



Il nodulo tiroideo

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“Slow Medicine”

Gruppo di lavoro AME “Per una medicina sostenibile”:

5 pratiche non consigliate perché non supportate dall’evidenza (3 relative alla tiroide):

- ✓ Ecografia di routine
- ✓ Terapia con L-tiroxina indiscriminata per gozzo nodulare
- ✓ fT3 di routine



AACE/ACE/AME Guidelines

AMERICAN ASSOCIATION OF CLINICAL ENDOCRINOLOGISTS, AMERICAN COLLEGE OF ENDOCRINOLOGY, AND ASSOCIAZIONE MEDICI ENDOCRINOLOGI MEDICAL GUIDELINES FOR CLINICAL PRACTICE FOR THE DIAGNOSIS AND MANAGEMENT OF THYROID NODULES – 2016 UPDATE **EXECUTIVE SUMMARY OF RECOMMENDATIONS**

Complete guidelines are available at <https://www.aace.com/publications/guidelines>

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on behalf of the AACE/ACE/AME Task Force on Thyroid Nodules**

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L'“epidemia” di noduli tiroidei



- ✓ Prevalenza negli adulti fino al 50-60%
- ✓ Asintomatici nella maggior parte dei casi
- ✓ Eutiroidismo nella maggior parte dei casi
- ✓ Basso rischio di malignità
- ✓ L'assenza di sintomi non esclude la malignità
- ✓ Ecografia consigliata in caso di:
 - i. Noduli palpabili
 - ii. Fattori di rischio

L'“epidemia” di noduli tiroidei



- E' aumentato il **riscontro incidentale** di piccoli noduli (ecoDoppler vasi collo, ecografie ghiandole salivari, TAC, RMN, PET)
- **Oltre il 90%** di questi non hanno impatto clinico
- **Fonte d'ansia** per i pazienti:
 - È benigno?
 - Può crescere nel tempo?
 - Può trasformarsi?



2 domande fondamentali

- Qual è il rischio di malignità?
- Quale follow-up dobbiamo attuare?

Rischio malignità

Classificazione ATA

Nodules **> 1cm** in greatest dimension (Strong recommendation, Moderate-quality evidence)

Nodules **> 1cm** in greatest dimension (Strong recommendation, Low-quality evidence)

Nodules **> 1.5 cm** in greatest dimension (Weak recommendation, Low-quality evidence)

NO

Risk of malignancy

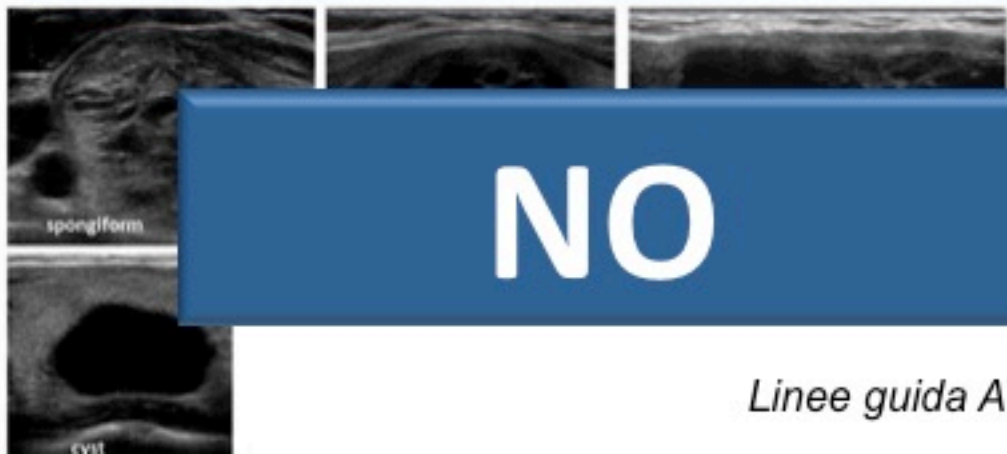
High Suspicion 70-90%

Intermediate Suspicion 10-20%

Low Suspicion 5-10%

Very low Suspicion <3%

Benign <1%



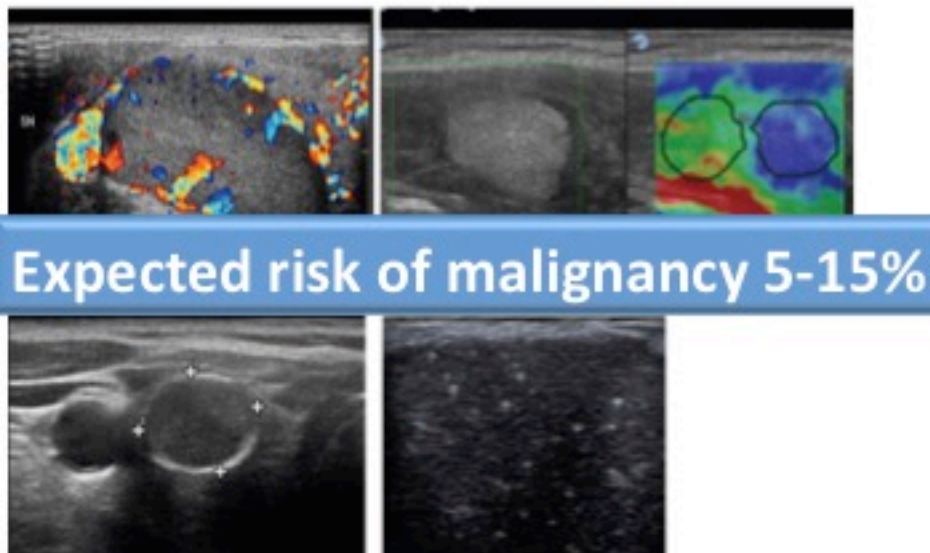
Rischio malignità

Classificazione AME-ACE-AACE



Low-Risk :

- ✓ Thyroid Cyst
- ✓ Mostly cystic nodule with reverberating artifacts
- ✓ Isoechoic spongiform nodule

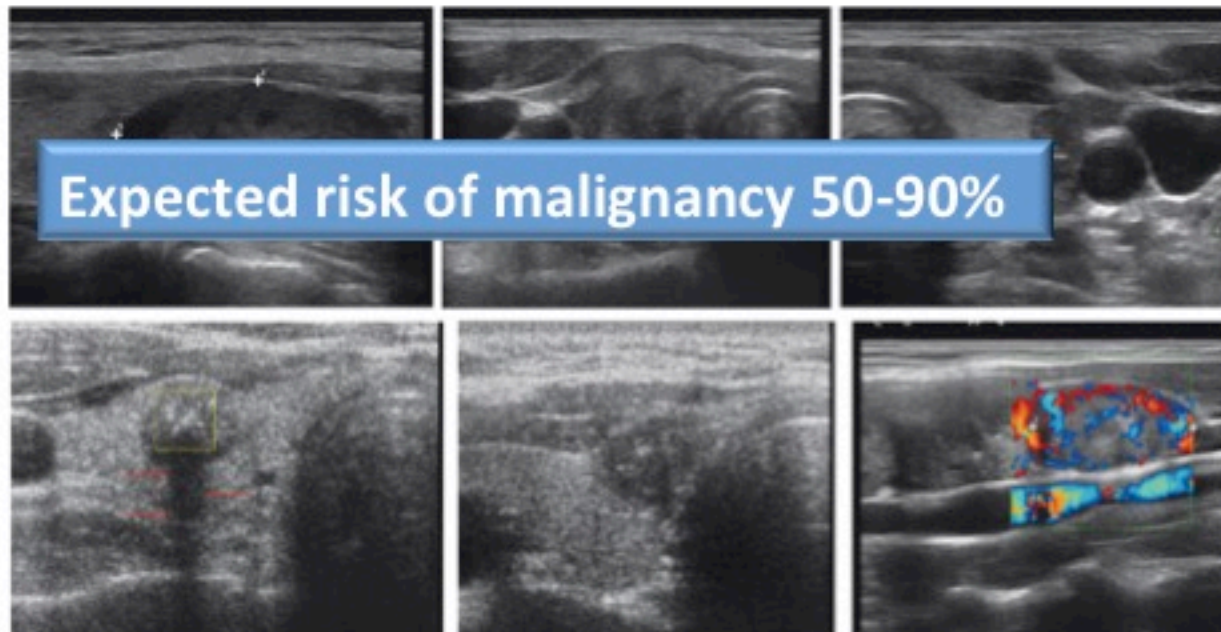


Intermediate Risk:

- ✓ Isoechoic nodule with central vascularity
- ✓ Isoechoic nodule with macrocalcifications
- ✓ Isoechoic nodule with indeterminate hyperechoic spots
- ✓ Isoechoic nodule with elevated stiffness on elastography

Rischio malignità

Classificazione AME-ACE-AACE



High-Risk:

- ✓ Marked hypoechoogenicity
- ✓ Microcalcifications
- ✓ Irregular (speculated) margins
- ✓ More tall than wide
- ✓ Extracapsular growth
- ✓ Suspicious regional lymph node



Quale follow-up?

Studio prospettico osservazionale multicentrico (8 centri italiani)





Original Investigation

The Natural History of Benign Thyroid Nodules

Cosimo Durante, MD, PhD; Giuseppe Costante, MD; Giuseppe Lucisano, MScStat; Rocco Bruno, MD; Domenico Meringolo, MD; Alessandra Paciaroni, MD; Efisio Puxeddu, MD, PhD; Massimo Torlontano, MD; Salvatore Tumino, MD; Marco Attard, MD; Livia Lamartina, MD; Antonio Nicolucci, MD; Sebastiano Filetti, MD

*Publicati i risultati dei primi
5 anni di follow-up*





Criteri d'inclusione

- ✓ Number: from 1 to 4
- ✓ Largest diameter: 4 to 40 mm
- ✓ Structure: solid or mixed (solid-cystic) with a fluid component representing no more than 75% of the total volume
- ✓ No evidence of malignancy
- ✓ No nodule-related signs or symptoms
- ✓ Euthyroidism
- ✓ No thyroid hormone therapy
- ✓ No history of surgical or nonsurgical thyroid interventions
- ✓ Serum thyroid antibody levels within normal limits
- ✓ No sonographic evidence of chronic autoimmune thyroiditis
- ✓ No clinical or sonographic evidence of acute thyroiditis

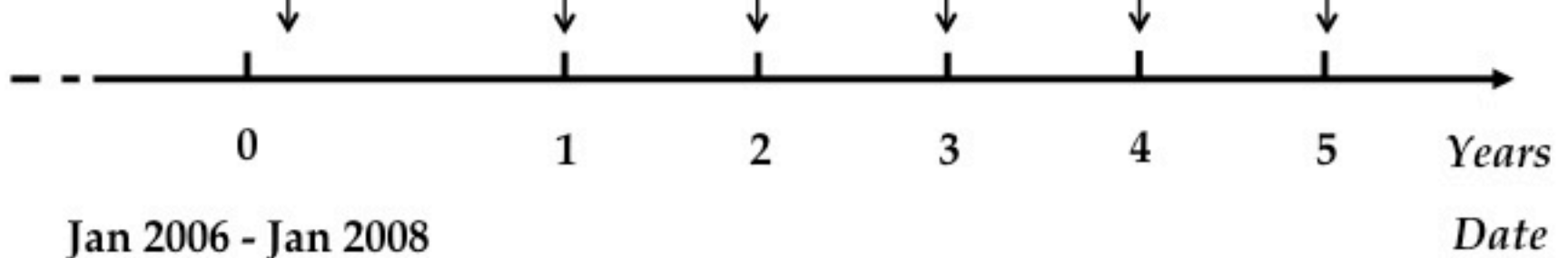


Methods

Check for
eligibility

Thyroid US; TSH,
fT4 Clinical data *

Thyroid US; TSH,
fT4 Clinical data *



* At each site, clinical and ultrasound assessment were performed by the same physician across all study period



Results (1)

*Study cohort (n=992)**

Characteristics	
Age – yrs (<i>mean±SD</i>)	52.3±13.7
Female – (<i>n; %</i>)	815 (82.1)
BMI – Kg/m² (<i>mean±SD</i>)	26.9±4.8
TSH – mIU/mL (<i>mean±SD</i>)	1.46±0.7
Uninodular goiter – (<i>n; %</i>)	594 (59.8)
Nodule maximum diameter – mm (<i>mean ±SD</i>)	14.24±8.1
Solid structure - (<i>n; %</i>)	806 (81.2)

* 630 cytologically and 937 sonographically benign nodules



Main outcomes and measures

Primary end-points

1. Incidence of *original nodule growth* (i.e., a nodule present at baseline)
2. Baseline factors predicting growth

Secondary end-point

1. Diagnosis of *thyroid cancer* arising in an original nodule



Methods

Clinical data

- Family history of nodular goiter
- Diagnosis (*incidentalomas, subclinical nodules, clinical nodules*)
- Birthplace, residency (*endemic/non-endemic areas*)
- Iodine salt supplementation
- Prior treatment with l-thyroxine
- BMI, Smoke
- ***In women:*** oligoamenorrhea, pregnancies, menopause, hormonal therapy (EP)



Methods

Statistical analysis

Baseline factors associated with nodule growth were identified by:

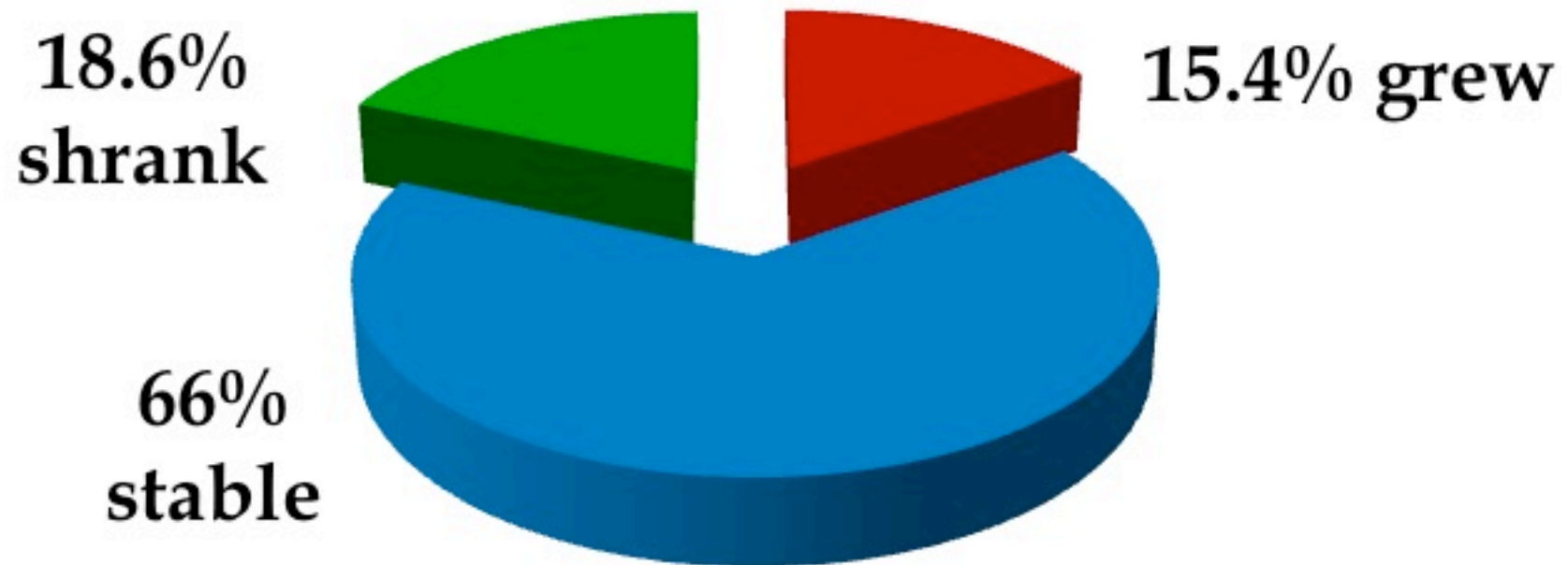
- **Multivariate backward logistic regression**
- **RECURSIVE Partitioning and Amalgamation (RECPAM):**
 - This method combines the advantages of standard logistic regression and tree-growing techniques
 - It provides information about the interactions between the several variables investigated
 - It allows us to identify distinct and homogeneous subgroups of patients characterized by different risks of nodule growth



Results (2)

Changes in size

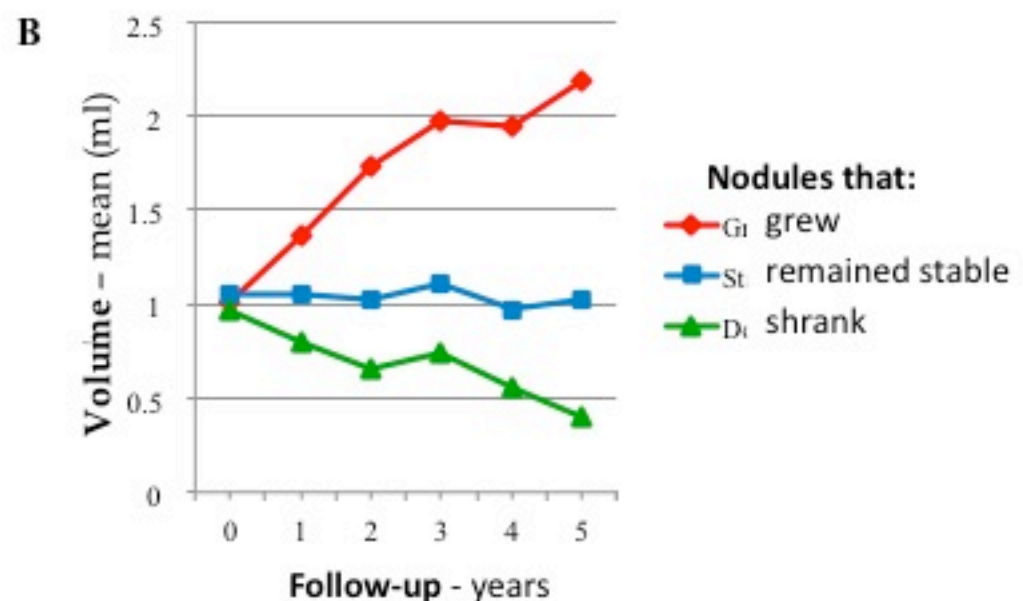
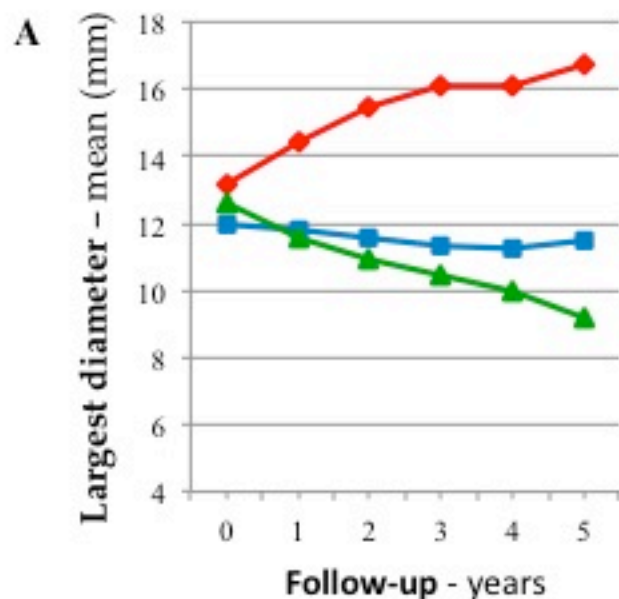
Patients (n=992)





Results (3)

Changes in the size



Mean changes in the largest diameters: +4.9 mm (95% CI 4.2 to 5.5)*

Mean changes in the volumes: +1.9 ml (95% CI 1.4 to 2.5)*

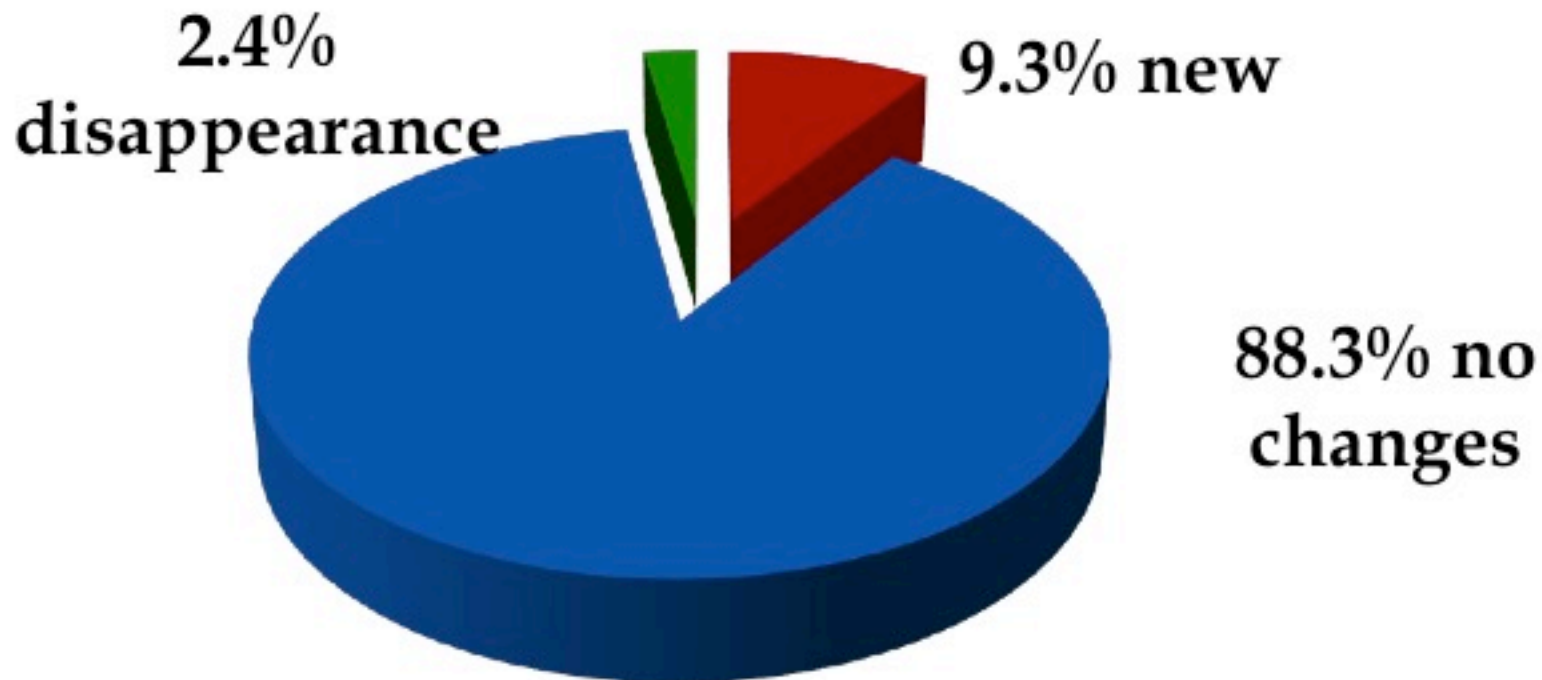
* ANOVA, longitudinal linear model with an unstructured correlation-type matrix



Results (4)

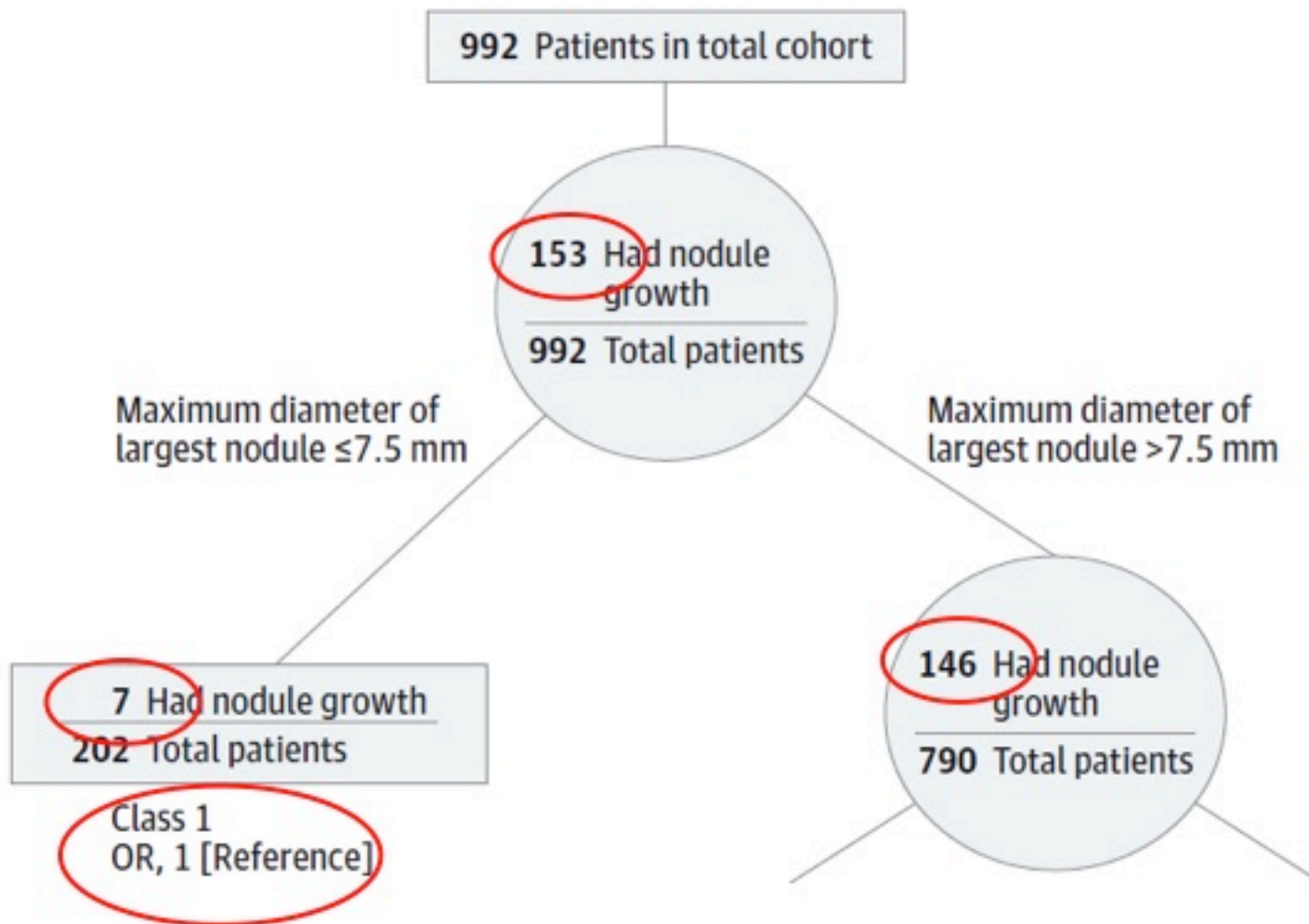
Changes in the number

Patients (n=992)





RECPAM analysis



RECPAM analysis

*6 sottogruppi a rischio crescente:
OR da 1 a 20*

146 Had nodule growth
790 Total patients

No. of nodules, 1

54 Had nodule growth
446 Total patients

Age >51 y

Age ≤51 y

20 Had nodule growth
217 Total patients

Class 2
OR, 2.8 (1.2-6.8)

34 Had nodule growth
229 Total patients

Class 3
OR, 4.9 (2.1-11.2)

No. of nodules >1

92 Had nodule growth
344 Total patients

Age >43 y

Age ≤43 y

60 Had nodule growth
269 Total patients

32 Had nodule growth
75 Total patients

Class 6
OR, 20.7 (8.6-50.1)

BMI ≤28.6

BMI >28.6

34 Had nodule growth
189 Total patients

Class 4
OR, 6.1 (2.6-14.2)

26 Had nodule growth
80 Total patients

Class 5
OR, 13.4 (5.5-32.6)



Results (5)

1

Single, small
nodule (≤ 7.5
mm).
Older age (> 43
yrs).

HR: 1

2

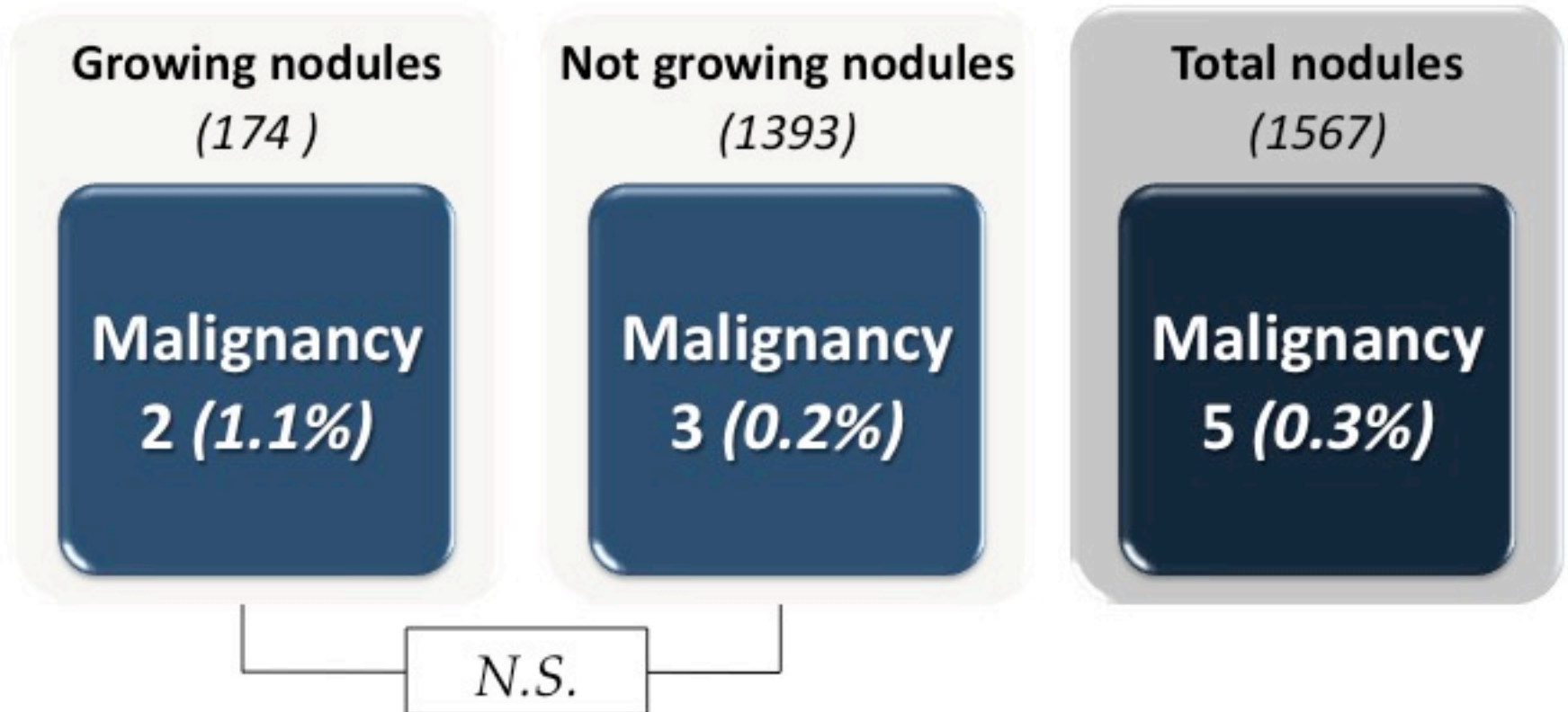
Multiple, large,
nodules (> 7.5
mm).
Younger age (≤ 43
yrs).

HR: 20.7



Results (6)

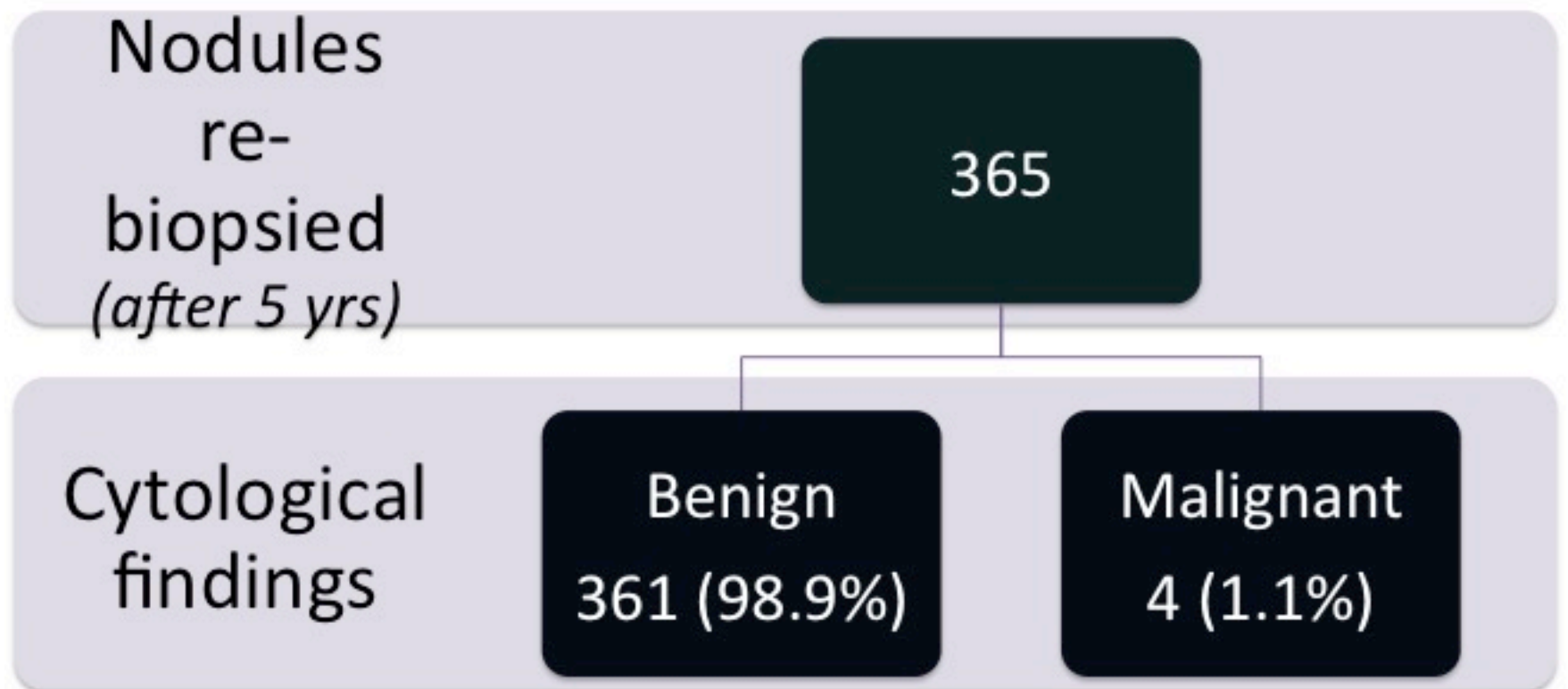
Growth and risk of thyroid cancer





Results (7)

Sensitivity of FNA



False negative results



In conclusione...

- Ad un follow-up di 5 anni quasi il 90% dei noduli rimangono stabili o si riducono
- Maggior rischio di crescita se dimensioni > 7.5 mm, noduli multipli, età ≤ 43 aa (OR 20.7); rischio alto anche se età > 43 aa e BMI > 28.6 (OR 13.4)
- Nuovi noduli solo nel 9% dei pazienti



In conclusione...

- Crescita non aumenta rischio di cancro
- La prevalenza di cancro è rara (7 casi, 0.7%): 5 in noduli preesistenti (2 aumentati di dimensioni), 1 "incidentale" dopo tiroidectomia, 1/93 noduli di nuova comparsa



In conclusione...

- ✓ La maggior parte dei noduli sono di piccole dimensioni e non avranno alcun impatto clinico in futuro
- ✓ La crescita di per sé non è un marker specifico di sospetta malignità
- ✓ L'ecografia combinata con il risultato citologico ha un ruolo determinante per distinguere i sottogruppi di pazienti a basso ed alto rischio (di malignità e crescita)