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The Value of Intra-Operative Frozen Section in Thyroid Neoplasm Management: Experience of One Center

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Abstract

Aim: To review our own experience with Frozen section (FS) in thyroid surgery and to assess its value in the management of patients with thyroid disease.

Methods: This retrospective study examined the results of 1110 frozen sections of thyroid specimens analyzed over the 10 year period from 2003 through 2012 and their correlations with the final histological examination. Deferred responses were not taken into account for statistical calculations.

Results: In our series, FS and final histopathological diagnosis agreed in 85.4% and disagreed in 5.5%. 9.1% of the cases were deferred. The global specificity and sensitivity of FS analysis for all histological subtypes were 99.3% and 64.7% respectively. Its sensitivity for papillary carcinoma was 61.7%, 83.3% for follicular carcinoma and 100% for anaplastic carcinoma. Discordances were due to 6 false-positive diagnoses and 55 false-negative (FN) diagnoses. 50% of FN was represented by papillary micro-carcinoma. The positive predictive value (PPV) of the FS examination was 94.4% and its negative predictive value (NPV) was 93.9%.

Conclusions: Our data supports the utility of intraoperative FS in the confirmation of malignancy of thyroid nodules. It's correlated with a high degree of specificity and an acceptable rate of sensitivity. Most of the discordances between FS and final histopathological diagnosis were explained by papillary microcarcinoma.

Keywords: Frozen section; Thyroid nodules; Accuracy

Introduction

Thyroid nodules represent a significant problem in the current clinical and surgical practice [1]. Due to their high incidence and malignant potential, careful evaluation is required in order to adopt optimal management and spare unnecessary surgery. FS biopsy of a thyroid nodule allows an intraoperative pathological diagnosis at the time of operation which may guide surgical strategy. For malignant nodules, total thyroidectomy should be performed to avoid patient the risk of a second surgery which increase disease spread, morbidity and complication rates. However In case of benignity, FS could alter operative management from aggressive to conservative surgery [2]. The aim of this study was to review the place of FS in thyroid surgery and to assess its value in the management of patients with thyroid disease.

Methods

The pathologic reports issued for all thyroid surgery specimens, submitted for intraoperative pathology examination at the Department of Pathology of Habib Thameur Hospital during the period from January 2003 to December 2012 were reviewed retrospectively. During this period, the results of fine needle aspiration (FNA) were not always available to pathologists at the time of intraoperative consultation. FS examination was performed on all thyroid specimens (thyroidectomy, lobectomy and loboisthemctomy). Each of the specimens was examined by any one of seven staff pathologists who selected areas for microscopic FS examination after gross inspection of the specimens. In most cases one block of tissue was examined. The tissue blocks were frozen in a cryostat at -20°C and followed by hematoxylin-eosin staining. Frozen tissues were then fixed in 10% neutral and processed for paraffin section. Touch preparations were routinely performed. In cases where the lesion was clearly benign or clearly malignant the surgeon was thus informed and was also given any more specific diagnostic information which could be provided. Pathologic reports were analyzed in regard to FS results final histopathology result and tumor size. Frozen-section analysis results for the thyroid gland are coded as malignant for all thyroid cancers, lymphoma, or metastatic diseases. Goiter, hyperplasia, thyroiditis, and adenoma are considered benign. Reports of using "favor" or "possible" for any malignancy or suspicious for capsular invasion, follicular neoplasm are coded as deferred (defer reporting results until permanent sections are reported). Definite pathologic categorization is based on permanent-section diagnosis. Permanent pathologic diagnoses were coded as malignant for any report of papillary, follicular, Hürthle cell, medullary, or anaplastic thyroid carcinoma. Micro carcinomas were included with papillary cancers. Lymphoma and metastatic disease involving the thyroid gland were coded as malignant. The maximum diameter of the tumor or the largest of multiple tumors was recorded for all malignant lesions. All remaining diagnoses were recorded as benign, including goiter, adenoma, Hürthle cell adenoma, hyperplasia, and thyroiditis. All histological diagnoses were performed in accordance with WHO guidelines.

The results were considered as follows:

A true positive (TP) is a positive result for malignancy with subsequent final histopathologic verification. A true negative (TN) is a negative result for malignancy with subsequent final histopathologic confirmation. A false positive (FP) is a positive result for malignancy at FS and benign results for the final histopathologic diagnosis. A false negative (FN) is a reading consistent with benign disease and malignant on final histopathologic diagnosis.

Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and accuracy for detection of malignancy are determined for frozen-section analysis according to the following equations: sensitivity=TP/(TP+FN); specificity=TN/(TN+FP); PPV=TP/(TP+ FP); NPV=TN/(TN+FN); and diagnostic accuracy=(TP+TN)/total cases.

Results

Intraoperative FS examinations of the thyroid were performed in 1110 thyroid specimens. Of these, the diagnosis was deferred in 102 cases (9%), positive for malignancy in108cases (9.7%), and benign in 902 cases (81.3%). Final pathology results revealed 920 benign lesions (82.9%) of all and 190 carcinomas (17.1%). On final histologic diagnosis, from the 902 benign diagnoses of the FS, 847 (93.3%) were TN and 55 (4.95%) were FN. 50% of FN were represented by papillary micro-carcinomas (tumor size<1 cm) which were accidentally discovered. The 108 malignant results of the FS were represented by 102 (94.4%) TP and 6 (0.55%) FP. The 102 TP were represented by 87 papillary carcinomas (PC), 5 follicular carcinomas (FC), 5 anaplastic carcinomas (AC), 4 medullary carcinomas (MC) and one poorly differentiated carcinoma. The 100 deferred results revealed 67 (67%) benign lesions and 33 (33%) carcinomas with 28 PC, 4 FC with micro-invasion and 1 poorly differentiated carcinoma. In our series, FS and final histopathological diagnosis agreed in 85.4% and disagreed in 5.5%. 9.1% of the cases were deferred (Table 1).

The sensitivity/specificity pairs of FS analysis for allhistological subtypes were 64.7%/99.3%, dropping to 53.1%/92% with calculation including deferred responses. The specificity for FS analysis for carcinoma diagnoses were unmoved with the histological subtype, however its sensitivity for papillary carcinoma was 61.7%, 83.3% for follicular carcinoma and 100% for anaplastic carcinoma. The positive predictive value of intraoperative FS result was 94.4% and the negative predictive value one was 93.9% with an accuracy of 85.4% (p<0.001).

	FS diagnoses			
	Benign	Malignant	Deferred	Total
Final histologic diagnoses				
Benign	847	6	67	920 (82.3%)
Malignant	55	102	33	190 (17.7%)
Papillary carcinoma	54	87	28	169
Follicular carcinoma	1	5	4	10
Anaplastic carcinoma	0	5	0	5
Poorly differentiated carcinoma	0	1	1	2
Medullary carcinoma	0	4	0	4
Total	902 (81.3%)	108 (9.7%)	100 (9%)	1110 (100%)

Table 1: Comparison of FS diagnoses with final histologic diagnoses.

Discussion

Generally, FS is considered to have enhanced specificity for diagnosing thyroid cancers [2]. Table 2 shows the different studies regarding the results obtained with the FS on the assessment of thyroid nodules. The sensitivity, specificity, PPV, NPV and accuracy of FS reported in the literature vary from 50% to 99%, 92% to 100%, 87% to 100%, 75% to 98.5%, and 69% to 98%, respectively. Our findings match those in the literature, with good accuracy.

Authors/year	FS	Cancer %	FP%	FN %	Deferred%	Ss %	Sp %	PPV %	NPV %	DA %
Proye 1980 [3]	674	7.4	0.3	1.5	2	80	99.7	95	98.5	96.5
Remsen 1984* [4]	240	18.3	0	0.8	0.4	-	100	100	-	99
Bugis 1986 [5]	182	13.7	0	3	2	64	100	100	95	95
Hwang 1987 [6]	319	26.3	1.25	3.5	1.25	-	-	-	-	95
Prey 1989 [7]	300	-	0	2.6	2.3	-	-	-	-	95
Rosen 1990 [8]	504	11	0	2	5	-	-	100	95	95
Rodriguez 1994* [9]	170	16	0	3.5	0.6	78	100	100	96	96
Godey 1996 [10]	2470	8.3	0	1.3	0.8	75	100	100	98	98
Sabel 1997* [11]	494	-	0.6	3	2	79	99	87	96	95
Aguilar 1997 [12]	326	17.2	0	6	7	50	100	100	91	91.5

Richards 2002 [13]	140	19.3	0	9	1.4	50	100	100	90	90
Leenhardt 2002 [14]	155	11	0.6	2.3	65	99	92	96	75	-
Caraci 2002 [15]	206	19.4	0.5	2	-	80	99	97	95	96
Cheng 2002 [16]	209	9.6	0	0.95	30	83	100	100	98.5	69
Wendum 2003 [17]	192	12.5	0	1	17	52	100	100	94	94.5
Boutin 2003* [18]	136	16	0	4	2	70	100	100	95	93.5
Lumachi 2003* [19]	606	17.5	0	3	-	92	100	100	-	-
Cerovix 2004* [20]	675	14.2	0	-	1	73	100	100	94	95
Cetin 2004* [21]	203	23.6	0	5	6	83	100	100	97	97
Campillo-soto 2006*[22]	179	-	-	-	-	-	100	100	90	91
Guiliani 2006* [23]	128	-	-	-	-	56.2	98.1	81.8	93.8	-
Zhang 2007* [24]	750	17	0	0,4	0,93	95.9	100	100	-	98.4
Makay 2007 * [25]	178	-	-	-	-	58.4	-	-	-	-
Chao 2007* [26]	569	18.1	0	2.3	15.1	82.1	100	100	95.8	96.5
Mekni 2008* [2]	1534	11	0.1	3	4.6	67	99.8	98	96.6	92
Fareh 2009* [27]	409	10.8	0	3.4	-	68.2	100	100	96.3	96.6
Our series *	1110	17.1	0.55	4.95	9	64.7	99.3	94.4	93.9	85.3

*the deferred responses are not included on calculation, FS: frozen section examination; Ss: sensitivity; Sp:specificity; FP: false positive; FN: false negative; PPV: positive predictive value; VPN: negative predictive value; DA: Diagnostic accurancy

Table 2: FS results in the assessment of thyroid nodules.

In our study, 4.95% of cases diagnosed by FS as benign lesions were FN. This result can be explained by a high rate of papillary microcarcinomas diagnosed only on final exam (50% of all FN). Malignant frozen-section diagnosis obtained 0.55% of FPs. Our findings indicate that FS is reliable in diagnosing benign and malignant tumors. Conversely, in 3.1% of those diagnosed as deferred frozen-section results, permanent-section examinations confirmed malignancy.

Usually, pathological diagnosis of papillary carcinoma in the thyroid is easy when compared follicular carcinoma. This is due to nuclear atypia which are specific of papillary carcinoma. However, our study showed opposite results, in fact we found that sensitivity of FS for papillary carcinoma is lower than that of follicular carcinoma. These particular and controverting results are due a high rate of follicular variety of papillary carcinoma in our series which diagnoses were challenging and habitually made after final histopathological examination. In the other hand, the major part of follicular carcinoma diagnosed were massively invasive making diagnosis easier. These are main reasons to explain lack of sensitivity of FS of papillary carcinoma compared to follicular carcinoma.

The true utility of this practice has long been debated. Proponents for routine use of intraoperative FS have demonstrated cost effectiveness and a reduced number of completion thyroidectomies. Others disagree on the basis that increased costs from additional operating time and pathologists needed to read the specimens are not justified by a significant benefit in patient outcomes [28]. However, FS is usually insufficient to determine true capsular or vascular invasion and deferral to a final pathologic diagnosis is often necessary in the setting of a follicular lesion [29]. Currently, preoperative fine needle aspiration (FNA) and intraoperative FS examination should be regarded as complementary procedures which, in some patients, may provide more diagnostic information than either procedure alone [8]. FS analysis often complements the fine needle aspiration cytology in cases with cytologic atypia or suspicious appearance, and is most useful at making a diagnosis of papillary thyroid carcinoma [28]. For FNA indeterminate specimens, a diagnostic thyroid lobectomy is often performed with intra-operative FS analysis in order to prevent a return trip to the operating room for completion thyroidectomy.

Conclusion

Our data supports the clinical usefulness of FS for the diagnosis and management of thyroid nodules. Future directions for the diagnosis and treatment of thyroid nodules should include addressing highly variable language used among pathologists in regard to thyroid intraoperative FS reporting. A standardized language may assist pathologists in their assessment as well as helping surgeons make decisions while in the operative theatre.

References

1. Irkorucu O, Tascilar O, Cakmak GK, Emre AU, Ucan HB, et al. (2007) Frozen section and fine needle aspiration biopsy in thyroid surgery-needles and sections. Indian J Surg 69: 140-144.

2. Mekni A ,Limaiem F , Cherif K, Chelly I, Sahtout S, et al. (2008) Value of intraoperative frozen section analysis in thyroid surgery a retrospective study of 1534 consecutive biopsies. Presse Med 37: 949-955.
3. Proye C, Lagache G, Trincoretto F, Miquel P, Bahon J, et al. (1980) Examen extemporané systématique ou sélectif dans la chirurgie des affections thyroïdiennes suspectes de malignité? Expérience de 674 examens en 6 ans. J Chir 117: 635-638.
4. Remsen KA, Lucente FE, Biller HF (1984) Reliability of frozen section diagnosis in head and neck neoplasms. Laryngoscope 94: 519-524.
5. Bugis SP, Young JE, Archibald SD, Chen VSM (1986) Diagnostic accurancy of fine needle aspiration biopsy versus frozen section in solitary thyroid nodules. Am J Surg 152: 411-416.
6. Hwang TS, Han EK, Kim CW, Chi JG, Park SH (1987) An evaluation of frozen section biopsy in 4434 cases. Korean Med Sci 2: 239-245.
7. Prey MU, Vitale T, Martin SA (1989) Guidelines for practical utilization of intra-operative frozen sections. Arch Surg 124: 331-335.
8. Rosen Y, Rosenblatt P, Saltzman E (1990) Intraoperative pathologic diagnosis of thyroid neoplasm. Report on experience with 504 specimens. Cancer 66: 2001-2006.
9. Rodriguez JM, Parrilla P, Sola J, Bas A, Aguilar J, et al. (1994) Comparison between preoperative cytology and intraoperative frozen section biopsy in the diagnosis of thyroid nodules. Br J Surg 81: 1151-1154.
10. Godey B, Le Clech G, Ingigues JP, Legall F, Beust L, et al. (1996) L'examen anatomopathologique extemporané dans la chirurgie des cancers thyroïdiens: intérêts et limites. Ann otolaryngol Chir Cervicofac 113: 219-224.
11. Sabel MS, Starem ED, Gianakakais LM, Dwarakanathan S, Prinz RA (1997) Use of needle aspiration biopsy and frozen section in the management of the solitary thyroid nodule. Surgery 12: 1021-1027.
12. Aguilar M, Conteras A, Gabilan I, Escobar L, Giron JA, et al. (1997) Thyroid nodules role of fine needle aspiration and intraoperative frozen section examination. ActaCytologica 41: 677-682.
13. Richrards ML, Chisholm R, Bruder JM, Strodel WE (2002) Is thyroid frozen section too much for too little? Am J Surg 184: 510-514.
14. Leenhardt L, Menegaux F, Franc B, Delbot T, Mansour G, et al. (2002) Selection of patients with solitary thyroid nodules for operation. Eur J surg 168: 236-241.
15. Caraci P, Aversa S, Mussa A, Pancani G, Ondolo C, et al. (2002) Role of fine needle aspiration biopsy and frozen section evaluation in the surgical management of thyroid nodules. Br J Surg 89: 797-801.
16. Cheng M, Morgan JL, Serpell JW (2002) Does frozen section have a role in the intraoperative management of thyroid nodules? ANZ J Surg 72: 570-572.
17. Wendum D, Fléjou JF (2003) Evaluation des examens extemporanés dans un service hospitalo-universitaire : analyse de 847 examens consécutifrozen section. Ann Pathol 23: 393-399.
18. Boutin P, Bozorg Grayeli A, Terrada C, Rondini-Gilli E, Mosnier I, et al. (2003) Results of fine needle aspiration biopsy frozen section diagnosis and definite histological results in thyroid pathology. Report of 163 cases. Rev Laryngol Otol Rhinol 124: 59-63.
19. Lumachi F, Borsato S, Tregnaghi A, Marino F, Poletti A, et al. (2004) Accuracy of fine needle aspiration cytology and frozen-section examination in patients with thyroid cancer. Biomed Pharmacother 58: 56-60.
20. Cerovix S, Ignjatovic M, Brajuskovic G, Knezevic-Usai S, Dimitrijevic J, et al. (2004) The value of intraoperative diagnosis in thyroid surgery. Arch oncol 12: 48.
21. Cetin B, Asian S, Hatiboglu C, Babacan B, Onder A, et al. (2004) Frozen section in thyroid surgery: is it a necessity? Can J Surg 47: 29-33.
22. Campillo-Soto A, Flores-Pastor B, Candel-Arenas M, Soria-Aledo V, Giménez-Bascuñana A, et al. (2006) Utility of frozen section in the surgical treatment of thyroid nodules. Cir Esp 79: 176-179.
23. Giuliani D, Willemsen P, Verhelst J, Kockx M, Vanderveken M (2006) Frozen section in thyroid surgery. Acta Chir Belg 106: 199-201.
24. ZW, Jin M (2007) The value of frozen section examination in thyroid surgery. Lin Chung Er Bi Yan Hou Tou Jing Wai Ke Za Zhi 221: 299-301.
25. Makay O, Icoz G, Gurcu B, Ertan Y, Tuncyurek M, et al. (2007) The ongoing debate in thyroid surgery: should frozen section analysis be omitted? Endocr J 54: 385-390.
26. Chao TC, Lin JD, Chao HH, Hsueh C, Chen MF (2006) Surgical treatment of solitary thyroid nodules via Fine-Needle Aspiration Biopsy and Frozen-Section Analysis. Annals of Surgical Oncology 14: 712-718.
27. Farah-Klibi F, Blel A, Neji O, Ferjaoui M, Ben Jilani S, et al. (2009) The value of intraoperative frozen section in surgical management of thyroid nodules Report of 409. Ann Pathol 29: 80-85.
28. Bomeli SR, LeBeau SO, Ferris RL (2010) Evaluation of a thyroid nodule. Otolaryngol Clin North Am 43: 229-238.
29. Kahme R, T Lee W, Puscas L, L Scher R, Shealy MJ, et al. (2013) Utility of intraoperative frozen section during thyroid surgery. Int J of Otolaryngol.