malignancy; overall predictive value is still low.

(Tuttle RM, Thyroid 1998; Tyler DS, Surgery 1994)

Revised American Thyroid Association Management Guidelines for Patients with Thyroid Nodules and Differentiated Thyroid Cancer

The American Thyroid Association (ATA) Guidelines Taskforce
on Thyroid Nodules and Differentiated Thyroid Cancer

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RECOMMENDATION 8

- The use of molecular markers (e.g., BRAF, RAS, RET=PTC, Pax8-PPAR γ , or galectin-3) may be considered for patients with indeterminate cytology on FNA to help guide management. Recommendation rating: C
- The panel cannot recommend for or against routine clinical use of 18FDG-PET scan to improve diagnostic accuracy of indeterminate thyroid nodules. Recommendation rating: I

RECOMMENDATION 9

- If the cytology reading reports a follicular neoplasm, a 123I thyroid scan may be considered, if not already done, especially if the serum TSH is in the low-normal range. If a concordant autonomously functioning nodule is not seen, lobectomy or total thyroidectomy should be considered. Recommendation rating: C



The American Thyroid Association (ATA) Guidelines Taskforce on Thyroid Nodules and Differentiated Thyroid Cancer

■ RECOMMENDATION 24

For patients with an isolated indeterminate solitary nodule who prefer a more limited surgical procedure, thyroid lobectomy is the recommended initial surgical approach. Recommendation rating: C

■ RECOMMENDATION 25

(a) Because of an increased risk for malignancy, total thyroidectomy is indicated in patients with indeterminate nodules who have large tumors (>4 cm), when marked atypia is seen on biopsy, when the biopsy reading is "suspicious for papillary carcinoma," in patients with a family history of thyroid carcinoma, and in patients with a history of radiation exposure. Recommendation rating: A

(b) Patients with indeterminate nodules who have bilateral nodular disease, or those who prefer to undergo bilateral thyroidectomy to avoid the possibility of requiring a future surgery on the contralateral lobe, should also undergo total or near-total thyroidectomy. Recommendation rating: C





AACE/AME/ETA Thyroid Nodule Guidelines

Follicular Lesions (Class 3)

Management:

- Repeated FNA biopsy of follicular lesions is not recommended because it does not provide additional information (Grade C; BEL 3)
- CNB is not recommended in the management of follicular lesions because it does not add additional information to FNA biopsy (Grade D; BEL 4)
- Molecular and histochemical markers are currently not recommended for routine use; their use may be considered in selected cases (Grade D; BEL 3)

Treatment

- Surgical excision is recommended for most follicular thyroid lesions (Grade B; BEL 3)
- Intraoperative frozen section is not recommended as a routine procedure (Grade D)
- Consider clinical follow-up in the minority of cases with favorable clinical, US, cytologic, and immunocytochemical features (Grade D)



CONSENSUS DOCUMENT

Cytological classification of thyroid nodules. Proposal of the SIAPEC-IAP Italian Consensus Working Group

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TIR 3/TYR 3

Action: Surgical excision of the lesion and histological examination.
Intraoperative histological examination is not recommended.
The surgical option should be evaluated in the clinical and imaging setting
(Thyler et al, Surgery 1994)



Uomo di 44 anni, con familiarità per neoplasia tiroidea e riscontro di nodulo tiroideo. Consigliereste:

- 1. Terapia soppressiva con l-tiroxina ed agoaspirato tiroideo**
- 2. Valutazione della funzionalità tiroidea (compresi ATG ed ATPO) ed agoaspirato tiroideo**
- 3. Valutazione della funzionalità tiroidea (compresi ATG, ATPO e calcitonina) ed ecografia tiroidea**
- 4. Supplementazione iodica e follow-up ecografico**

Nodulo tiroideo in uomo con familiarità per ca tiroideo

La Calcitonina nella patologia nodulare tiroidea

→ 8 casi di CT elevata su 1385 pazienti con nodulo tiroideo (0.57%)

Pacini et al. J Clin Endocrinol Metab. 1994; 78:826-9

→ 4 casi di CT elevata su 469 pazienti con nodulo tiroideo (0.84%)

Rieu et al Clin Endocrinol (Oxf). 1995;42:453-60

→ 16 casi di CT elevata su 1167 pazienti con nodulo tiroideo (1.37%)

Niccoli et al. J Clin Endocrinol Metab. 1997;82:338-41

→ 13 casi di CT elevata su 1062 pazienti con nodulo tiroideo (1.22%)

Vierhapper et al. J Clin Endocrinol Metab. 1997;82:1589-93

TUTTI casi confermati all'istologia

Nodulo tiroideo in uomo con familiarità per ca tiroideo

La Calcitonina nella patologia nodulare tiroidea

Screening dei livelli di calcitonina in 10,864 pazienti con nodulo tiroideo

Prevalenza = 0.40% (44 pazienti)

Sensibilità diagnostica migliore rispetto al FNAB

Diagnosi precoce

Il Carcinoma midollare della tiroide non è un riscontro infrequente in pazienti con nodulo tiroideo (~ 1 su 250 pazienti)

La valutazione routinaria dei livelli basali di Calcitonina dovrebbe far parte del work-up diagnostico del paziente con nodulo tiroideo

Elisei et al. J Clin Endocrinol Metab 89: 163–168, 2004

Nodulo tiroideo in uomo con familiarità per ca tiroideo

ORIGINAL ARTICLE

Endocrine Care

Calcitonin Measurement in the Evaluation of Thyroid Nodules in the United States: A Cost-Effectiveness and Decision Analysis

Kevin Cheung, Sanziana A. Roman, Tracy S. Wang, Hugh D. Walker, and Julie Ann Sosa

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J Clin Endocrinol Metab, June 2008, 93(6):2173–2180

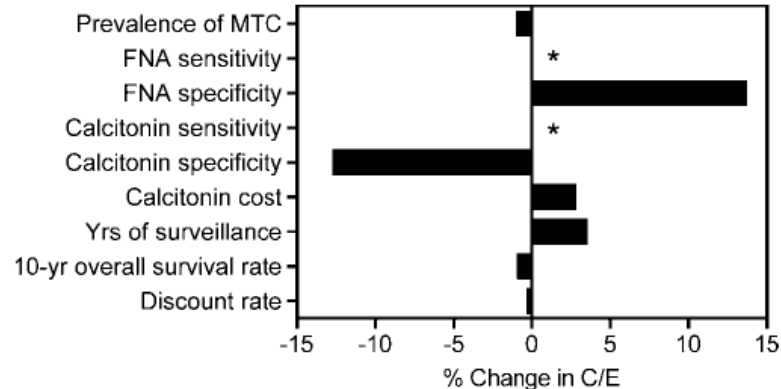


FIG. 4. Impact on C/E of a 1% increase in sensitivity analysis variables compared with base-case analysis. Vertical line at zero represents the base case; horizontal bars to the right represent reduced C/E, and horizontal bars to the left represent improved C/E. FNA, Fine needle aspiration.

Nodulo tiroideo in uomo con familiarità per ca tiroideo

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ORIGINAL STUDIES, REVIEWS,
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THYROID CANCER AND NODULES

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■ RECOMMENDATION 4

The panel cannot recommend either for or against the routine measurement of serum calcitonin. Recommendation rating: I

“ However, most studies rely on pentagastrin stimulation testing to increase specificity. This drug is no longer available in the United States, and there remain unresolved issues of sensitivity, specificity, assay performance and cost effectiveness. A recent cost-effectiveness analysis suggested that calcitonin screening would be cost effective in the United States (38). However, the prevalence estimates of medullary thyroid cancer in this analysis included patients with C-cell hyperplasia and micromedullary carcinoma, which have an uncertain clinical significance. If the unstimulated serum calcitonin determination has been obtained and the level is greater than 100 pg/mL, medullary cancer is likely present.”



Donna di 51 anni, con nodulo del lobo tiroideo destro a citologia Thy 3, sottoposta a lobectomia destra. L'esame istologico mostra Carcinoma papillare var. follicolare 27 x 12 x 19 mm. Focale infiltrazione senza superamento della capsula tiroidea. Margine di resezione indenni. Ritenete che:

1. La procedura chirurgica possa essere considerata conclusa
2. La paziente debba essere sottoposta a tiroidectomia di completamento
3. Non sia possibile assumere questa decisione senza prima eseguire altri accertamenti
4. La paziente debba essere sottoposta a tiroidectomia di completamento solo se c'è sospetto di malattia residua.

Totalizzazione della tiroidectomia

pTNM	T2, Nx, Mx
Stage	II

ETA consensus:

Completion thyroidectomy should be proposed in the case of:

- large tumor
- multifocality
- extrathyroidal extension
- vascular invasion
- evidence of local or distant metastases
- previous history of radiation exposure
- unfavorable histology

Totalizzazione della Tiroidectomia

ATA guidelines:

■ RECOMMENDATION 29

Completion thyroidectomy should be offered to those patients for whom a near-total or total thyroidectomy would have been recommended had the diagnosis been available before the initial surgery. This includes all patients with thyroid cancer except those with small (<1 cm), unifocal, intrathyroidal, node-negative, low-risk tumors. Therapeutic central neck lymph node dissection should be included if the lymph nodes are clinically involved. Recommendation rating: B

Schlinkert RT et al, Mayo Clin Proc 1997

Bilimoria KY et al, Ann Surg 2007

Tuttle RM et al, Thyroid 1998

Totalizzazione della tiroidectomia

ATA guidelines:

COMPLETION THYROIDECTOMY MAY BE NECESSARY WHEN THE DIAGNOSIS OF MALIGNANCY IS MADE AFTER LOBECTOMY

To provide complete resection of multicentric disease (*Pacini F. et al, Thyroid 2001*)

To allow radioiodine postoperative therapy (*Kim ES et al, Clin Endocrinol (Oxf) 2004*)

High rate of cancer in the opposite lobe when multifocal disease is present in the ipsilateral lobe (*Pacini F et al, Thyroid 2001*)

NB THE SURGICAL RISKS OF TWO-STAGE THYROIDECTOMY (LOBECTOMY FOLLOWED BY COMPLETION THYROIDECTOMY)

ARE SIMILAR TO THOSE OF A NEAR-TOTAL OR TOTAL THYROIDECTOMY

Erdem E et al, Eur J Sur Oncol 2003

Chirurgia vs Terapia ablativa con ^{131}I

ATA guidelines:

■ RECOMMENDATION 30

Ablation of the remaining lobe with radioactive iodine has been used as an alternative to completion thyroidectomy (189). It is unknown whether this approach results in similar long-term outcomes. Consequently, routine radioactive iodine ablation in lieu of completion thyroidectomy is not recommended. Recommendation rating: D

Randolph GW et al, Thyroid 2002

Lobectomy vs Tiroidectomia di completamento

ATA guidelines:

Noduli con citologia maligna = Class VI BSTR

■ RECOMMENDATION 26

For patients with thyroid cancer >1 cm, the initial surgical procedure should be a near-total or total thyroidectomy unless there are contraindications to this surgery. Thyroid lobectomy alone may be sufficient treatment for small (<1 cm), low-risk, unifocal, intrathyroidal papillary carcinomas in the absence of prior head and neck irradiation or radiologically or clinically involved cervical nodal metastases. Recommendation rating: A

Extent of Surgery Affects Survival for Papillary Thyroid Cancer

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TABLE 2. Cox Proportional Hazards Analysis Stratified by Tumor Size Demonstrating the Risk of Recurrence and Death for Patients Who Underwent Lobectomy Compared to Total Thyroidectomy for PTC

	Hazard Ratio (95% Confidence Interval)				
	All Patients	< 1.0 cm	≥ 1.0 cm	1.0–2.0 cm	2.1–4.0 cm
No. patients	42,952	10,247	32,705	12,778	16,365
Recurrence					
Total thyroidectomy	1.00 (Referent)	1.00 (Referent)	1.00 (Referent)	1.00 (Referent)	1.00 (Referent)
Lobectomy	1.57 (1.20–2.06) <i>P</i> = 0.001	1.01 (0.77–1.32) <i>P</i> = 0.24	1.15 (1.02–1.30) <i>P</i> = 0.04	1.24 (1.01–1.54) <i>P</i> = 0.04	1.26 (1.03–1.42) <i>P</i> = 0.03
Survival					
Total thyroidectomy	1.00 (Referent)	1.00 (Referent)	1.00 (Referent)	1.00 (Referent)	1.00 (Referent)
Lobectomy	1.21 (1.07–1.44) <i>P</i> = 0.027	1.02 (0.74–1.41) <i>P</i> = 0.83	1.31 (1.07–1.60) <i>P</i> = 0.009	1.49 (1.02–2.17) <i>P</i> = 0.04	1.31 (1.01–1.69) <i>P</i> = 0.04

NO DIFFERENCE IN OUTCOMES BETWEEN TOTAL THYROIDECTOMY AND LOBECTOMY IN NODULES < 1 CM

TOTAL THYROIDECTOMY FOR PTC IS ASSOCIATED WITH LOWER RISK OF RECURRENCE AND DEATH FOR CANCER ≥ 1 CM



FIGURE 1. Recurrence rates after surgery for patients with PTC (A) by tumor size and (B) by extent of surgery.

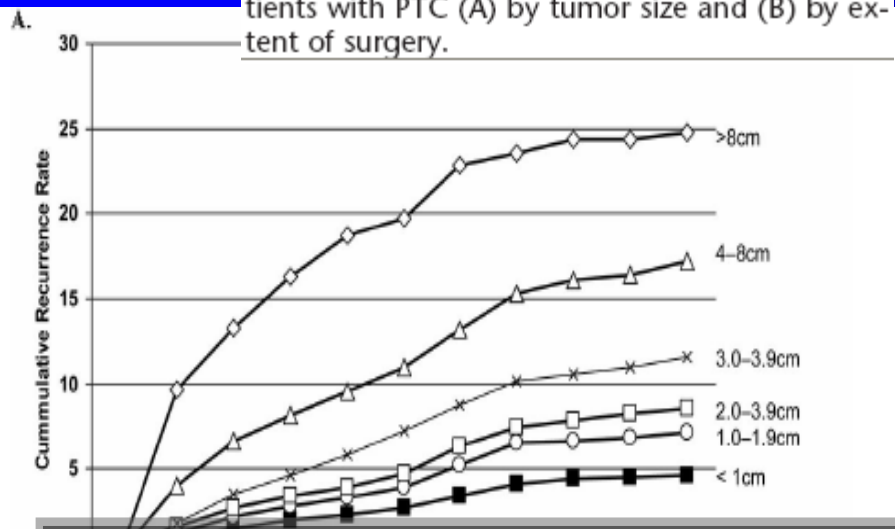
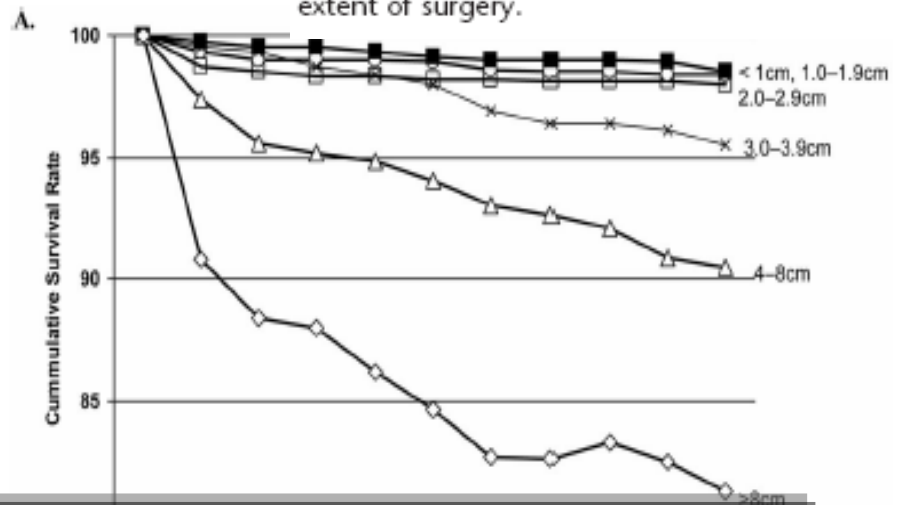
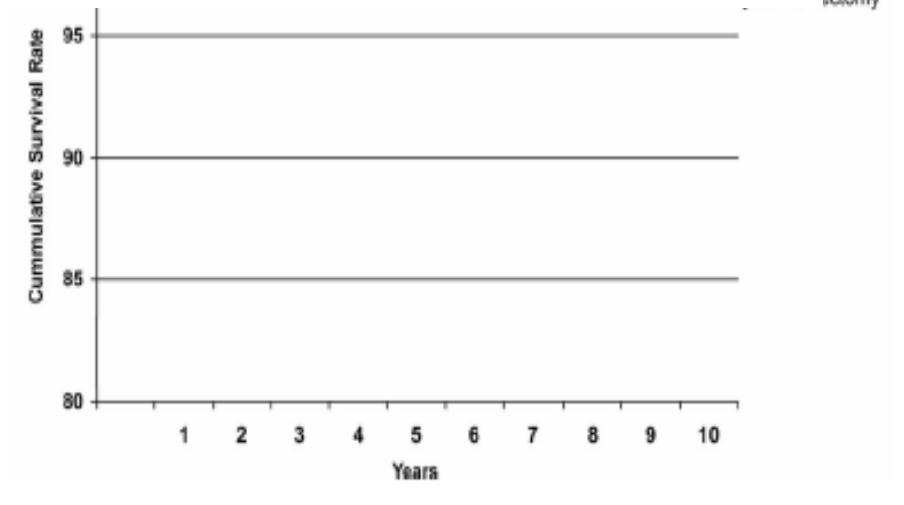
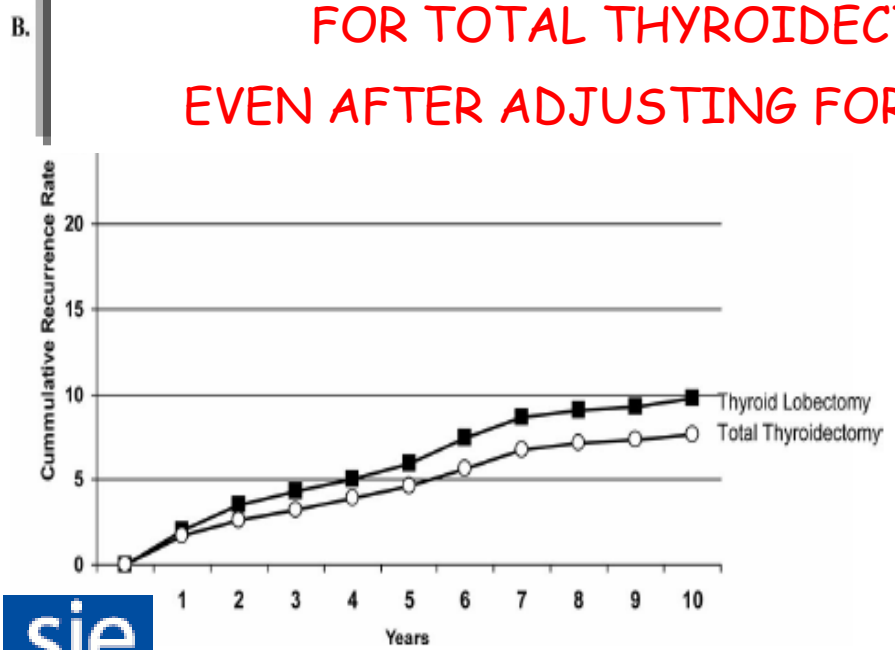


FIGURE 2. Relative survival rates after surgery for patients with PTC (A) by tumor size and (B) by extent of surgery.



THIS STUDY FIRST CLEARLY DEMONSTRATE A SURVIVAL BENEFIT FOR TOTAL THYROIDECTOMY IN TUMORS 1.0 CM, EVEN AFTER ADJUSTING FOR OTHER LOW-RISK FEATURES.



Uomo di 67 anni, sottoposto a tiroidectomia totale per PTC (T1N1M0) quattro anni fa. 6 mesi fa riscontro di Tg basale (con metodica ultrasensibile) dosabile, attualmente in crescita. Consigliereste:

- 1. Ulteriore valutazione dei livelli di Tg e degli anticorpi anti Tg**
- 2. Valutazione dei livelli di Tg dopo stimolo con TSH ricombinante, ecografia del collo**
- 3. Valutazione dei livelli di Tg dopo stimolo con TSH ricombinante**
- 4. Scintigrafia diagnostica con I¹³¹**



Esiti di PTC con Tg in aumento

ORIGINAL ARTICLE

Endocrine Care

Long-Term Surveillance of Papillary Thyroid Cancer Patients Who Do Not Undergo Postoperative Radioiodine Remnant Ablation: Is There a Role for Serum Thyroglobulin Measurement?

Cosimo Durante, Teresa Montesano, Marco Attard, Massimo Torlontano, Fabio Monzani, Giuseppe Costante, Domenico Meringolo, Marco Ferdeghini, Salvatore Tumino, Livia Lamartina, Alessandra Paciaroni, Michela Massa, Laura Giacomelli, Giuseppe Ronga, and Sebastiano Filetti, on behalf of the PTC Study Group

J Clin Endocrinol Metab, August 2012, 97(8):2748–2753

290 DTC a basso rischio (criteri ATA) trattati con la sola tiroidectomia (RRA-) seguiti con US e Tg ogni anno

vs.

495 DTC trattati con tiroidectomia ed ablazione del residuo (RRA+)

Dopo 2.5-22 anni di follow-up

livelli finali di Tg indosabili (<1 ng/ml) in 95% dei pz RRA-
in 99% dei pz RRA+

I livelli di Tg calano spontaneamente anche nei pz RRA- entro 5-7 anni, diventando indosabili

I livelli di Tg sono utili nel follow up anche dei pz che non vanno incontro ad ablazione

ATA risk stratification		
Low risk	Intermediate risk	High risk
<ul style="list-style-type: none"> No local or distant metastases All macroscopic tumor has been resected No tumor invasion of locoregional tissues or structures No aggressive histology or vascular invasion If ^{131}I was given, no ^{131}I uptake outside the thyroid bed on the post-therapeutic WBS 	<ul style="list-style-type: none"> Microscopic invasion of tumor into the perithyroidal soft tissues at initial surgery Cervical lymph node metastases or ^{131}I uptake outside the thyroid bed on the post-therapeutic WBS or Tumor with aggressive histology or vascular invasion 	<ul style="list-style-type: none"> Macroscopic tumor invasion Incomplete tumor resection Distant metastases Thyroglobulinemia out of proportion to what is seen on the post-ablative scan
ETA risk stratification		
Very low risk	Low risk	High risk
<ul style="list-style-type: none"> Complete surgery Patients with unifocal microcarcinoma (<1 cm) with no extension beyond the thyroid capsule and without lymph node metastases 	<ul style="list-style-type: none"> No local or distant metastases No tumor invasion of locoregional tissues or structures No aggressive histology or vascular invasion 	<ul style="list-style-type: none"> Less than total thyroidectomy Tumor invasion of locoregional tissues or structures Cervical lymph node metastases Distant metastases Aggressive histology or vascular invasion

Esiti di PTC con Tg in aumento

Ann Surg Oncol (2012) 19:3479–3485
DOI 10.1245/s10434-012-2391-6

Annals of
SURGICAL ONCOLOGY
OFFICIAL JOURNAL OF THE SOCIETY OF SURGICAL ONCOLOGY

ORIGINAL ARTICLE – ENDOCRINE TUMORS

Is There a Role for Unstimulated Thyroglobulin Velocity in Predicting Recurrence in Papillary Thyroid Carcinoma Patients with Detectable Thyroglobulin after Radioiodine Ablation?

Hilda Wong, MBBS¹, Kai P. Wong, MBBS², Thomas Yau, MBBS¹, Vikki Tang, BS¹, Roland Leung, MBBS¹, Joanne Chiu, MBBS¹, and Brian Hung-Hin Lang, MS²

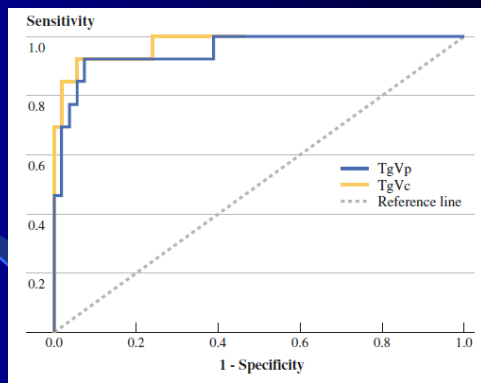


FIG. 2 Receiver–operating characteristics (ROC) curve of primary TgV (TgVp) and cumulative TgV (TgVc)

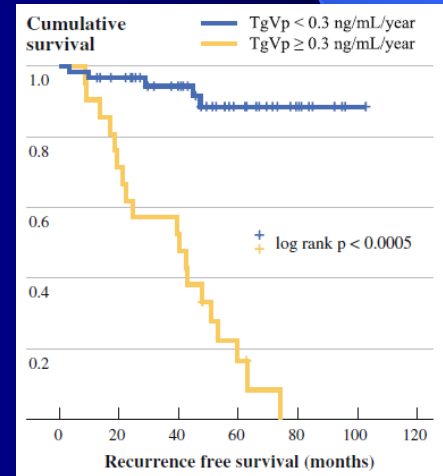
La velocità di crescita dei livelli basali di Tg
 ➔ predice la recidiva con elevata sensibilità e specificità
 ➔ è un fattore prognostico per la sopravvivenza
 in pazienti trattati con tiroidectomia con o senza ablazione del residuo

TABLE 3 Comparison of baseline TgI, simultaneous TSH values, and TgVp in patients with and without recurrent disease^a

Characteristic	Recurrent disease	No recurrence	<i>p</i> value ^b
TgI	7.25 (0.3 to 4800.0)	1.25 (0.3 to 117.0)	<0.005
Simultaneous TSH			
With Tg1	0.03 (0.03 to 3.70)	0.06 (0.03 to 5.00)	0.064
With Tg2	0.03 (0.03 to 4.00)	0.03 (0.03 to 3.50)	0.810
With Tg3	0.03 (0.03 to 2.00)	0.03 (0.03 to 4.00)	0.283
TgVp	16.03 (–29.20 to 5383.75)	–0.67 (–27.31 to 6.80)	<0.005
Total no. of patients	29	58	

^a Data are presented as median (range)

^b Mann–Whitney *U* test



Esiti di PTC con Tg in aumento

Endocrine Journal 2013, 60 (4), 415-421

ORIGINAL

Relationship of biochemically persistent disease and thyroglobulin-doubling time to age at surgery in patients with papillary thyroid carcinoma

Akira Miyauchi¹, Takumi Kudo², Minoru Kihara¹, Takuya Higashiyama¹, Yasuhiro Ito¹, Kaoru Kobayashi¹ and Akihiro Miya¹

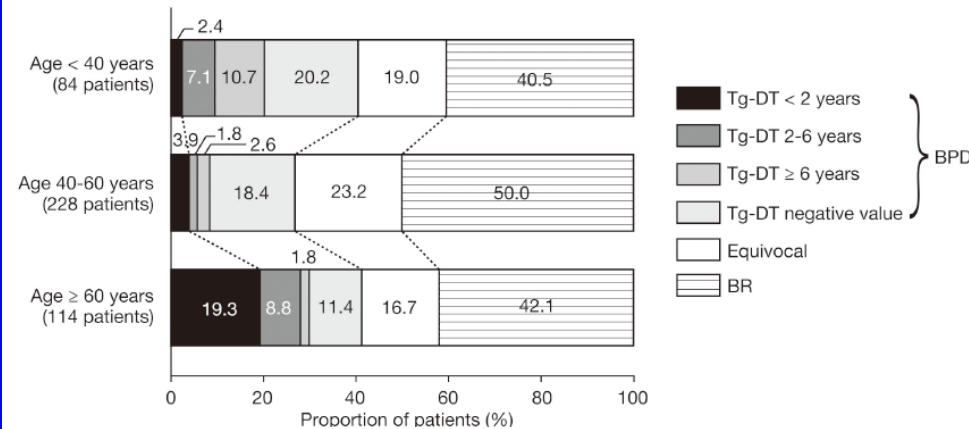


Table 2 Proportion of the patients with biochemically persistent disease (BPD) according to their age at surgery

Age at Surgery	No. of patients	(%)	No. of patients with BPD	Proportion of pts. with BPD (%)
<40 years	84	20	34	41
40 to 59 years	228	54	61	27
≥60 years	114	27	47	41
All ages	426	100	142	33

**p* = 0.0261
***p* = 0.0094

BPD: Biochemically persistent disease.

Fisher's exact test: *:*p* = 0.0261, **: *p* = 0.0094

In 142 pazienti

→ N1b

→ Dimensioni ≥4 cm

→ Estensione extra-tiroidea
si associano a malattia
biochimica persistente

Il tempo di raddoppiamento dei
livelli di Tg correla con l'età
all'intervento di tiroidectomia

Esiti di PTC con Tg in aumento

THYROID
Volume 19, Number 11, 2009
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DOI: 10.1089/thy.2009.0110

ORIGINAL STUDIES, REVIEWS,
AND SCHOLARLY DIALOG
THYROID CANCER AND NODULES

Revised American Thyroid Association Management
Guidelines for Patients with Thyroid Nodules
and Differentiated Thyroid Cancer

The American Thyroid Association (ATA) Guidelines Taskforce
on Thyroid Nodules and Differentiated Thyroid Cancer

■ RECOMMENDATION 44

Periodic serum Tg measurements and neck ultrasonography should be considered during follow-up of patients with DTC who have undergone less than total thyroidectomy, and in patients who have had a total thyroidectomy but not RAI ablation. While specific cutoff levels during TSH suppression or stimulation that optimally distinguish normal residual thyroid tissue from persistent thyroid cancer are unknown, rising Tg values over time are suspicious for growing thyroid tissue or cancer. Recommendation rating: B

■ RECOMMENDATION 45

(a) In low-risk patients who have had remnant ablation and negative cervical US and undetectable TSH-suppressed Tg within the first year after treatment, serum Tg should be measured after thyroxine withdrawal or rhTSH stimulation approximately 12 months after the ablation to verify absence of disease. Recommendation rating: A



Donna di 51 anni, con nodulo del lobo tiroideo destro a citologia Thy 3, sottoposta a lobectomia destra, con esame istologico compatibile con Carcinoma papillare var. follicolare, senza superamento della capsula tiroidea. Margine di resezione indenni. Viene sottoposta a tiroidectomia di completamento.

Ritenete che la terapia adiuvante/ablativa con radioiodio sia:

- 1) Indicata
- 2) Non indicata
- 3) Indicata ma a basse dosi
- 4) Subordinata a tireoglobulina positiva

DEPENDING ON THE RISK STRATIFICATION OF THE INDIVIDUAL PATIENTS THE ROLE OF POSTOPERATIVE RAI MAY BE:

ABLATION of normal thyroid remnant

1. absence of abnormal uptake in a diagnostic WBS
2. undetectable basal and stimulated (<1 ng/ml) serum Tg)

ADJUVANT THERAPY of microscopic residual diseases

THERAPY of known RAI avid metastatic foci

PERMITS POSTABLATIVE I131 TOTAL BODY SCANNING

EFFICACY OF RAI DEPENDS ON:

- patients preparation
- tumor specific characteristic
- site of disease
- dosage



The American Thyroid Association (ATA)
and
National comprehensive Cancer Network (NCCN)



RECOMMEND A RISK ADAPTED APPROACH TO RAI REMNANT ABLATION

BASED ON AN UNDERSTANDING OF AN INDIVIDUALIZED ESTIMATES OF:

- RISK OF SPECIFIC MORTALITY (based on TNM ed età) (tabella 1)
- RISK OF RECURRENCE (ATA/ETA) (tabella 2);
- POTENTIAL BENEFIT IN INIZIAL STAGING ANF FOLLOW-UP (tabella 2)

PROVIDES DEFINITIVE RECCOMENDATION FOR RAI TREATMENT ONLY FOR PATIENTS AT THE EXTREME ENDS OF THE RISK SPECTRUM (VERY HIGH RISK AND VERY LOW RISK PATIENTS),

WHILE PROVIDE ONLY GENERAL GUIDANCE AND SUGGESTIONS FOR THE MAJORITY OF POTIENTS THAT FALL IN THE INTERMEDIE RISK GROUP ("SELECTIVE USE OF RAI").



The American Joint Committee on Cancer (AJCC) has designated staging by TNM classification to define thyroid cancer.[1]

TX	Primary	Stage	T	N	M										
T0	No evidence of tumor	<i>Papillary or follicular (differentiated)</i>													
T1	Tumor ≤ 1 cm	YOUNGER THAN 45 YEARS													
T1a	Tumor ≤ 0.5 cm	I	Any T	Any N	M0										
T1b	Tumor > 0.5 cm, ≤ 1 cm	II	Any T	Any N	M1										
T2	Tumor > 1 cm, ≤ 2 cm	45 YEARS AND OLDER													
T3	Tumor > 2 cm, ≤ 4 cm	45 YEARS AND OLDER													
T4a	Modest tumor extension	III	<table border="1"> <thead> <tr> <th>Stage</th> <th>I</th> <th>II</th> <th>III</th> <th>IV</th> </tr> </thead> <tbody> <tr> <td>Survival rate follow-up 11.3 yr</td> <td>98.3%</td> <td>84.2%</td> <td>70.0%</td> <td>38.1%</td> </tr> </tbody> </table> <p style="text-align: right;"><i>Loh et al., JCE&M 1997</i></p>			Stage	I	II	III	IV	Survival rate follow-up 11.3 yr	98.3%	84.2%	70.0%	38.1%
Stage	I	II				III	IV								
Survival rate follow-up 11.3 yr	98.3%	84.2%	70.0%	38.1%											
T4b	Very extensive tumor	IV													
cT4a	Intrathyroidal	IVA	T4a	N0	M0										
cT4b	Anathyroidal	IVB	T4a	N1a	M0										
NX	Regional lymph nodes not assessed		T4a	N1b	M0										
N0	No regional lymph node metastasis		T1	N1b	M0										
N1	Regional lymph node metastasis		T2	N1b	M0										
N1a	Metastasis to ipsilateral lymph nodes		T3	N1b	M0										
N1b	Metastasis to contralateral lymph nodes, mediastinal lymph nodes, or distant lymph nodes		T4a	N1b	M0										
M0	No distant metastasis		T4b	Any N	M0										
M1	Distant metastasis	Stage IVC	Any T	Any N	M1										

^a Reprinted with permission from AJCC: Thyroid. In: Edge SB, Byrd DR, Compton CC, et al., eds.: AJCC Cancer Staging Manual. 7th ed. New York, NY: Springer, 2010, pp 87-96.



ATA RISK OF RECURRENCE CLASSIFICATION AFTER INITIAL SURGERY

Low risk	
(i) No local or distant mets (ii) All macroscopic tumor has been resected (iii) There is no tumor invasion of locoregional tissues or structures (iv) Tumor does not have aggressive histology (e.g., tall cell, insular, columnar cell carcinoma) or vascular invasion (v) If I-131 is given, there is no I-131 uptake outside the thyroid bed on the first posttreatment whole-body RAI scan	(T1-T2, N0-Nx)
Intermediate risk	
(i) Microscopic invasion of tumor into the perithyroidal soft tissue at initial surgery (ii) Cervical LN mets or I-131 uptake outside the thyroid bed on the post-treatment whole-body RAI scan done after thyroid remnant ablation (iii) Tumor with aggressive history or vascular invasion	T3, N0/N1
High risk	
(i) Macroscopic tumor invasion (ii) Incomplete tumor resection (iii) Distant mets (iv) Possibly thyroglobulinemia out of proportion to what is seen on the post-treatment scan	(T4, M1)

TABLE 5: Criteria for distinguishing low-risk and high-risk well-differentiated carcinoma based on the AGES (age, grade, extrathyroid extent, and size) classification system.

Low	High
Women < 50 years	Women ≥ 50 years
Men < 40 years	Men ≥ 40 years
Well-differentiated tumor	Poorly differentiated tumor (tall cell, columnar cell, or oxyphilic variants)
Tumor < 4 cm in diameter	Tumors ≥ 4 cm in diameter
Tumor confined to thyroid	Local invasion
No distant metastases	Distant metastases

**AGES classification criteria
(age, grade, extrathyroidal extent, size)**



RAI ABLATION IS RECOMMENDED IN:

- large tumors (>4 cm) regardless of age;
- gross extrathyroidal extension;
- distant metastases;
- Follicular and hurtle cell thyroid cancer

RAI ABLATION IS NOT RECOMMENDED FOR:

- small papillary thyroid cancer (T1a, N0)

"SELECTIVE USE" OF RAI ABLATION IN:

- intrathyroidal 1-4 cm papillary thyroid cancer;
- any size tumor with minor extrathyroidal extension;
- degree of loco regional lymph node involvement



ATA/NCCN NOTE THAT "BECAUSE EITHER CONFLICTING OR INADEQUATE DATA, THEY CANNOT RECOMMEND EITHER FOR OR AGAINST RAI ABLATION FOR ALL PATIENTS IN THE SELECTIVE USE CATEGORY,

HOWEVER, "SELECTED PATIENTS" WITH HIGHER RISK FEATURES MAY BENEFIT FROM RAI ABLATION, WHILE THE PRESENCE OF ANY SINGLE RISK FEATURE DOES NOT MANDATE RAI ABLATION

HIGHER RISK FEATURES INCLUDED:

- worrisome histological subtype (tall cell, columnar, insular or solid variants, poorly differentiated ca, follicular ca. hürthle cell thyroid cancer)
- intrathyroidal vascular invasion
- macroscopic multifocal disease (>1 cm)

OTHER IMPORTANT VARIABLE IN THE DECISION MAKING PROCESS:

- increase ATG antibody
- non stimulated post operative basal Tg >5 ng/ml or stimulated >10 ng/ml
- BRAF status

Factors	Description	Expected Benefit				Strength of evidence
		Decreased risk of death	Decreased risk of recurrence	May facilitate initial staging and followup	RAI ablation usually recommended	
T1	≤1 cm, intrathyroidal or microscopic multifocal	No	No	Yes	No	E
	1-2 cm, intrathyroidal	No	Conflicting data	Yes	<u>Selective use</u>	I
T2	>2-4 cm, intrathyroidal	No	Conflicting data	Yes	<u>Selective use</u>	C
T3	>4 cm,					
	<45 years	No	Conflicting data	Yes	Yes	B
	≥45 years	Yes	Yes	Yes	Yes	B
	Any size, any age, minimal extrathyroidal extension	No	Inadequate data	Yes	<u>Selective use</u>	I
T4	Any size with gross extrathyroidal extension	Yes	Yes	Yes	Yes	B
NX, N0	No metastatic nodes documented	No	No	Yes	No	I
N1	<45 years	No	Conflicting data	Yes	<u>Selective use</u>	C
	>45 years	Conflicting data	Conflicting data	Yes	<u>Selective use</u>	C
M1	Distant metastases present	Yes	Yes	Yes	Yes	A

ATA 2009 Thyroid cancer guidelines



UNCERTAINTY OVER RAI DOSAGE REQUIRED FOR EFFECTIVE ABLATION.

ATA 2009 and European 2006 consensus report, suggest that clinicians can choose between low or high dose

■ RECOMMENDATION 36

The minimum activity (30–100 mCi) necessary to achieve successful remnant ablation should be utilized, particularly for low-risk patients. Recommendation rating: B

The use of reduced dose of radiiodine has important advantages: lower side effects especially risk of second primary cancer, improve the patient's quality of life, Spend less time in hospital, Reduces financial costs incurred by the health service provider, Reduces exposure of radioiodine in the environments

NCCN guidelines recommend using 30 to 100 mCi in cases of papillary, follicular, Hurtle cell carcinoma >1 cm, with nodal or distant metastases or with aggressive histology when there is suspected or proven thyroid bed uptake in total body radioiodine scan after thyroidectomy. report, suggest tht clinicians can choose between low or high dose



*Three trials have compared 1100 MBq with 1800 MBq RAI activity
Bal CS. et al 2004, Gawkowska et al. (2001), Sirisalipoch. (2004)*

*Two randomized trial have compared 1800 MBq with 3700 MBq RAI activity
BAL et al, (1996), Sirisalipoch. W (2004).*

Systematic review and meta-analysis, including all randomized trials, of low activity versus high activity radioiodine ablation after thyroidectomy: provides some evidence from randomized trials that a lower activity of radioiodine ablation is as effective as higher dose after surgery in patients with DTC with lower toxicity. (Valachis A, Nearchou A; Acta Ocol 2013).

However administration of the smaller activity is associated with fewer common adverse effects and does not result in more repeat treatment.

combination with either thyrotropin alfa or thyroid hormon withdrawal before ablation
CONCLUSION: Low dose radioiodine plus thyrotropin alfa was effective as high dose radioiodine with a lower rate of adverse events. (Ujjal Mallik, F.R.C.R et al; N Eng J M 2012)

The timing of RRA seems to have no effect on the long-term outcome of the disease. Therefore, urgency for radioiodine ablation in patients with low-risk thyroid cancer is not recommended. (Tsirona et al 2013).

*HiLo trial, 2012 was a multicentric trial which enrolled 438 patients who had DTC stages T1 to T3 with possible spread of nearby lymph node but without metastases distant, with primary outcome successful ablation in low vs. high RAI dose and in rTSH vs. THW RAI preparation. **CONCLUSION:** There were no differences in successful ablation among patients receiving low-dose RAI, high-dose RAI, rTSH, or THW.*

*The ESTIAMBL trial (2012) randomized study that included 752 patients with low-risk thyroid cancer (T1N0M0, T1N1aM0, T1N1bM0, and T2N0M0). **CONCLUSION:** This study again demonstrated that successful ablation could be achieved equally well with low vs. high RAI dosing and with rTSH vs. THW, suggesting that low-dose RRA plus rTSH may work equally as well as high dosing and THW with fewer side-effects.*

In DTC patients at intermediate risk, high RAI activities at ablation have no major advantage over low activities". (Castagna MG, Eur J Endocrinol, 2013)

"Most low-risk to intermediate-risk patients who do warrant RRA can be prepared with recombinant human thyroid-stimulating hormone and given the smallest dose possible (30 to 50 mCi of iodine 131) for successful remnant ablation"

(Haugen BR, Endocrin practise 2012)

EFE 2013

Trattamento RAI con ^{131}I (70 mCi)

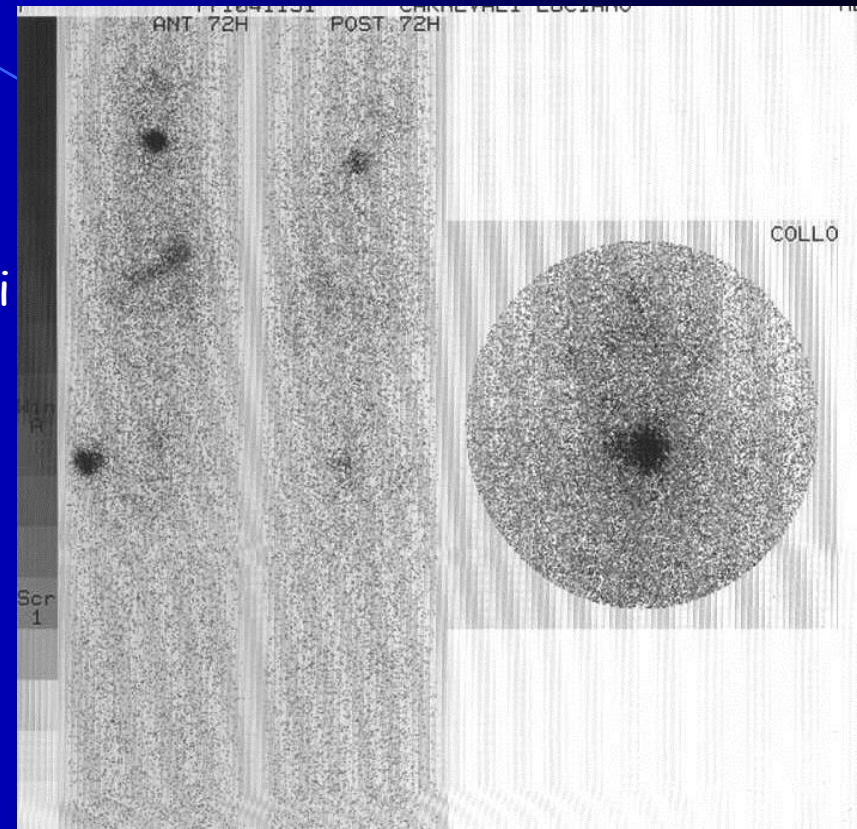
^{131}I -WBS: presenza di discreta captazione cervicale mediana riferibile in prima ipotesi a residuo tiroideo

Ecografia cervicale: **NEGATIVA**

Tg withdraw T4 = 25 ng/ml

TSH = 142 $\mu\text{U}/\text{ml}$

Tg Ab = 35 UI/ml



Uomo di 62 anni, sottoposto a tiroidectomia totale per carcinoma follicolare, con metastasi ossee femorali sintomatiche non iodocaptanti alla scintigrafia diagnostica. Trattereste il paziente con:

- 1. Dose terapeutica di I131 dopo sospensione della terapia con LT4**
- 2. Radioterapia esterna**
- 3. Terapia chirurgica**
- 4. Terapia con inibitori delle tirosino chinasi**



La gestione del paziente con metastasi ossee deve considerare :

- 1) la presenza o il rischio di fratture patologiche, soprattutto a carico delle articolazioni che supportano il peso corporeo
- 2) il rischio di compromissione neurologica da lesioni vertebrali
- 3) la presenza di dolore
- 4) la capacità di captare lo iodio
- 5) l'esposizione midollare a radiazioni ionizzanti (metastasi pelviche)

Bernier et al. 2001 J Clin Endocrinol Metab 86:1568–1573.

Zettinig et al. 2002 Clin Endocrinol (Oxf) 56:377–382



Esiti di FTC con M+ ossee non iodocaptanti

clinical practical guidelines

Annals of Oncology 23 (Supplement 7): vii110-vii119, 2012
doi:10.1093/annonc/mds230

Thyroid cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up[†]

F. Pacini¹, M. G. Castagna¹, L. Brilli¹ & G. Pentheroudakis², on behalf of the ESMO Guidelines Working Group*

¹Department of Internal Medicine, Endocrinology and Metabolism and Biochemistry, Section of Endocrinology and Metabolism, University of Siena, Siena, Italy;

²Department of Medical Oncology, Medical School, University of Ioannina, Ioannina, Greece

Table 3. Therapeutic effects of different TKIs in clinical trials enrolling patients with MTC or DTC

Drug	Histotype	No. patients	Phase	PR (%)	SD (%)	SD>6 months (%)	mPFS (weeks)
Motesanib	MTC	91	II	2	81	48	48
	DTC	93	II	14	67	35	40
Sunitinib	MTC	23	II	35	57		28
	MTC	6	II		83		
	MTC	15	II	33	27		
Vandetanib	DTC	31	II	14	68		
	MTC	30	II	20	73	53	
	MTC	19	II	16	64	53	
Sorafenib	MTC	331	III	45	42	83	30.5 months
	MTC	16	II	6	87	56	60
	DTC	41	II	15		53	79
	DTC	30	II	23			
XL184	DTC	31	II	25	34		
	MTC	37	I	29		41	
Axitinib	MTC	11	I	18	27		
	DTC	45	II	31	42		
Pazopanib	DTC	37	II	49			

MTC, medullary thyroid cancer; DTC, differentiated thyroid cancer; PR, partial response; SD, stable disease; mPFS, median progression-free survival.



Esiti di FTC con M+ ossee non iodocaptanti

In 109 pazienti con metastasi ossee da DTC

22% sono andati all'intervento con resezione completa
(maggiore successo nei pz <45 anni)

55% sono andati all'intervento con resezione parziale

23% non sono andati all'intervento

**Miglioramento della sopravvivenza
solo nel primo gruppo**

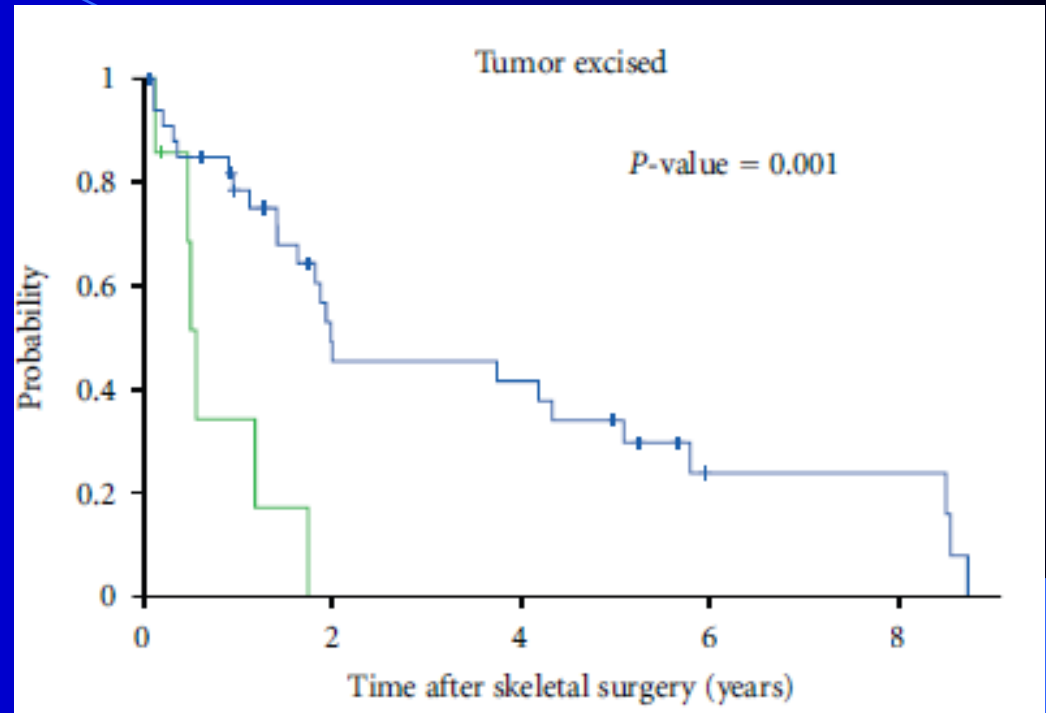
Bernier et al. 2001 J Clin Endocrinol Metab 86:1568–1573



Esiti di FTC con M+ ossee non iodocaptanti

presentation with a
single bone metastasis

complete bone
metastasis resection



improved patient and
implant survival

Satcher et al. Int J Surg Oncol 2012, 12

Esiti di FTC con M+ ossee non iodocaptanti

THYROID
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DOI: 10.1089/thy.2009.0110

ORIGINAL STUDIES, REVIEWS,
AND SCHOLARLY DIALOG
THYROID CANCER AND NODULES

Revised American Thyroid Association Management Guidelines for Patients with Thyroid Nodules and Differentiated Thyroid Cancer

The American Thyroid Association (ATA) Guidelines Taskforce on Thyroid Nodules and Differentiated Thyroid Cancer

■ RECOMMENDATION 60

Complete surgical resection of isolated symptomatic metastases has been associated with improved survival and should be considered, especially in patients <45 years old with slowly progressive disease (320,363). Recommendation rating: B

■ RECOMMENDATION 62

When skeletal metastatic lesions arise in locations where acute swelling may produce severe pain, fracture, or neurologic complications, external radiation and the concomitant use of glucocorticoids to minimize potential TSH-induced and/or radiation-related tumor expansion should be strongly considered (392). Recommendation rating: C



Donna di 51 anni, sottoposta a tiroidectomia totale per Carcinoma papillare variante follicolare e sottoposta a trattamento con ^{131}I . Dopo 12 mesi esegue test con rhTSH (AbTg 22 ng/ml):

US collo: metastasi lcv

Confermata con FNAB

Quale ritenete il trattamento più indicato ?

	Basale	3 gg	5 gg
TSH ($\mu\text{U/ml}$)	0,1	147	12,4
Tg (ng/ml)	3	17,8	11,5

1. Nuovo trattamento con ^{131}I
2. Chirurgia
3. Chirurgia subito seguita da ^{131}I
4. Nessuno: "wait and see"

Ecografia del collo: altamente sensibile nel riconoscimento di metastasi in regione cervicale anteriore nei pazienti con CDT. (Pacini F et al, 2003).

La **misurazione della Tg** nel liquido di lavaggio aumenta la sensibilità dell'agoaspirato dei linfonodi cervicali che appaiono sospetti all'ecografia (Snozek et al, 2007)

Metastasi lcv possono occasionalmente essere scoperte dall'ecografia del collo anche con livelli di Tg sierica indosabili dopo stimolo con rhTSH (David A et al 2001)

When the thyroid is still present, neck node metastasis in the central compartment are often obscured from US detection. LNMs are found in 40-60% of patients undergoing central neck dissection



Value of Preoperative Ultrasonography in the Surgical Management of Reoperative Thyroid Cancer

● true-positive rate	56.7%
● true-negative rate	13.8%
● false-positive rate	3.7%
● false-negative rate	6.0%
● sensitivity	90.4%
● specificity	78.9%
● positive predictive value	93.9%
● overall accuracy	87.9%

Stulak et al., Arch Surg. 2006;141:489-496

Le metastasi scoperte nel corso del follow-up sono verosimilmente manifestazioni di **PERSISTENZA DI MALATTIA NON ERADICATA CON IL TRATTAMENTO INIZIALE**.

La gerarchia dei trattamenti per la malattia metastatica è nell'ordine:

- **ESCISSIONE CHIRURGICA LOCOREGIONALE IN PZ POTENZIALMENTE CURABILI**
- **LA TERAPIA CON RADIOIODIO PER TUMORI IODOCAPTANTI**
- **LA RADIO TERAPIA ESTERNA**
- **"WAIT AND SEE" CON MALATTIA ASINTOMATICA STABILE O LENTAMENTE PROGRESSIVA**

La chirurgia è il trattamento di scelta per le recidive loco-regionali (linfonodi cervicali e/o tessuti molli nel collo) (Kloss RT et al, 2005).

QUAL E' LA GESTIONE CHIRURGICA METASTASI LOCOREGIONALI ?

▪ RACCOMANDAZIONE 50

- a) La dissezione completa dei compartimenti centrale o laterali del collo, risparmiando le strutture vitali non coinvolte dalla malattia, dovrebbe essere attuata nei pazienti con persistenza o recidiva di malattia confinata al collo. Grado di raccomandazione: B
- b) La dissezione limitata dei compartimenti centrale o laterali del collo, può essere un'alternativa ragionevole ad una dissezione più estesa e radicale in pazienti con recidiva di malattia che hanno già subito precedenti interventi allo stesso livello e/o radioterapia esterna. Grado di raccomandazione: C

Benché alcune metastasi linfonodali possano essere trattate con radioiodio, può essere necessario più di un trattamento a seconda dell'istologia, delle dimensioni e del numero di metastasi.

Un po' di letteratura.....

La dissezione completa dei compartimenti centrale o laterale del collo dovrebbe essere attuata nei pz con persistenza/recidiva malattia confinata al collo

- La **dissezione bilaterale del compartimento centrale** può migliorare la sopravvivenza e ridurre il rischio di recidiva a livello linfonodale.
Tisell LE, Nilsson B, 1996 World J Surg
- Inoltre, la dissezione del compartimento centrale **selettiva unilaterale** aumenta la percentuale di pazienti che risultano liberi da malattia con livelli di Tg indosabili dopo 6 mesi dall'intervento chirurgico.
Sywak M, Cornford L, 2006 Surgery
- Altri studi sulla dissezione del compartimento centrale bilaterale hanno mostrato un aumento della morbidità (lesioni del nervo laringeo ricorrente, ipoparatiroidismo transitorio) rispetto alla linfadenectomia selettiva unilaterale.
Lee YS, Kim SW, 2007 World J Surg



- **RACCOMANDAZIONE 27¹**

- a) La dissezione del compartimento centrale del collo (livello VI) in pazienti con coinvolgimento clinico dei linfonodi del compartimento centrale o laterocervicali, deve essere effettuata in concomitanza con la tiroidectomia totale per assicurare una completa liberazione da malattia della sezione centrale del collo. Grado di raccomandazione: B
- b) La dissezione profilattica del compartimento centrale (ipsi- o bilaterale) può essere praticata in pazienti con CPT senza coinvolgimento linfonodale clinicamente evidente, in particolare in casi di tumore primitivo in fase avanzata (T3 o T4). Grado di raccomandazione: C
- c) La tiroidectomia totale o quasi-totale può essere praticata senza dissezione profilattica del compartimento centrale per tumori di piccole dimensioni (T1 o T2), non invasivi, carcinomi papilliferi con linfonodi negativi e per la maggior parte dei carcinomi follicolari. Grado di raccomandazione: C

Per quei pazienti in cui il coinvolgimento linfonodale sia clinicamente evidente, la resezione chirurgica potrebbe portare ad una riduzione dei tassi di recidiva di malattia e possibilmente di mortalità

- **Raccomandazione 28²**

La dissezione terapeutica del compartimento linfonodale laterocervicale deve essere eseguita in pazienti in cui la biopsia linfonodale abbia dimostrato la presenza di malattia metastatica a tale livello. Grado di raccomandazione: B

ATA guidelines

■ RECOMMENDATION 48

- (a) Following surgery, cervical US to evaluate the thyroid bed and central and lateral cervical nodal compartments should be performed at 6–12 months and then periodically, depending on the patient's risk for recurrent disease and Tg status. Recommendation rating: B
- (b) If a positive result would change management, ultrasonographically suspicious lymph nodes greater than 5–8 mm in the smallest diameter should be biopsied for cytology with Tg measurement in the needle washout fluid. Recommendation rating: A
- (c) Suspicious lymph nodes less than 5–8 mm in largest diameter may be followed without biopsy with consideration for intervention if there is growth or if the node threatens vital structures. Recommendation rating: C

ALGORITMO per la GESTIONE del CDT a 6-12 MESI dall'ABLAZIONE DEL RESIDUO

