CONGRESSO CATARINENSE DE ENDOCRINOLOGIA E METABOLOGIA

Carcinoma Diferenciado de Tireoide: acompanhamento e armadilhas

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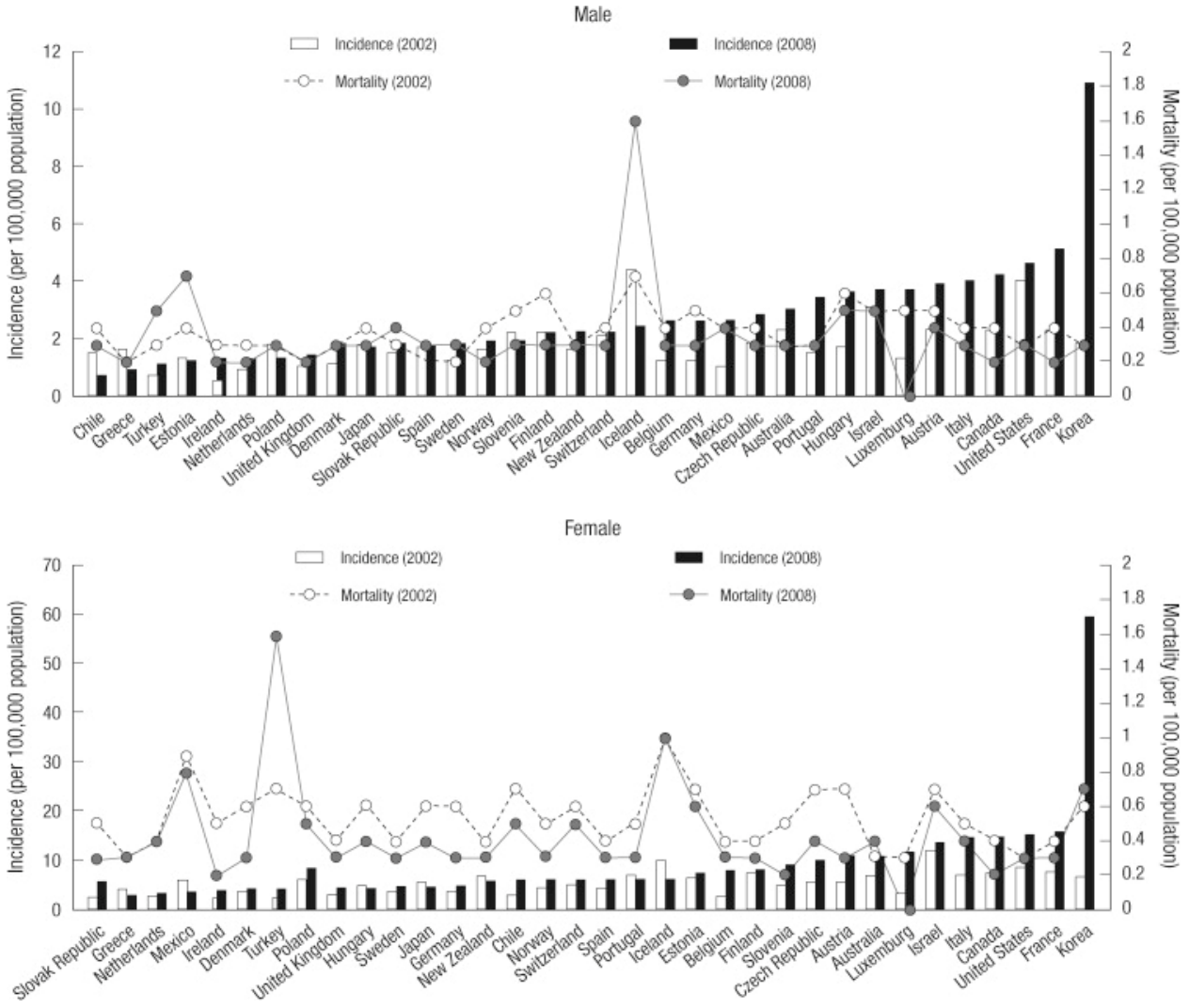
2019

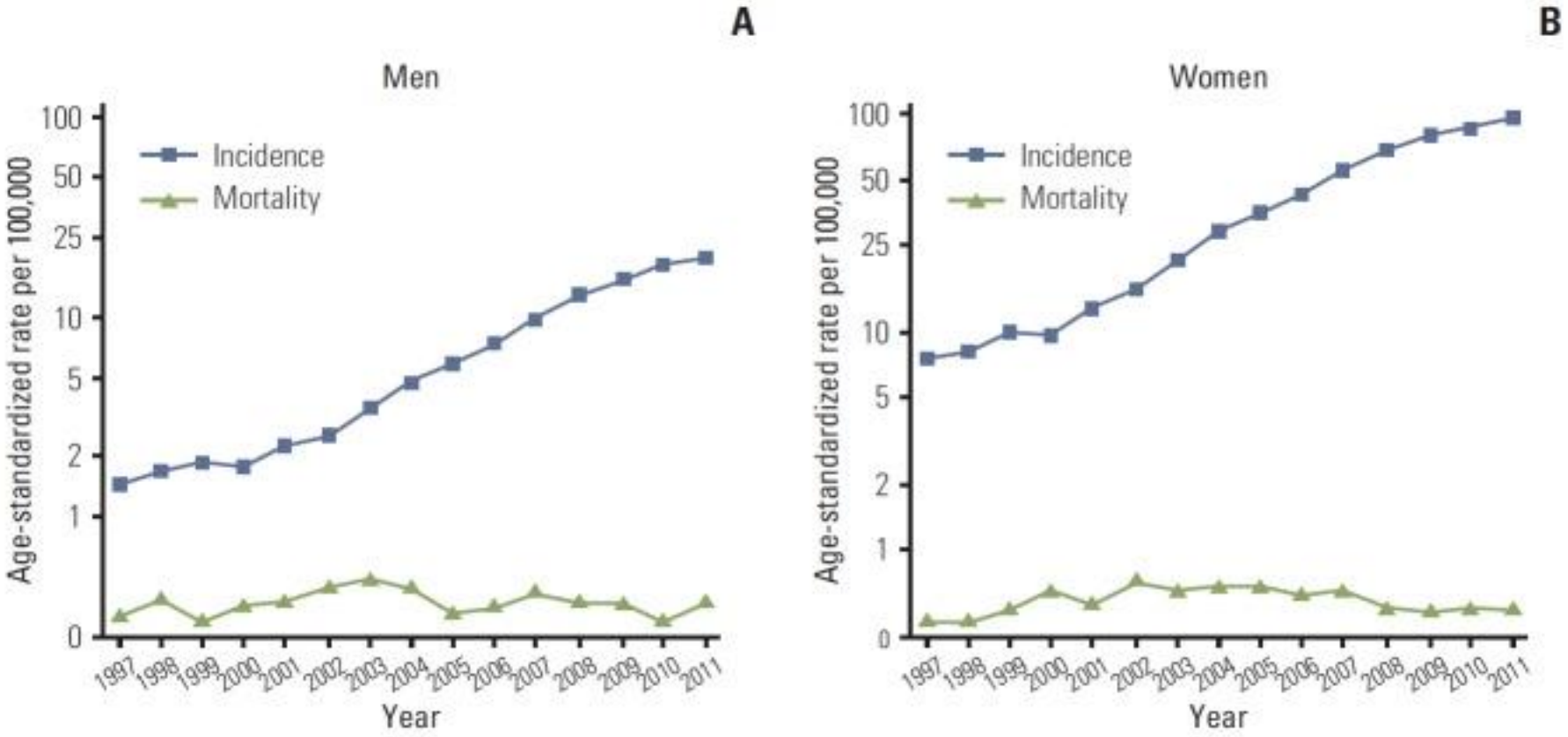
Roteiro

- Epidemiologia
- Sistemas de estratificação de risco
- Seguimento Clínico
- Armadilhas no seguimento clíncico

Incidência x Mortalidade CDT



Age-Period-Cohort Analysis of Thyroid Cancer Incidence in Korea



Sobrevida do CDT

Percent surviving at least 5 years

98.1%

2008-14 data from the National Cancer Institute's Surveillance, Epidemiology and End Results Program

Evolução na Estratificação de Risco

Características clinicopatológicas identificadas nos primeiros meses do diagnóstico

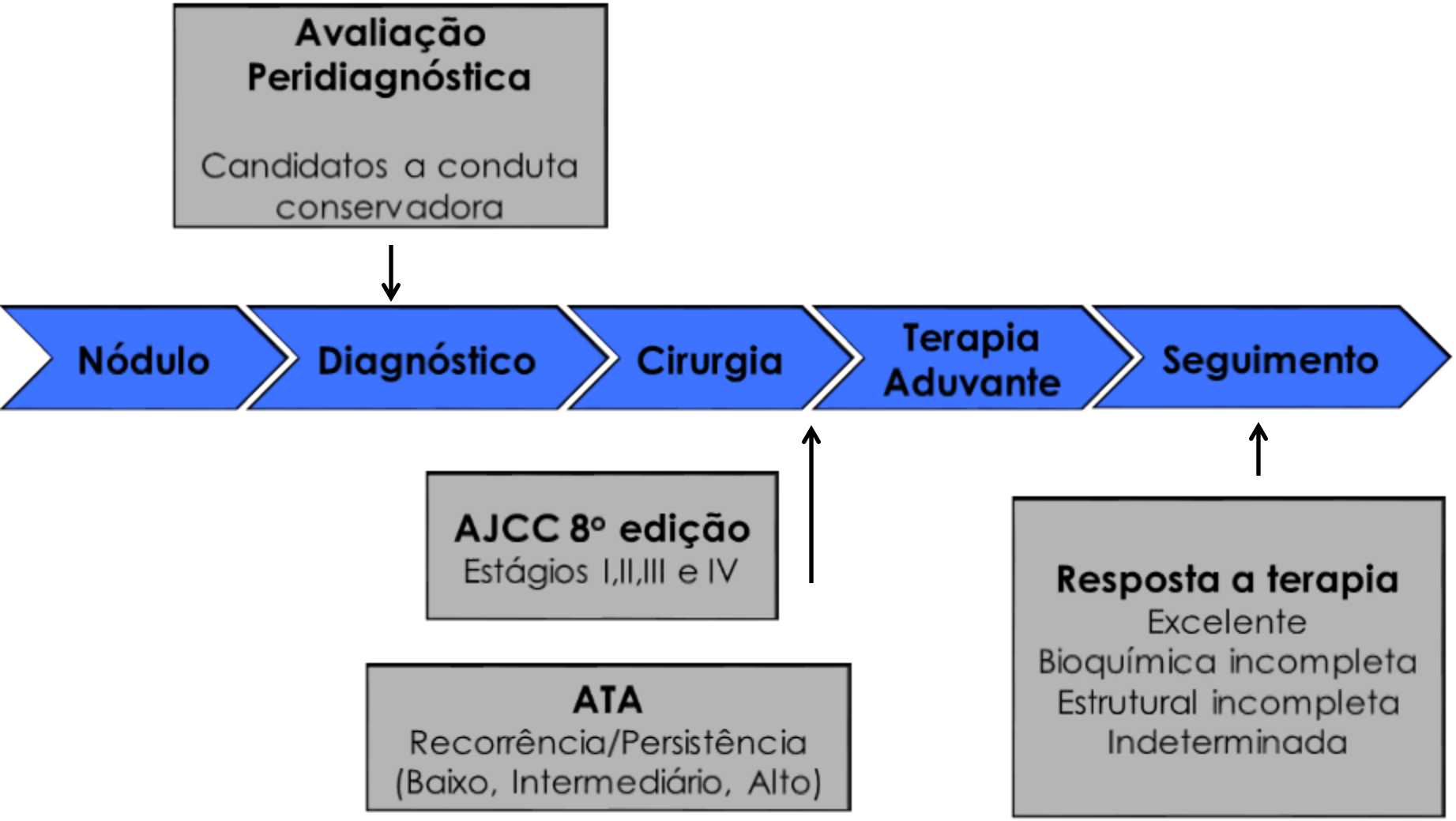
Risco de mortalidade/prognóstico

Evolução na Estratificação de Risco

- Avaliação atual inclui outros desfechos:
  - Risco de doença persistente após a terapia inicial
  - Risco de doença bioquímica ou estrutural recorrente
  - Probabilidade de remissão logo após a terapia inicial

Avaliação Dinâmica

Estratificação Risco CDT



Tuttle RM et al , J Clin Endocrinol Metab, 2019

AJCC/TNM 8th Edition (Mortalidade)

Updated American Joint Committee on Cancer/
Tumor-Node-Metastasis Staging System for Differentiated
and Anaplastic Thyroid Cancer (Eighth Edition):
What Changed and Why?

R. Michael Tuttle,[1] Bryan Haugen,[2] and Nancy D. Perrier[3]

T Category	*T Criteria*
TX	Primary tumor cannot be assessed
T0	No evidence of primary tumor
T1	Tumor ≤ 2 cm in greatest dimension limited to the thyroid
T1a	Tumor ≤ 1 cm in greatest dimension limited to the thyroid
T1b	Tumor > 1 cm but ≤ 2 cm in greatest dimension, limited to the thyroid
T2	Tumor > 2 cm but < 4 cm in greatest dimension limited to the thyroid
T3*	Tumor > 4cm limited to the thyroid, or gross extrathyroidal extension invading only strap muscles
T3a*	Tumor > 4 cm limited to the thyroid
T3b*	Gross extrathyroidal extension invading only strap muscles (sternohyoid, sternothyroid, thyrohyoid, or omohyoid muscles) from a tumor of any size
T4	Includes gross extrathyroidal extension into major neck structures
T4a	Gross extrathyroidal extension invading subcutaneous soft tissues, larynx, trachea, esophagus, or recurrent laryngeal nerve from a tumor of any size
T4b	Gross extrathyroidal extension invading prevertebral fascia or encasing carotid artery or mediastinal vessels from a tumor of any size
Note: All categories may be subdivided: (s) solitary tumor and (m) multifocal tumor (the largest tumor determines the classification).	

Tuttle et al, Thyroid. 2017 Jun;27(6):751-756.

AJCC/TNM 8th Edition- "N"

Updated American Joint Committee on Cancer/
Tumor-Node-Metastasis Staging System for Differentiated
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What Changed and Why?

R. Michael Tuttle,[1] Bryan Haugen,[2] and Nancy D. Perrier[3]

Definition of Regional Lymph Node (N)

N Category	*N Criteria*
NX	Regional lymph nodes cannot be assessed
N0	No evidence of regional lymph nodes metastasis
N0a*	One or more cytological or histologically confirmed benign lymph node
N0b*	No radiologic or clinical evidence of locoregional lymph node metastasis
N1*	Metastasis to regional nodes
N1a*	Metastasis to level VI or VII (pretracheal, paratracheal, or prelaryngeal/Delphian or upper mediastinal) lymph nodes. This can be unilateral or bilateral disease.
N1b*	Metastasis to unilateral, bilateral, or contralateral lateral neck lymph nodes (Levels I, II, III, IV, or V) or retropharyngeal lymph nodes

Tuttle et al, Thyroid. 2017 Jun;27(6):751-756.

AJCC/TNM 8th Edition- Estadiamento

Updated American Joint Committee on Cancer/
Tumor-Node-Metastasis Staging System for Differentiated
and Anaplastic Thyroid Cancer (Eighth Edition):
What Changed and Why?

R. Michael Tuttle,[1] Bryan Haugen,[2] and Nancy D. Perrier[3]

When age at diagnosis is…	*And T is…*	*And N is…*	*And M is…*	*Then the stage group is…*
< 55 yrs	Any T	Any N	M0	I
	Any T	Any N	M1	II
≥ 55 yrs	T1	N0/NX	M0	I
	T1	N1	M0	II
	T2	N0/NX	M0	I
	T2	N1	M0	II
	T3a/T3b	Any N	M0	II
	T4a	Any N	M0	III
	T4b	Any N	M0	IVA
	Any T	Any N	M1	IVB

Tuttle et al, Thyroid. 2017 Jun;27(6):751-756.

Risco de Recorrência/Persistência

Table 3
Comparison of risk of recurrent/persistent disease staging systems

Risk	ATA	ETA	LATS
Very low	—	All of the following: Unifocal <1 cm N0M0, no ETE	All of the following: Unifocal <1 cm N0M0, no ETE
Low	All of the following: Any size, intrathyroidal N0M0 All macroscopic tumor resected No ETE No aggressive histology No vascular invasion No ^{131}I uptake outside thyroid bed on the posttreatment scan, if performed	All of the following: Unifocal/multifocal 1–4 cm, intrathyroidal N0M0 No ETE No aggressive histology No vascular invasion No ^{131}I uptake outside thyroid bed on the posttreatment scan, if performed	All of the following: 1–4 cm intrathyroidal N0M0
Intermediate	Any of the following: N1 Minor ETE Tumor with aggressive histology Vascular invasion ^{131}I uptake outside thyroid bed on the posttreatment scan, if performed	—	—
High	Any of the following: Incomplete tumor resection Macroscopic ETE Distant metastases Inappropriate postoperative Tg	Any of the following: N1 >4 cm Macroscopic ETE Distant metastases	Any of the following: N1 >4 cm (>45 y) Macroscopic ETE (>45 y) Residual disease Distant metastases Aggressive histology

Momesso et al, Endocrinol Metab Clin North Am. 2014 Jun;43(2):401-21 2014

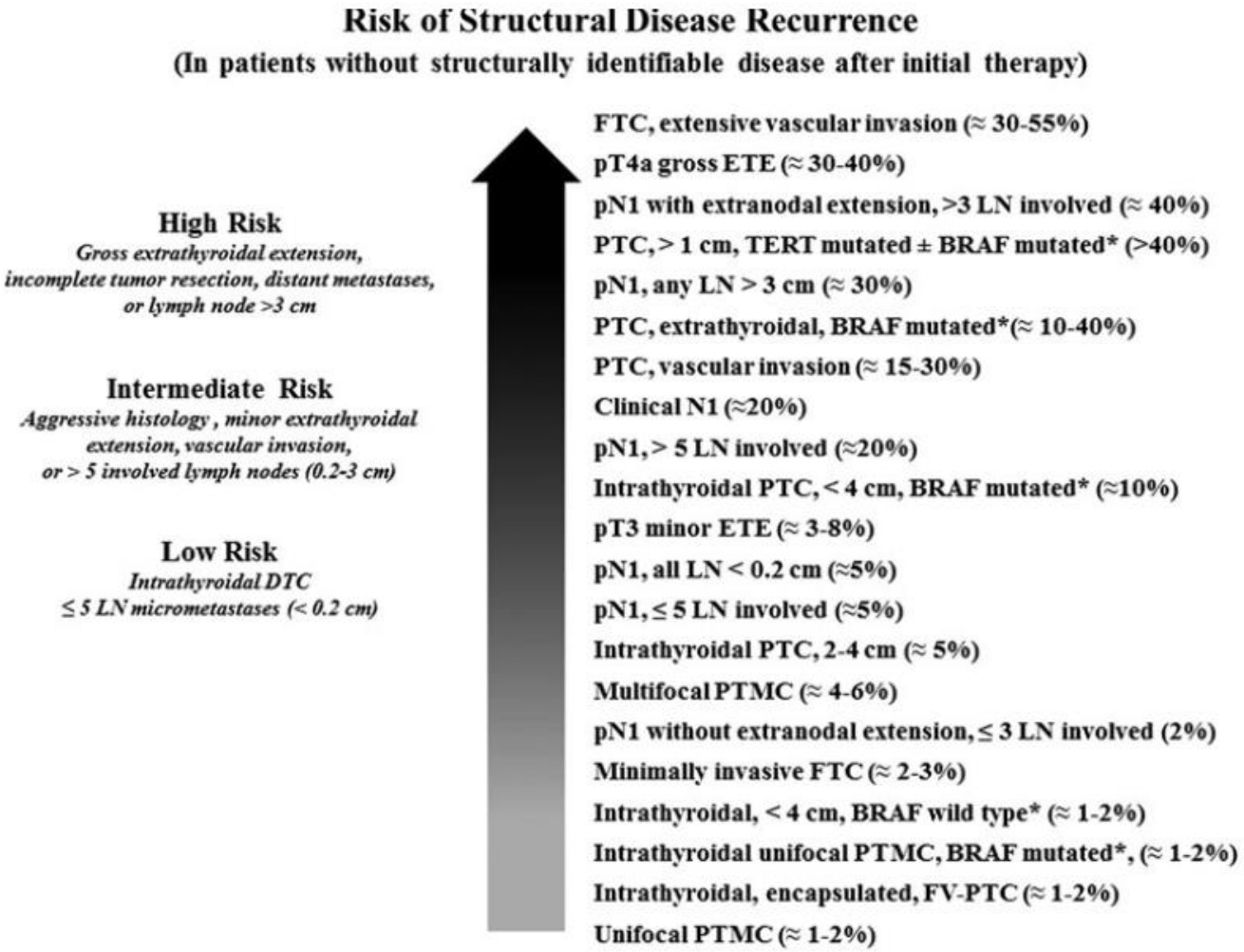
ATA Risk Stratification(2015)

TABLE 11. ATA 2009 RISK STRATIFICATION SYSTEM WITH PROPOSED MODIFICATIONS

ATA low risk	Papillary thyroid cancer (with all of the following): • No local or distant metastases; • All macroscopic tumor has been resected • No tumor invasion of loco-regional tissues or structures • The tumor does not have aggressive histology (e.g., tall cell, hobnail variant, columnar cell carcinoma) • If ^{131}I is given, there are no RAI-avid metastatic foci outside the thyroid bed on the first posttreatment whole-body RAI scan • No vascular invasion • Clinical N0 or ≤5 pathologic N1 micrometastases (<0.2 cm in largest dimension)[a] Intrathyroidal, encapsulated follicular variant of papillary thyroid cancer[a] Intrathyroidal, well differentiated follicular thyroid cancer with capsular invasion and no or minimal (<4 foci) vascular invasion[a] Intrathyroidal, papillary microcarcinoma, unifocal or multifocal, including *BRAF*^{V600E} mutated (if known)[a]
ATA intermediate risk	Microscopic invasion of tumor into the perithyroidal soft tissues RAI-avid metastatic foci in the neck on the first posttreatment whole-body RAI scan Aggressive histology (e.g., tall cell, hobnail variant, columnar cell carcinoma) Papillary thyroid cancer with vascular invasion Clinical N1 or >5 pathologic N1 with all involved lymph nodes <3 cm in largest dimension[a] Multifocal papillary microcarcinoma with ETE and *BRAF*^{V600E} mutated (if known)[a]
ATA high risk	Macroscopic invasion of tumor into the perithyroidal soft tissues (gross ETE) Incomplete tumor resection Distant metastases Postoperative serum thyroglobulin suggestive of distant metastases Pathologic N1 with any metastatic lymph node ≥3 cm in largest dimension[a] Follicular thyroid cancer with extensive vascular invasion (> 4 foci of vascular invasion)[a]

ATA, 2015

ATA Risk Stratification



ATA, 2015

Avaliação Dinâmica Risco

Estimating Risk of Recurrence in Differentiated Thyroid Cancer After Total Thyroidectomy and Radioactive Iodine Remnant Ablation: Using Response to Therapy Variables to Modify the Initial Risk Estimates Predicted by the New American Thyroid Association Staging System

R. Michael Tuttle,[1] Hernan Tala,[1] Jatin Shah,[2] Rebecca Leboeuf,[1] Ronald Ghossein,[3] Mithat Gonen,[4] Matvey Brokhin,[1] Gal Omry,[1] James A. Fagin,[1] and Ashok Shaha[2]

TABLE 7. IMPACT OF RESPONSE TO INITIAL THERAPY ASSESSMENT ON INITIAL ESTIMATES OF RISK

	ATA initial risk of recurrence classification (n = 471)		
	Low	*Intermediate*	*High*
Initial estimate of risk of persistent structural or recurrent disease	3% (3/104)	18% (43/241)	66% (83/126)
Modified estimate of risk of persistent structural or recurrent disease based on response to initial therapy			
Excellent response ($n = 159$)	2% (1/59)	2% (2/86)	14% (2/14)
Acceptable response ($n = 95$)	0% (0/30)	0% (0/56)	0% (0/9)
Incomplete response ($n = 217$)	13% (2/15)	41% (41/99)	79% (81/103)

Tuttle MR et al, Thyroid. 2010 Dec;20(12):1341-9

Estadiamento Dinâmico do CDT

- RESPOSTA EXCELENTE
- RESPOSTA BIOQUÍMICA INCOMPLETA
- RESPOSTA ESTRUTURAL INCOMPLETA
- RESPOSTA INDETERMINADA

Estadiamento Dinâmico do CDT

- **RESPOSTA EXCELENTE**
  - Nenhuma evidência de doença clínica, bioquímica ou estrutural

  (TG suprimida < 0.2ng/mL ou TG estimulada <1ng/mL)

- **RESPOSTA BIOQUÍMICA INCOMPLETA**
  - TG elevada ou AATG em ascenção, sem doença localizável

  (TG suprimida ≥ 1ng/mL ou TG estimulada ≥ 10ng/mL)

- **RESPOSTA ESTRUTURAL INCOMPLETA**
  - Persistência ou detecção de metástases locoregionais ou à distância, independente dos níveis de TG ou AATG

- **RESPOSTA INDETERMINADA**
  - Alterações bioquímicas ou estruturais inespecíficas

  (TG suprimida 0.2-1ng/mL ou TG estimulada 1-10ng/mL ou ATG estável ou em queda)

Atualização Avaliação Dinâmica

Update on Differentiated Thyroid Cancer Staging

Denise P. Momesso, MD[a], R. Michael Tuttle, MD[b,*]

Table 4
ATA initial risk stratification systems and clinical outcomes

ATA Risk	Initial Treatment	Study	NED (%)	Persistent/ Recurrent[a] (%)	Dead (%)
Low	TT and RAI	Tuttle et al,[5] 2010	86	14	0
		Castagna et al,[9] 2011	91	9	0
		Vaisman et al,[6] 2012	88	12	0
		Pitoia et al,[8] 2013	78	22	0
	TT or TL No RAI	Vaisman et al,[46] 2011	99	1	0
		Schvartz et al,[47] 2012	99	1	0
		Durante et al,[48] 2012	99	1	0
Intermediate	TT and RAI	Tuttle et al,[5] 2010	57	43	0
		Vaisman et al,[6] 2012	63	36	1
		Pitoia et al,[8] 2013	52	48	0
	TT or TL No RAI	Vaisman et al,[46] 2011	92	8	0
High	TT and RAI	Tuttle et al,[5] 2010	14	68	18
		Vaisman et al,[6] 2012	16	68	16
		Pitoia et al,[8] 2013	31	69	0[b]

Momesso et al, Endocrinol Metab Clin North Am. 2014 Jun;43(2):401-21 2014

Atualização Avaliação Dinâmica

Update on Differentiated Thyroid Cancer Staging

Denise P. Momesso, MD[a], R. Michael Tuttle, MD[b,*]

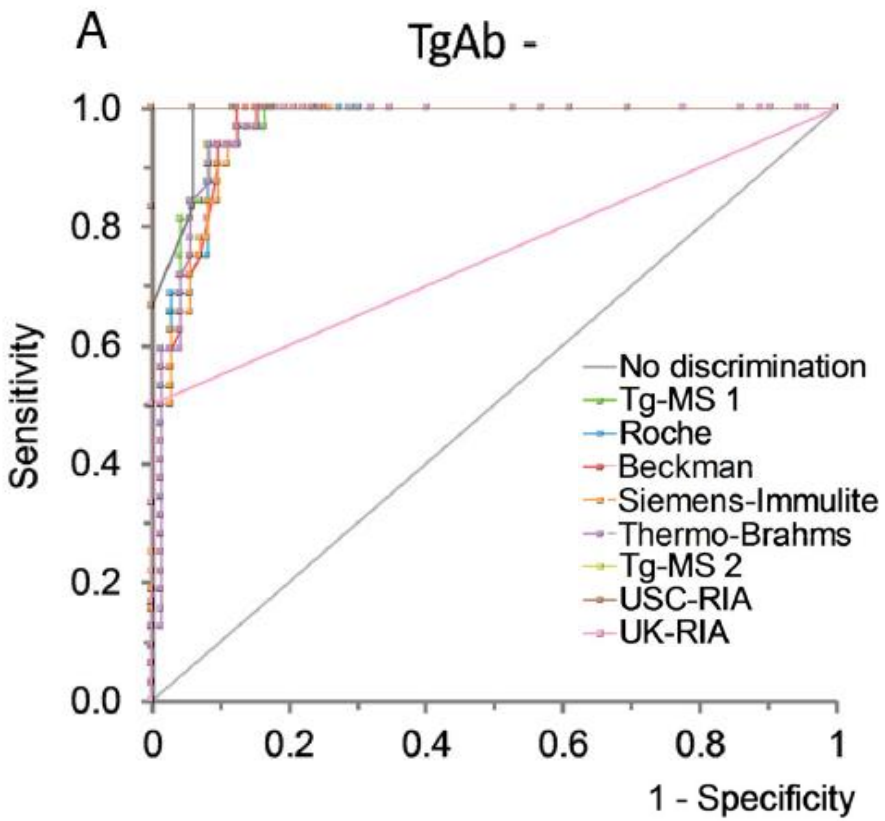
Resposta	TT + RAI	TT s/ RAI	Lobectomia
Excelente	TG não estimulada: <0.2 ng/mL ou TG estimulada <1ng/mL ATG indetectável Imagem negativa	TG não estimulada: <0.2 ng/mL ou TG estimulada <2ng/mL ATG indetectável Imagem negativa	TG estável, não estimulada <30ng/mL ATG indetectável Imagem negativa
Bioquímica Incompleta	TG não estimulada: >1 ng/mL ou TG estimulada > 10 ng/mL ou Aumento de TG e ATG Imagem negativa	TG não estimulada: >5 ng/mL ou TG estimulada > 10 ng/mL ou Aumento de TG e ATG Imagem negativa	TG não estimulada: >30 ou Aumento de TG e ATG Imagem negativa
Estrutural Incompleta	Doença estrutural, independente da TG /ATG	Doença estrutural, independente da TG /ATG	Doença estrutural, independente da TG /ATG
Indeterminada	TG não estimulada: 0.2-1 ng/mL ou TG estimulada 1-10ng/mL ou ATG estável/declínio Imagem/PCI inespecífico	TG não estimulada: 0.2-5 ng/mL ou TG estimulada 2-10ng/mL ou ATG estável/declínio Imagem/PCI inespecífico	ATG estável/declínio Imagem inespecífica

Momesso et al, Endocrinol Metab Clin North Am. 2014 Jun;43(2):401-21 2014

Armadilhas no seguimento do CDT

Tireoglobulina

- Variabilidade interensaio

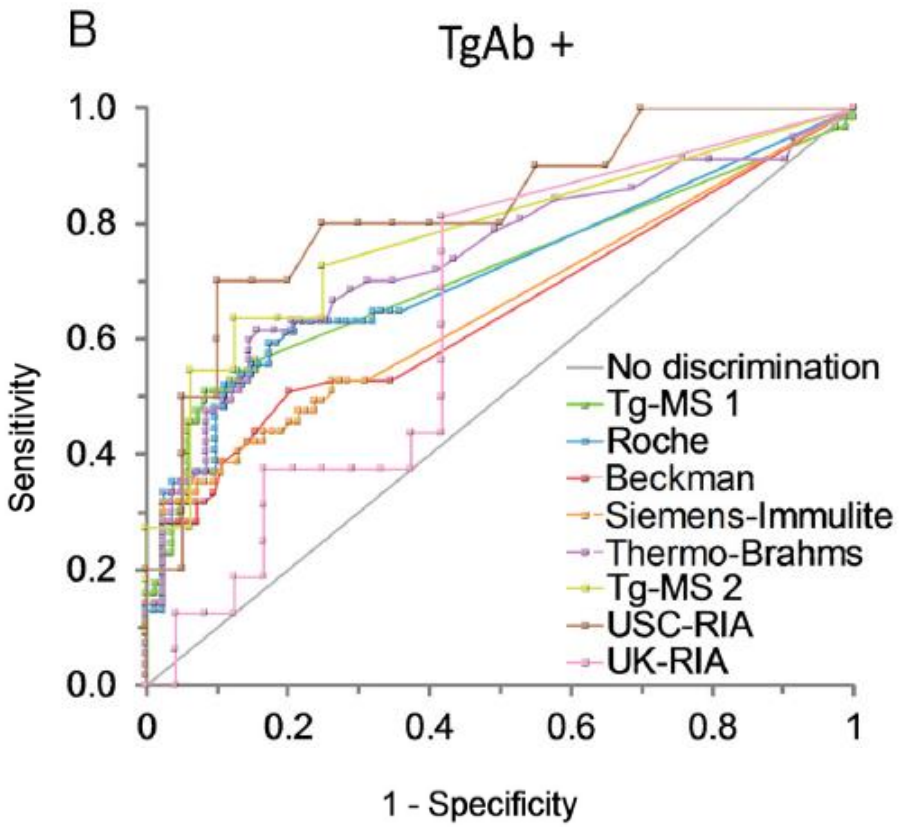


TgAb -	Cutoff assay FS* Sensitivity	Specificity
Tg-MS 1	100% (32/32)	84% (61/73)
Tg-MS 2	100% (6/6)	94% (16/17)
Beckman	100% (32/32)	79% (58/73)
Roche	100% (32/32)	74% (54/73)
Siemens Immulite	97% (31/32)	85% (62/73)
Thermo Brahms	100% (32/32)	75% (54/72)
USC-RIA	100% (6/6)	83% (5/6)
UK-RIA	100% (6/6)	100% (8/8)

Netzel et al, J Clin Endocrinol Metab. 2015 Aug;100(8):.

Tireoglobulina

- Presença de ATG +



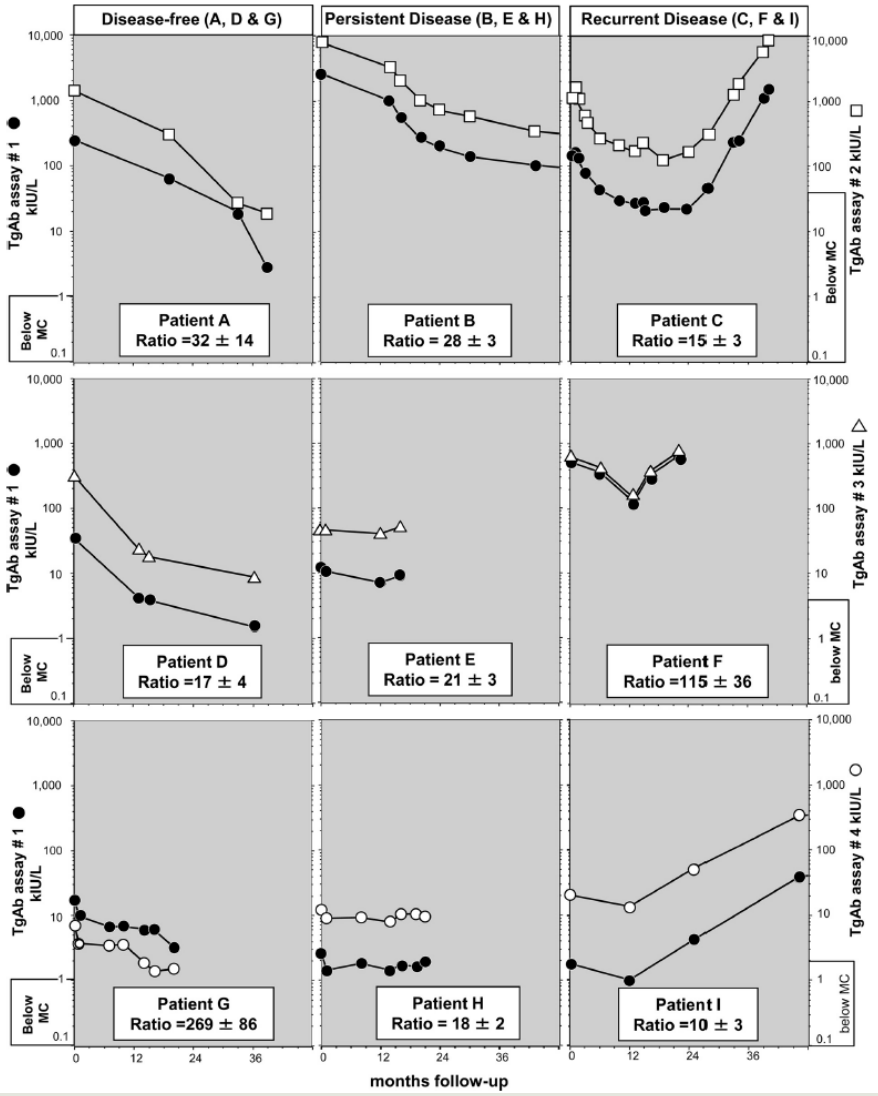
TgAb +	Cutoff assay FS* Sensitivity	Specificity
Tg-MS 1	56% (32/57)	85% (71/84)
Tg-MS 2	55% (6/11)	94% (15/16)
Beckman	53% (30/57)	65% (55/84)
Roche	63% (34/54)	77% (62/81)
Siemens Immulite	30% (16/57)	90% (76/84)
Thermo Brahms	68% (39/57)	71% (59/83)
USC-RIA	60% (9/15)	45% (9/20)
UK-RIA	81% (13/16)	58% (14/24)

Netzel et al, J Clin Endocrinol Metab. 2015 Aug;100(8):.

ATG- Diferentes Ensaios Laboratoriais

Clinical Utility of Thyroglobulin Antibody (TgAb) Measurements for Patients with Differentiated Thyroid Cancers (DTC)

Carole A. Spencer



Anti-Tireoglobulina

CLINICAL CONSEQUENCES OF A CHANGE IN ANTI-THYROGLOBULIN ANTIBODY ASSAYS DURING THE FOLLOW-UP OF PATIENTS WITH DIFFERENTIATED THYROID CANCER

Diane Donegan, MB, CHB[1]; Bryan McIver, MD, PhD[2]; Alicia Algeciras-Schimnich, PhD[3]

Table 1
TgAb Status Using the Beckman Access and Roche Elecsys Assays

	Beckman Access (IU/mL)	
Roche Elecsys (IU/mL)	Positive (≥4)	Negative (<4)
Positive (≥22)	111	117
Negative (<22)	7	1,222

ATG como marcador tumoral

Thyroglobulin antibody (TgAb) methods – Strengths, pitfalls and clinical utility for monitoring TgAb-positive patients with differentiated thyroid cancer

Carole Spencer, Shireen Fatemi

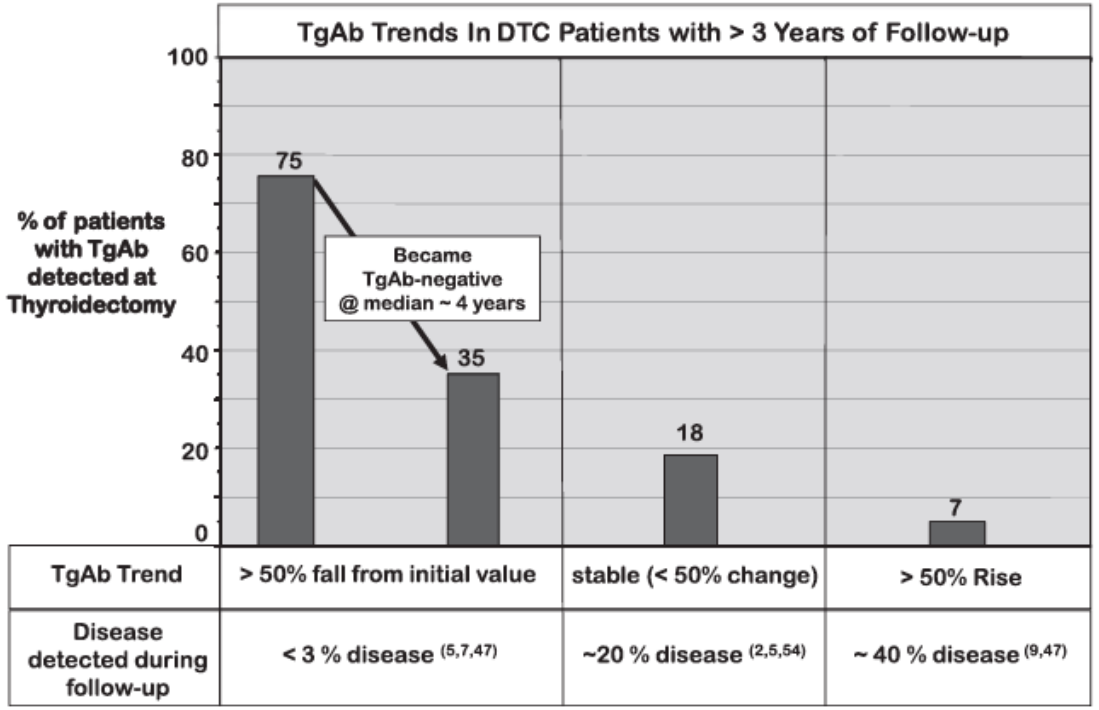


Fig. 4. Trends in TgAb concentrations versus the risk of having persistent or recurrent disease detected during follow-up of DTC patients with detectable TgAb at the time of initial treatment.

Elevações esperadas de Tg e ATG

Clinical Utility of Thyroglobulin Antibody (TgAb) Measurements for Patients with Differentiated Thyroid Cancers (DTC)

Carole A. Spencer

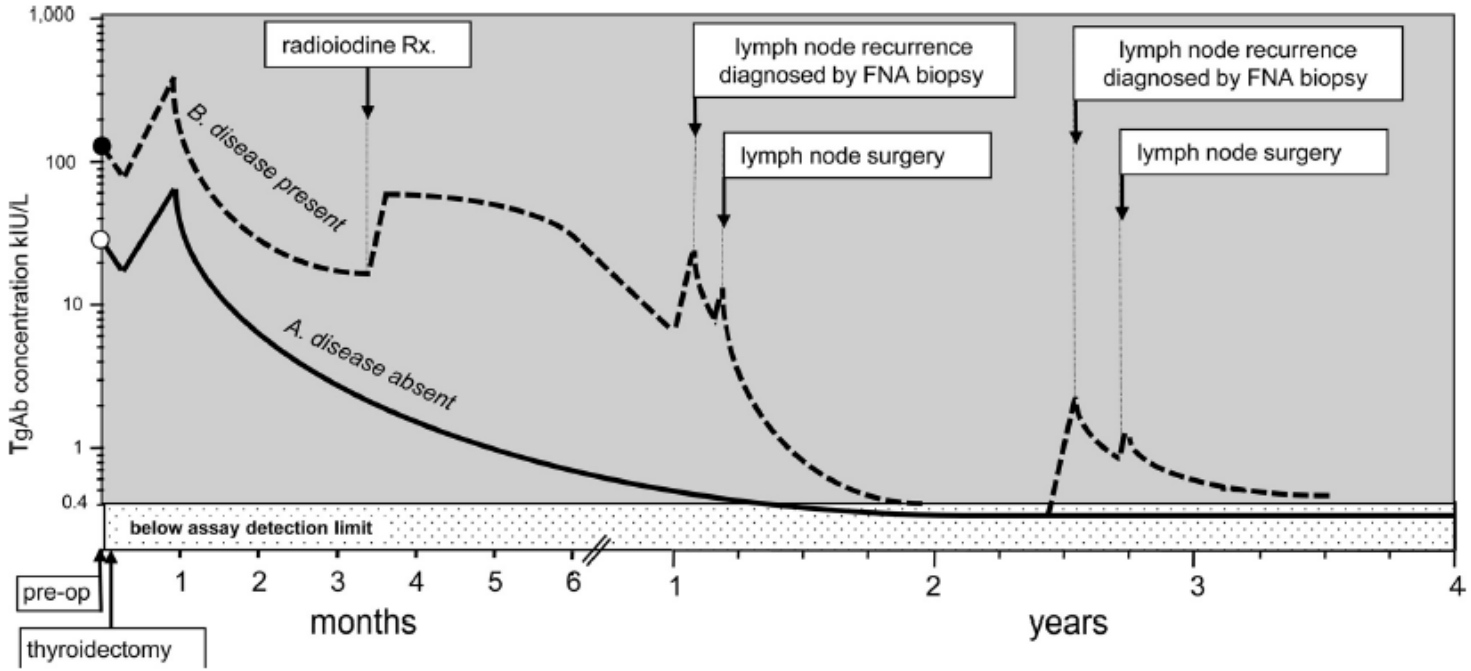


FIG. 1. Typical changes in TgAb trends after thyroidectomy in patients rendered disease-free by surgery (pattern A) *vs.* patients with persistent/recurrent disease (pattern B). TgAb concentrations may rise or become detectable *de novo* in response to increases in Tg antigen after thyroidectomy, lymph node recurrence(s), lymph node resection(s) FNA biopsy of metastatic lymph nodes, or radioiodine therapy.

Valores elevados de Tg

- **RESPOSTA EXCELENTE**
  - Nenhuma evidência de doença clínica, bioquímica ou estrutural

  (TG suprimida < 0.2ng/mL ou TG estimulada <1ng/mL)

- **RESPOSTA BIOQUÍMICA INCOMPLETA**
  - TG elevada ou AATG em ascenção, sem doença localizável

  (TG suprimida ≥ 1ng/mL ou TG estimulada ≥ 10ng/mL)

- **RESPOSTA ESTRUTURAL INCOMPLETA**
  - Persistência ou detecção de metástases locoregionais ou à distância, independente dos níveis de TG ou AATG

- **RESPOSTA INDETERMINADA**
  - Alterações bioquímicas ou estruturais inespecíficas

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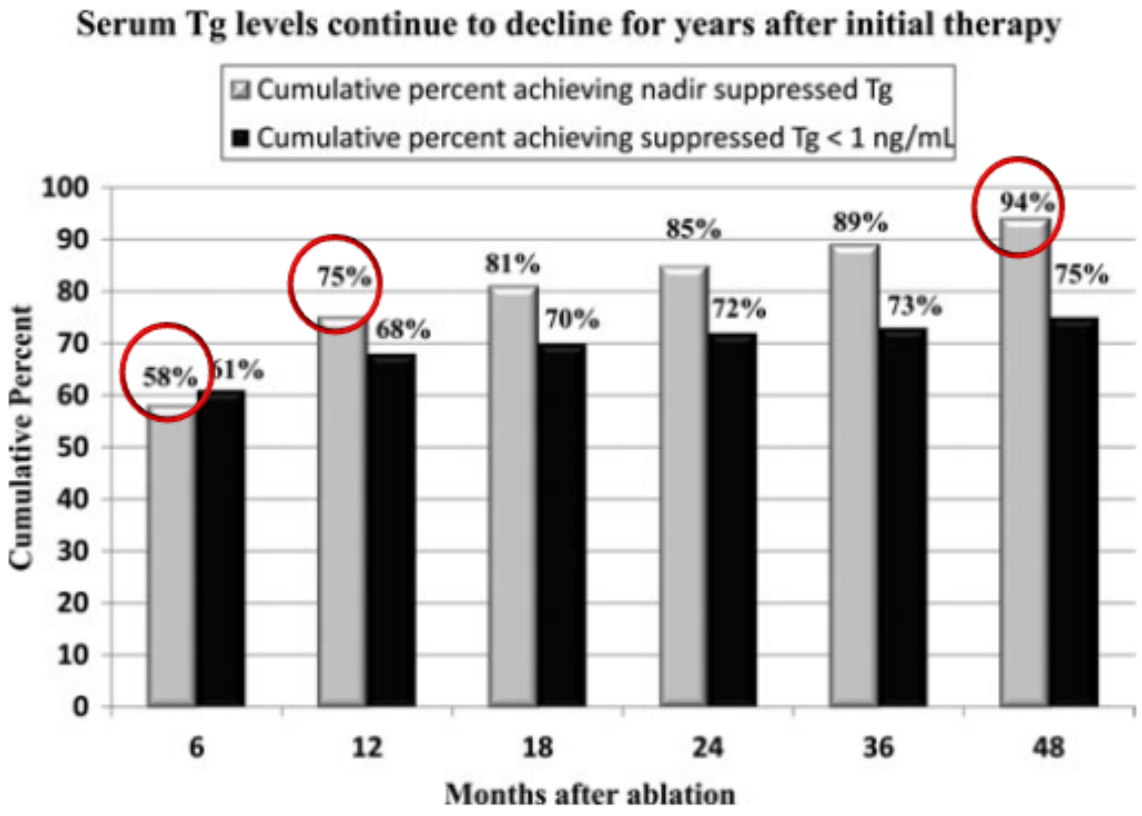
- **RESPOSTA INDETERMINADA**
  - Alterações bioquímicas ou estruturais inespecíficas

  (TG suprimida 0.2-1ng/mL ou TG estimulada 1-10ng/mL ou ATG estável ou em queda)

Tireoglobulina

Even Without Additional Therapy,
Serum Thyroglobulin Concentrations Often Decline for Years
After Total Thyroidectomy and Radioactive Remnant Ablation
in Patients with Differentiated Thyroid Cancer



Padovani et al, Thyroid. 2012 Aug;22(8):778-83.

USG cervical

2013 European Thyroid Association Guidelines for Cervical Ultrasound Scan and Ultrasound-Guided Techniques in the Postoperative Management of Patients with Thyroid Cancer

L. Leenhardt[a] M.F. Erdogan[b] L. Hegedus[c] S.J. Mandel[d] R. Paschke[e]
T. Rago[f] G. Russ[a]

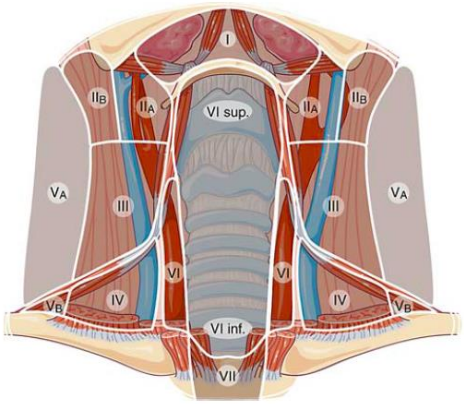


Table 2. Reported range of the diagnostic value of US signs for the detection of cervical metastatic lymph nodes from thyroid carcinoma

Sign	Sensitivity, %	Specificity, %	NPV, %	PPV, %	Accuracy, %	% of normal LN with the sign
Microcalcifications	5–69	93–100	33–60	88–100	56–72	0
Cystic aspect	10–34	91–100	30–66	77–100	48–65	0
Peripheral vascularization	40–86	57–93	31–70	77–80	54–71	1–18
Hyperechogenicity	30–87	43–95	38–84	66–96	56–90	4–17
Round shape	37	70	45	63		4–36
Hilum present	0–0.5					29–48
Absent vascularization	0					33–36

USG cervical

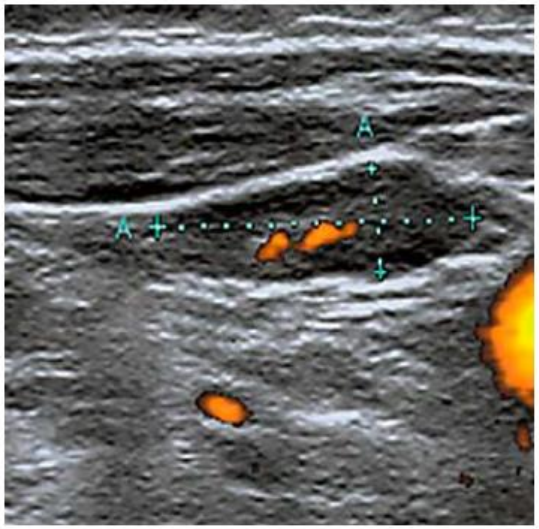


Fig. 3. Normal lymph node.

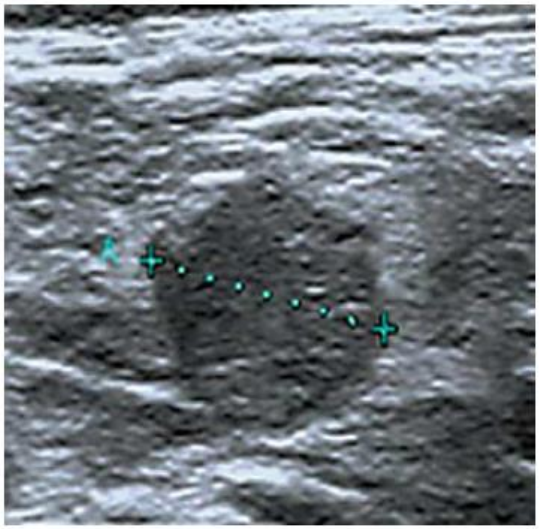


Fig. 4. Indeterminate cervical lymph node: absence of hilum and round shape.

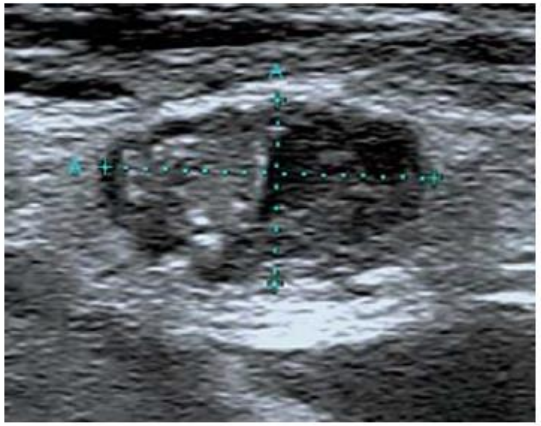


Fig. 5. Cervical lymph node metastasis.

NORMAL:
- Hilo preservado
- Formato oval
- Vascularização hilar ou ausente
- Sem outras carac suspeitas

INDETERMINADO:
- Ausência de hilo
+
- Formato arredondado
- > ou = 8 mm nível II ou > ou = 5mm nível III e IV
- Vascularização central

SUSPEITO P/ MALIGNIDADE:
- Microcalcificações
- Aparência parcialmente cística
- Vascularização periférica ou difusa
- Hiperecoico

PCI- Resultados falso-positivos

Mucoepidermoid Parotid Gland Tumor Found on Follow-up Radioiodine Scan for Differentiated Papillary Thyroid Cancer

Chinna Naik and Sandip Basu

CASE REPORT Open Access

Selectively false-positive radionuclide scan in a patient with sarcoidosis and papillary thyroid cancer: a case report and review of the literature

Nicole L Lebo[1], Francois Raymond[2] and Michael J Odell[1*]

Incidental Gallbladder Cancer Visualized From Posttreatment 131I Whole-Body Scan

Yoch Anongpornjossakul;Chirawat Utamakul;Wichana Chamroonrat;Arpakorn Kositwattanarerk;Kanungnij Thamnirat;Chanika Sritara;

PCI- Resultados falso-positivos

Pitfalls and Limitations of Radionuclide Imaging in Endocrinology

Kanhaiyalal Agrawal, MBBS, MD,[*] Abdulredha A.H. Esmail, MD,[†]
Gopinath Gnanasegaran, MBBS, MSc, MD, FRCP,[*]
Shaunak Navalkissoor, FRCP,[‡] Bhagwant Rai Mittal, MD, DNB, FICN, FAMS,[§]
and Ignac Fogelman, BSc, MD, FRCP[*,‖]

Table 5 Potential False-Positive and False-Negative Causes on the Whole-Body Radiolodine Scintigraphy

False-Positive Causes	False-Negative Causes
External surface contamination through saliva, sweat, and vomit	Loss of differentiation of thyroid cancer cells
Ectopic normal thyroid tissue	Microscopic metastases
Physiological uptake in lacrimal and salivary glands, eutopic or ectopic gastric mucosa, gastrointestinal tract, breast, liver, and urinary tract excretion	Improper patient preparation before WBS (eg, iodine contamination, TSH $<$ 30 mIU/L)
Neoplasms of nonthyroidal origins (gastric adenocarcinoma, meningioma, lung cancers, teratomas, uterine fibromyoma, ovarian adenocarcinoma, and ovarian cystadenoma)	Defective iodine-trapping mechanism

Agrawal K et al, Semin Nucl Med. 2015 Sep;45(5):440-57

Considerações Finais

- Um aumento na incidência do CT tem sido descrito em todo o mundo, principalmente microcarcinomas e sem impacto significativo da mortalidade;
- A visão atual de estratificação de risco começa desde a avaliação do nódulo tireoidiano até a resposta ao tratamento e seguimento clínico;
- Em pacientes com ATG+, a TG não pode ser considerada inicialmente como marcador tumoral;
- Na presença de ATG+, mudanças nos valores de ATG (mesmo ensaio) representam um melhor marcador tumoral do que os ensaios imunométricos de Tg

- Valores persistentes de ATG + ou aumento nos níveis de ATG devem ser apropriadamente investigados;
- Deve-se considerar as situações em que se espera um aumento nos valores de TG e/ou ATG não relacionado a progressão tumoral;
- Valores elevados de Tg e /ou ATG sem doença estrutural identificada, deve-se considerar o acompanhamento conservador sem terapia adjuvante;
- Correlacionar os achados do USG cervical com a estratificação de risco e resposta ao tratamento.

Obrigada!

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