Hôpitaux Universitaires Paris Centre

COCHIN
BROCA
HÔTEL-DIEU

Prise en charge des nodules indéterminés de Bethesda

Terminologie de Bethesda: analyse critique des résultats

B.Cochand-Priollet

Club Thyroïde Ile de France
28 juin 2014

Bethesda 2007

9 Sessions

- Epidémiologie
- Clinique et ex cliniques/biologiques
- Ex radiologiques
- Indications de ponction
- Techniques de ponction
- Techniques cytologiques
- Techniques ancillaires
- Terminologie
- CAT

Bethesda 2007

Bethesda Terminologie 2010

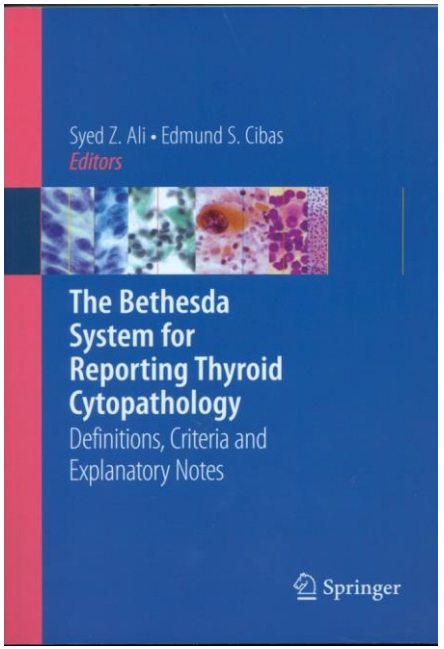
- **2007/2009/2010**
- **Recommandée par**

HAS, SFE, EFCS

- **Nombreux pays européens(Croatie,**

Finlande, Espagne, Grèce, Portugal,Tchèquie,Turquie……)

S F C C



Cytopathology 2010;21:86-92
Ann Pathol 2012; 3:177-83
DMEV 2010;13:191-5

Catégories diagnostiques de BSRCT

Catégories diagnostiques	Risque de malignité (%)	Attitude thérapeutique
Non diagnostique	?	Seconde ponction échoguidée dans un délai de 3 à 6 mois
Bénin	0 - 3	Surveillance clinique, échographique dans un délai de 6 à 18 mois pendant 5 ans
Lésion folliculaire de signification indéterminée	5 - 15	Seconde ponction dans un délai de 6 mois
Néoplasme folliculaire et néoplasme à cellules oncocytaires	15 - 30	Contrôle chirurgical (Lobectomie)
Suspect de malignité	60 – 75	Thyroïdectomie subtotale ou totale
Malin	97 - 99	Thyroïdectomie totale

Bethesda : Objectifs

Comparer les données entre différents services/pays

Améliorer la reproductibilité inter et intra observateurs

Faciliter la communication entre pathologistes, cliniciens, chirurgiens et radiologues

Optimiser la cytopathologie thyroïdienne :
Epidémiologie – Pathologie
Gestion des patients

Comparer les données entre différents services/pays

Auteurs	Nombre de cas	Non diagn	Bénin	LFSI ou ASI	NF/ NFHC	SM	Malin
Theoharis et al 2009	3207	11.1%	73.8%	3%	5.5%	1.3%	5.2%
Broome et al 2011	282	4%	48%	29% (20%)	12% (36%)	10%	11%
Crowe et al 2011	110	1.8%	31.8%	40% (18.2%)	14.6% (18.8%)	0%	11.8% (100%)
Vickie et al 2011	3080	18.6% (8.9%)	59% (1.1%)	3.4% (17%)	9.7% (25.4%)	2.3% (70%)	7% (98.1%)
Cochand-Priollet et al 2009/2010	2277	14.1% (0.6%)	64.9% (0.2%)	9.2% (17.2%)	5.6% (9%FN/ 25%FNHC)	4.2% (66%)	2% (100%)
Bethesda		<15% ?	60% 0 à 3%	<7% 5 à 15%	6-11% 15 à 30%	2-8% 60 à 75%	3-7% 97 à 99 %

Comparer les données entre différents services/pays

Auteurs	Nombre de cas	Non diagn	Bénin	LFSI ou ASI	NF/ NFHC	SM	Malin
Mastorakis et al Cytopathology 2012	500	NA	49%	9.4% (23.4%)	1.2%	10.6%	26.8% (100%)
	500	NA	72.2%	5% (8%)	2.2%	3.2%	12.2% (100%)
Elsheikh et al 2012	1382	20.1%	39% (3%)	27.2% (6%)	8.4% (22%)	2.6% (56%)	2.7% (100%)
Firat P et al 2012	764	11.7%	64.1%	9.8% (36%)	3.7% (45%)	3.5% (100%)	7.2% (100%)
Mondal SK et al 2013	1020	1.2% (0%)	87.5% (4.5%)	1% (20%)	4.2% (30.6%)	1.4% (75%)	10% (97.8%)
Park JH et al 2014	1730	13.3% (35.3%)	40.6% (5.6%)	9.1% (69%)	0.4% (50%)	19.3% (98.7%)	17.3% (98.9%)
Bethesda		<15% ?	60% 0 à 3%	<7% 5 à 15%	6-11% 15 à 30%	2-8% 60 à 75%	3-7% 97 à 99 %

Comparer les données en France

Auteurs	Nombre de cas	Non diagn	Bénin	LFSI ou ASI	NF/ NFHC	SM	Malin
Royer B et al 2012	9970	4%	74%	10.5%	6% (14%)	3%	2.5%
Cochand-Priollet B et al 2012	2210	14.3%	65.5%	11% (23.6%)	4.9% (15.2%)	2.3% (58.7%)	2% (100%)
Lacoste-Collin L et al 2012	1317	31.6%	48%	7.8% (18.5%)	7% (22.2%)	3% (55.6%)	2.6% (100%)
Bethesda		<15% ?	60% 0 à 3%	<7% 5 à 15%	6-11% 15 à 30%	2-8% 60 à 75%	3-7% 97 à 99 %

- **BSRTC autorise les comparaisons**
- **Fait ressortir les « insuffisances » au niveau des cytopathologistes ou des préleveurs**
- **Epidémiologie du K de la thyroïde**

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Pathak P Diagn Cytopathol 2014

- **415 cas indéterminés**
- **3 lecteurs**
- **Reclasser en BSRTC**
- **Fleiss'kappa score: 0,6561**

κ	Interpretation
< 0	Désaccord
0.0 — 0.20	Accord très faible
0.21 — 0.40	Accord faible
0.41 — 0.60	Accord modéré
0.61 — 0.80	Accord fort
0.81 — 1.00	Accord presque parfait

Améliorer la reproductibilité inter et intra observateurs

Ali SZ Acta Cytol 2013

- Meta-analyse NFHC
- 47 349 cas/14 publications post BSRTC
- 13024 cas/5 publications pré BSRTC

- **Résultats:**

nb de cas 6.1 à 7.4%;
CC: 55 à 61%;
%K: 22 à 28%

Olson MT Acta Cytol 2014

- Meta-analyse SM
- 50 192 cas/12publications post BSRTC
- 51 863 cas/13 publications pré BSRTC

Table 2. Summary of prospective studies in the pre- and post-TBSRTC periods

	SPTC rate	Surgical follow-up rate of SPTC	Malignant rate
Pre-TBSRCT studies [14, 16, 18, 19, 23]	4.5% (537/12,041)	82.9% (445/537)	62.5% (278/445)
Post-TBSRCT studies [9, 11, 30]	3.1% (341/11,175)	84.2% (287/341)	80.5% (231/287)
p	<0.00001	0.61508	<0.00001

Améliorer la reproductibilité inter et intra observateurs

CYTOLOGICAL CRITERIA and Risk of malignancy	AA Renshaw Cancer Cytopathol 2011	MH Luu Acta Cytol 2011	MT Olson Acta Cytol 2011	S Onder Cytopathol 2013
Microfollicular architecture but sparse cellularity	21-34%		27%	6.9%
Predominant oncocytic cells and low cellularity				0%
Predominant oncocytic cells and goiter or Hashimoto				
Cytological atypias suggesting papillary carcinoma	39%	32.3%	48%	28%
Atypical « cyst lining cells »				
Cytological atypias	50%			22%
Cytological atypias due to technical artifact				
Abnormal lymphocytic population				
% FLUS/AUS/% malignant	8%/25%	3.2%/26%	3.3%/32%	6.7%/18.9%

Critères cytologiques	820 critères	
I. Architecture micro-folliculaire	24,5%	6,9% - 34% dans la littérature
II. Important population oncocytaire avec une faible cellularité	3,6%	
III. Atypies liées à des artéfacts de préparation	0%	Absent en milieu liquide
IV. Importante population oncocytaire avec une riche cellularité pouvant s'intégrer dans un goitre ou une thyroïdite	2%	
V. Atypies cytonucléaires pouvant suggérer un carcinome papillaire mais un contingent de cellules vésiculaires bénignes	34%	28% – 58% dans la littérature
VI. Atypies pouvant suggérer des cellules en bordure de kyste	0%	Identifiable en milieu liquide
VII. Atypies cytologiques	22,1%	22% - 50% dans la littérature
VIII. Population lymphocytaire atypique	0%	Recrutement-dépendant
IX. Autre : cellules géantes, faible cellularité, absence de colloïde	13,8%	Importance de la qualité du prélèvement

LFSI: 11% dont 23.6% K

La catégorie des LFSI n'est pas un « fourre tout »

Améliorer la reproductibilité inter et intra observateurs

- **Meilleure classification pour les catégories indéterminées III, IV et V**
- **Application de critères stricts pour la catégorie III**
- **Reproductibilité dans cette catégorie**

Bethesda : Objectifs

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In Germany, about 59 000 thyroid operations are performed each year for uni- or multinodular goiter, most of them for diagnostic purposes. The rate of detection of thyroid cancer in such operations is relatively low, at 1:15.

- **Augmentation notable du % de cancers dans les thyroïdes opérées (14% à 50%)**
- **Augmentation de la spécificité 50% cat IV et V; 100% cat VI**

Kocjan G Acta Cytol 2011

- **Combinaison TI-RADS/BSRTC**
- **Score Ti-RADS 3 et 4A combinés avec Cat III BSRTC: VNP: 90%**
- **Score TI-RADS 4B et 5 combinés avec Cat III, IV et V BSRTC: risque de malignité élevé > 75%**

Maia FF Clin Endocrinol 2014

Int J Surg. 2014 May 22. pii: S1743-9191(14)00112-5. doi: 10.1016/j.ijsu.2014.05.013. [Epub ahead of print]

Controversies in the surgical management of thyroid follicular neoplasms. Retrospective analysis of 721 patients.

Conzo G[1], Calò PG[2], Gambardella C[3], Tartaglia E[3], Mauriello C[3], Della Pietra C[3], Medas F[2], Cruz RS[2], Podda F[2], Santini L[3], Troncone G[4].

Author information

Abstract

The most appropriate surgical management of "follicular neoplasm/suspicious for follicular neoplasm" lesions, is still controversial. Analysing and comparing the experience of two units for endocrine surgery, we retrospectively evaluated 721 patients, surgically treated after a follicular neoplasm diagnosis. Total thyroidectomy was routinely performed in one Institution, while in the other one it was selectively carried out. The main criteria leading to hemythyroidectomy were a single nodule, the age ≤45 years, the absence of thyroiditis or clinical/intraoperative suspicion of malignancy. Total thyroidectomy was performed in 402/721 patients (55.7%), hemythyroidectomy in 319/721 cases (44.2%) and a completion thyroidectomy in 51/319 cases (15.9%). The overall malignancy rate was 24% (176/721 patients), respectively 16% (51/319 patients) following hemythyroidectomy, and 31% (125/402 patients) following total thyroidectomy. Definitive recurrent laryngeal nerve paralysis and permanent hypoparathyroidism were not reported in hemythyroidectomy patients in which lower mean hospitalization and costs were observed. Considering the low-risk of follicular neoplasm solitary lesions, hemythyroidectomy is still the safest standard of care with lower hospitalization and costs. In case of multiglandular disease or thyroiditis, that might be associated with a higher risk of cancer, total thyroidectomy should be recommended. Further investigation is warranted to achieve a better preoperative follicular neoplasm diagnostic accuracy in order to reduce the amount of unnecessary surgical operations with a diagnostic aim.

721 patients

Lobectomie indiquée : nodule unique; absence de TL; absence de signes cliniques -Rx de malignité (K:16%)

Thyroïdectomie totale indiquée: TH multinodulaire; TL; Signes suspects de malignité (K: 31%)

Bethesda : Objectifs

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Réticences et critiques

Pathologe. 2012 Jul;33(4):324-30. doi: 10.1007/s00292-012-1575-y.

[Bethesda classification of fine needle punctures of the thyroid. Much ado about nothing really new?].

[Article in German]

Schäffer R[1], Schmid KW, Tötsch M.

Author information

Abstract

The Bethesda system for reporting thyroid cytopathology was published in 2008 (Baloch et al. 2008, Cytojournal 5:6; Baloch et al. 2008, Diagn Cytopathol 36:425-437) offering a classification system which is closely related to clinical data. The aim was to ensure adequate terminology without risk of errors in understanding, to advise clinicians concerning therapeutic options in relationship to cytological diagnoses as well as to facilitate the comparison of cytology data at national and international levels. However, mainly due to specific US American (both medical and legal) demands, this classification system is not yet fully appreciated in most European countries. The reasons are various: (a) Criteria for representative material are much more restrictive than those commonly used and in Germany a higher number of (unnecessary) repunctures would be the consequence. (b) It remains doubtful whether the introduction of a new and rather heterogeneous category of "atypia of undetermined significance or follicular lesion of undetermined significance" would contribute to a substantial decrease of findings classified as "follicular neoplasia". Furthermore it is unlikely that clinicians would be willing to accept the recommended conservative approach with repuncture if a new diagnostic category is associated with a calculated risk of malignancy in 5-15% cases. (c) Until now an integration of new developments in molecular markers into the Bethesda system is missing. Thus, for experienced cytologists the Bethesda system for reporting thyroid cytopathology offers very limited benefits in comparison to the currently used, established and highly accepted classification systems. However, a positive argument remains the fact that an internationally accepted classification system may improve the comparability of the results of national and international studies on thyroid findings.

Résultats antérieurs

Inclusion des cas correspondant aux nodules kystiques (macrophages seuls)
ND « nodules kystiques » : 6.2%

Réticences et critiques

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Re ponction après LFSI

- **86 deuxièmes ponctions (24%)**

CATEGORIES	RESULTATS (%)
BENIN	**42 (48.8%)**
LFSI	**17 (19.8%)**
NF	**6 (7%)**
SM	**12 (13.9%)**
MALIN	**0 (0%)**
ND	**9 (10.5%)**

LFSI Re-classés : 69.7% Littérature : 62 à 76%

Réticences et critiques

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Ann Surg. 2014 Jul;260(1):163-8. doi: 10.1097/SLA.0000000000000215.

A clinical algorithm for fine-needle aspiration molecular testing effectively guides the appropriate extent of initial thyroidectomy.

Yip L[1], Wharry LI, Armstrong MJ, Silbermann A, McCoy KL, Stang MT, Ohori NP, LeBeau SO, Coyne C, Nikiforova MN, Bauman JE, Johnson JT, Tublin ME, Hodak SP, Nikiforov YE, Carty SE.

Author information

Abstract

OBJECTIVE: To test whether a clinical algorithm using routine cytological molecular testing (MT) promotes initial total thyroidectomy (TT) for clinically significant thyroid cancer (sTC) and/or correctly limits surgery to lobectomy when appropriate.

BACKGROUND: Either TT or lobectomy is often needed to diagnose differentiated thyroid cancer. Determining the correct extent of initial thyroidectomy is challenging.

METHODS: After implementing an algorithm for prospective MT of in-house fine-needle aspiration biopsy specimens, we conducted a single-institution cohort study of all patients (N = 671) with nonmalignant cytology who had thyroidectomy between October 2010 and March 2012, cytological diagnosis using 2008 Bethesda criteria, and 1 or more indications for thyroidectomy by 2009 American Thyroid Association guidelines. sTC was defined by histological differentiated thyroid cancer of 1 cm or more and/or lymph node metastasis. Cohort 2 patients did not have MT or had unevaluable results. In cohort 1, MT for a multigene mutation panel was performed for nonbenign cytology, and positive MT results indicated initial TT.

RESULTS: MT guidance was associated with a higher incidence of sTC after TT ($P = 0.006$) and a lower rate of sTC after lobectomy ($P = 0.03$). Without MT results, patients with indeterminate (follicular lesion of undetermined significance/follicular or oncocytic neoplasm) cytology who received initial lobectomy were 2.5 times more likely to require 2-stage surgery for histological sTC ($P < 0.001$). In the 501 patients with non-sTC for whom lobectomy was the appropriate extent of surgery, lobectomy was correctly performed more often with routine preoperative MT ($P = 0.001$).

CONCLUSIONS: Fine-needle aspiration biopsy MT for BRAF, RAS, PAX8-PPARγ, and RET-PTC expedites optimal initial surgery for differentiated thyroid cancer, facilitating succinct definitive management for patients with thyroid nodules.

Aragon P
Ann Surg Oncol 2014

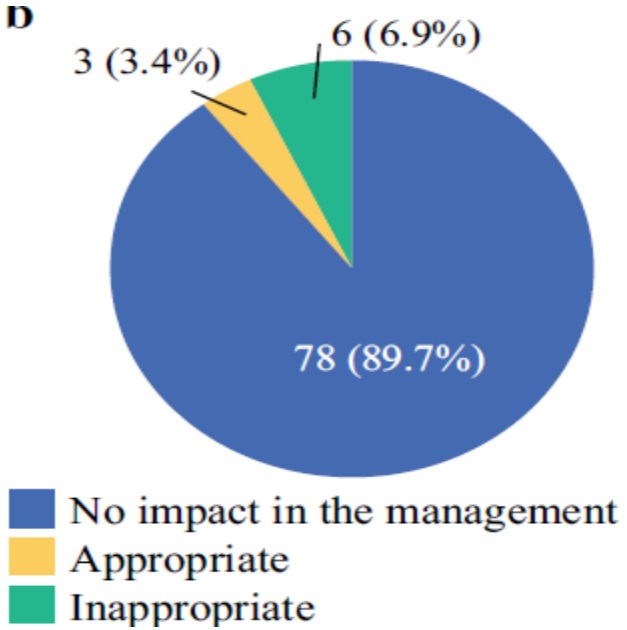

TABLE 2 Cases with change in the surgical management based on molecular test

	FNA diagnosis	Nodule size (cm)	History, signs and symptoms	Management based on algorithm	Molecular test	Actual surgery performed	Final path report	Change in the surgical management
1	PTC	1.3	MNG	TT+CLND	*BRAF* negative	TT	FVPTC	Undertreatment
2	SFM	2.1	Hypothyroidism	TT	GEC positive	TT+CLND	ADN	Overtreatment
3	SFM	1.8	MNG	TT	*BRAF* positive	TT+CLND	PTC	Appropriate
4	AUS	1	Hypothyroidism FHx of thyroid cancer	TT	GEC positive	TT+CLND	FA	Overtreatment
5	AUS	2.1	Uninodular	HT	GEC positive	TT	ADN, and LcT	Overtreatment
6	AUS	3.9	Compressive symptoms FHx of thyroid cancer	TT	GEC positive	TT+CLND	FVPTC	Appropriate
7	Benign	1.8	MNG and hypothyroidism	Repeat FNA	GEC positive	TT+CLND	FVPTC	Appropriate
8	Benign	1.8	MNG	Repeat FNA	GEC positive	TT	MNH	Overtreatment
9	Insufficient	2.4	MNG	Repeat FNA	GEC positive	TT+CLND	FA, and MNH	Overtreatment

FNA fine needle aspiration, *PTC* papillary thyroid cancer, *AUS* atypia of undetermined significance, *SFM* suspicious for malignancy, *MNG* multinodular goiter, *FHx* family history, *TT* total thyroidectomy, *CLND* central lymph node dissection, *HT* hemithyroidectomy, *FVPTC* follicular variant of PTC, *FA* follicular adenoma, *ADN* adenomatoid nodule, *MNH* multinodular hyperplasia, *LcT* lymphocytic thyroiditis

Conclusion

- **Compréhension du BSRTC**
- **Enseignement**
- **Publications**
- **Faire évoluer**