The role of intraoperative frozen sections for thyroid nodules

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Summary

The role of intraoperative frozen sections (FS) during thyroidectomy is controversial. Aim: to evaluate the role of FS for thyroid nodules management. Patients and methods: All patients who had thyroid surgery for nodular disease and previous USG-guided FNAB in 2006 were prospectively analyzed. They underwent intraoperative FS evaluation, and the biopsy material was classified as benign, malignant or follicular neoplasm. FNAB, FS and paraffin sections were compared. Results: Under the FS, 54% of the nodules were benign, 30% were follicular neoplasms, and 16% were malignant. All cases considered benign and malignant under the FS evaluation were confirmed through the histological “paraffin” analysis. Since it is not considered a definitive indication for total thyroidectomy, if the follicular neoplasms were classified as “benign” under the FS, their sensitivity, specificity, positive and negative predictive values and global diagnostic accuracy were 69%, 100%, 100%, 91.5% e 77%, respectively. Among the 42 cases classified as “follicular neoplasm” under the FNAB, in 1 case the FS conclusion was for papillary carcinoma, in 3 cases as benign (all confirmed through the “paraffin”); and 38 cases continued as “follicular pattern”, being 29 follicular adenomas and 9 carcinomas through the “paraffin”. Conclusion: The FS is only indicated when the FNAB reports “follicular neoplasm”.

References

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INTRODUCTION

The fact that fine needle aspiration (FNA) is a highly accurate preoperative method to be used for the diagnosis of thyroid nodules in cancer detection, and the so-called “follicular neoplasia” still is a dilemma. The value of the intra-operative frozen section (FS) remains controversial while its potential to help the surgeon decide between hemithyroidectomy or total thyroidectomy. The method can potentially avoid a second surgery to remove the contralateral lobe should the surgical specimen reveal malignancy in the histopathology included in paraffin and, alternatively, it can avoid an unnecessary total thyroidectomy which will cause the patient to have to replace levothyroxine forever and increase the chance of the patient developing hypoparathyroidism and damage to the recurrent laryngeal nerve.

The goal of the present investigation is to assess the value of the frozen section regarding decision making when facing a nodular disease of the thyroid gland.

MATERIALS AND METHODS

During the year of 2006, in a prospective study, 126 patients were consecutively submitted to thyroidectomy because of a thyroid nodular disease, and the nodules were previously assessed by guided FNA. All the patients were submitted to FNA performed by the same ultrasound operator and pathologist and the pathology interpretation was carried out by the same pathologist who participated in the harvesting of the material. During surgery, all the specimens were submitted to intraoperative frozen section test. The histopathology diagnosis of the material embedded in paraffin was available. The present study was approved by the Ethics in Research Committee of the local institution.

The FNA is conducted through a 20mL plastic syringe with a 21 gauge needle. Ultrasound was performed by means of a 10MHz probe and a minimum of three aspirations was normally used without local anesthesia. In case of mixed nodules, the liquid component was initially emptied, and the puncture was repeated afterwards. The material collected was assessed by the pathologist, and the liquid was previously centrifuged. All the material collected was fixed in alcohol and dyed by Papanicolaou or HE. The frozen section exam was made with one or two representative sections of the area most likely to present capsular invasion.

The cytopathology specimens were classified as inconclusive, benign (colloid nodule, cyst or thyroiditis), malignant and suspected malignant (specimens which definition of malignancy could not be established, presenting a follicular pattern). The presence of monomorphic epithelial cells or slightly pleomorphic, frequently grouped in micro-follicles or in syncytial masses and showing nuclei with atypia or eosinophilic aspect of Hurthle cells, were all considered follicular pattern. As to the frozen sections, the surgical specimens were classified into inconclusive, benign, malignant and follicular pattern.

The frozen section was compared to the histopathology exam (paraffin), considered gold standard. True positive and true negative cases were defined with basis on the histopathology confirmation of the frozen section, of carcinoma or benign lesion, respectively. Thus, the disagreeing results were classified into false-positive and false-negative. Sensitivity, specificity, the predictive values of the negative and positive tests and the accuracy were calculated.

Following that, the FNA findings were compared to those from the frozen section and the impact of each one in the establishment of the surgical approach (partial or total thyroidectomy) was assessed.

RESULTS

Comparing the FS with the paraffin histopathology (Gold Standard).

In the present sample, there was no FS deemed inconclusive: 68 nodules (54%) were benign, 38 (30%) were follicular neoplasias (we must wait for the results of the paraffin study for a detailed investigation of vascular and capsular invasion) and 20 (16%) were malignant. Figure 1 compares the FS findings with the histopathology (“paraffin”).

Figure 1. Comparing the FS and the paraffin histopathology.

| OT        | histopathology |
|-----------|----------------|
| Benign    | Benign 68      |
| Follicular| Benign 29      |
| Malignant | Malignant 9    |
|           | Malignant 20   |

Figure 2. Comparing the FS and the paraffin findings, considering the suspicious punctions (follicular pattern) as being benign.

| OT        | histopathology |
|-----------|----------------|
| Benign    | Benign 97      |
|           | Malignant 9    |
| Malignant | Malignant 20   |
Table 1. FS results in the assessment of thyroid nodules.

| Author                  | n   | Sensitivity | Specificity | PPV  | PNV  | Accuracy |
|-------------------------|-----|-------------|-------------|------|------|----------|
| Bugis et al., 1986⁴     | 198 | 95%         |             |      |      |          |
| Shaha et al., 1990⁵     | 190 | 95%         |             |      |      |          |
| Rosen et al., 1990⁶     | 457 | 53%         | 100%        | 100% | 97,8%|          |
| Shaha et al., 1990⁷     | 38  | 95%         |             |      |      |          |
| Irish et al., 1992⁸     | 137 | 87%         |             |      |      |          |
| Kingston et al., 1992⁹  | 395 | 52%         | 100%        | 100% | 73%  | 79%      |
| Gibbet et al., 1995¹⁰   | 85  | 95%         |             |      |      |          |
| McHenry et al., 1996¹¹  | 76  | 93%         | 100%        |      |      |          |
| Godei et al., 1996¹²    | 2470| 74%         | 100%        |      |      |          |
| Morosini et al., 1997¹³ | 812 | 91,3%       | 100%        |      |      |          |
| Paphavast et al., 1997¹⁴| 1023| 78%         | 99%         | 90%  | 98%  |          |
| Chang et al., 1997¹⁵    | 586 | 97%         |             | 95%  | 92,6%|          |
| Linder et al., 1997¹⁶   | 73  | 83%         |             | 95%  |      |          |
| Mulcahy et al., 1998¹⁷  | 66  | 95%         |             |      |      |          |
| Chen et al., 1998¹⁸     | 57  | 23%         |             |      |      |          |
| Hamming et al., 1998¹⁹  | 240 | 67%         | 99%         | 98%  | 87%  | 89%      |
| Tworek et al., 1998²⁰   | 68  | 98%         |             |      |      |          |
| Boyd et al., 1998²¹     | 151 | 86%         | 99%         |      |      |          |
| Ng SC et al., 1999²²    | 34  | 100%        | 86%         |      |      |          |
| Chow et al., 1999²³     | 84  |             |             |      |      |          |
| Multanen et al., 1999²⁴| 335 | 74,6%       |             |      |      |          |
| Taneri et al.2000²⁵     | 63  | 28,5%       | 77,5%       |      |      |          |
| Piraino et al., 2000²⁶  | 85  | 89,4%       |             |      |      |          |
| Lin et al., 2000²⁷      | 63  | 87%         |             |      |      |          |
| Leteurtre et al., 2001²⁸| 63  | 17%         |             |      |      |          |
| Tamimi et al., 2001²⁹   | 61  | 60%         | 100%        |      |      |          |
| Bastagli et al., 2001³⁰ | 155 | 42,9%       | 100%        | 100% | 8,5% | 92%      |
| Lee et al., 2002³¹      | 1076|             |             |      |      |          |
| Abboud et al., 2003³²   | 113 | 68%         | 99%         |      |      |          |
| Pisanu et al., 2003³³   | 36  | 33,3%       |             |      |      |          |
| Boutin et al., 2003³⁴   | 163 | 73%         | 99%         |      |      |          |
| Kesmodel et al., 2003³⁵ | 42  | 36%         |             |      |      |          |
| Saydam et al., 2003³⁶   | 67  | 100%        | 87%         |      |      |          |
| Calcut et al., 2004³⁷   | 152 | 67%         | 100%        | 100% |      |          |
| Lumachi et al., 2004³⁸  | 606 | 83%         | 100%        |      |      |          |
| Cetin et al., 2004³⁹    | 203 | 87,1%       | 100%        |      |      |          |
| Rios et al., 2004⁴⁰     | 197 | 19%         | 100%        | 100% | 93%  | 93%      |
| Pisanu et al., 2004⁴¹   | 41  | 33,3%       |             |      |      |          |
| Furlan et al., 2004⁴²   | 56,1%|             |             |      |      |          |
| Sahin et al., 2005⁴³    | 84  | 100%        |             |      |      |          |
| Chao et al., 2005⁴⁴     | 135 | 40%         | 100%        | 100% | 92%  | 92,9%    |
| Dzodic et al., 2006⁴⁵   | 40  | 77,7%       | 100%        | 100% | 94%  | 95%      |
| Giuliani et al., 2006⁴⁶ | 417 | 56,25%      | 98,16%      | 81,81%| 93,85%|          |
| Olson et al., 2008⁴⁷    | 236 | 25%         |             |      |      |          |
| Miller et al., 2007⁴⁸   | 205 | 23%         | 99%         |      |      |          |
Among the 20 cases considered malignant at the FS, two were thyroid medullary carcinomas and all the others were papilliferous carcinoma. Among the cases classified as follicular pattern (38), 29 were benign (follicular adenomas) and nine malignant, two cases of follicular carcinoma and seven of papilliferous carcinoma - follicular variant.

If we disregard the follicular pattern punctures, the predictive values for the negative (benign puncture) and positive (malignant puncture) tests add up to 100%. However, should the FS be suspicious (follicular pattern), it is one indication to perform total thyroidectomy, for the lack of criteria to conclude for malignancy - if classified as “benign”, we found a new status (Figure 2).

In this new status, considering the follicular pattern cases (wait for “paraffin” result) as “benign” in the FS, the following values were found: sensitivity = 69%; specificity = 100%; predictive value for the positive test = 100%; predictive value for the negative test = 91.5%; and accuracy = 77%.

Comparing FS with FNA

All the cases had been submitted to FNA in the preoperative test. Thus, of the 126 nodules punctured, 65 (51.6%) were benign, 42 (33.3%) were follicular neoplasia and 19 (15.1%) were malignant. Cross these data with those obtained from the FS exam, we noticed the following:

1) the 19 cases characterized as “malignant” by the FNA were confirmed by the FS and the paraffin;
2) the 65 cases characterized as benign in the FNA were confirmed by the FS and by the paraffin;
3) considering the 42 cases reported as follicular neoplasia by the FNA, we had:
   - in one case, the FS found the criteria matching those of papilliferous carcinoma (confirmed by the paraffin test);
   - in three cases, FS found enough criteria to define it as benign (confirmed by the paraffin test);
   - in the remaining 38 cases, the FS kept the appearance of a follicular pattern, suggesting that one should wait for the paraffin results; of these, 29 came as follicular adenomas and nine came as carcinoma, two follicular carcinoma and seven papilliferous of the follicular variant.

DISCUSSION

Table 1 shows the study regarding the results obtained with the FNA on the assessment of thyroid nodules.²⁻⁴⁻⁸

Our findings match those in the literature, with good accuracy, nonetheless, it also fails when compared to the so called “follicular pattern”. Thus, specificity and positive predictive value are high. We found 100% for both, matching a good part of the data in the literature. This means that, when the FS method points to a cancer possibility, such result is highly reliable. The “follicular pattern” results come with the pathologist’s recommendation of waiting for the “paraffin” result, because the criteria necessary for the final diagnosis of malignancy were not found, thus not systematically recommending total thyroidectomy. With this, on the 2x2 Table such conclusion was classified as “benign” and this justifies the 69% sensitivity in our sample. Now, when the FNA is considered, the finding of “follicular neoplasia” is a criterion for surgical indication, thus, it must be classified as “malignant”.¹

There was a strong correlation between the benign and malignant findings among the FNA guided by ultrasound, FS and histopathology, embedded in “paraffin” (Gold Standard). Thus, when the FNA shows it is benign, or malignant, the FS did not add information. Now, within the 42 cases of “follicular neoplasia” seen at the FNA, in a FS found malignancy criteria, with an impact on the treatment decision and, in three, it was defined that it was a benign lesion.

CONCLUSION

The FS is only indicated in cases which the FNA yielded results of “follicular neoplasia”.

REFERENCES

1. Rocha RP, Almeida JPA, Couto Netto SD, Silva RABN, Pfuetzemreiter EG, Dedivitis RA. Puncção aspirativa por agulha fina guiada por ultrasonografia para nósulos tireoidianos. Rev Bras Cir Cabeça Pescoço. 2007;56(4):186-8.
2. Gallcut RA, Selvaggi SM, Mack E, Oszog O, Warner T, Chen H. The utility of frozen section evaluation for follicular thyroid lesions. Ann Surg Oncol. 2004;11(1):94-8.
3. Wong Z, Matha C, Craik J, Carter J, Harman CR. Role of intraoperative fine-needle biopsy in the management of thyroid nodules. ANZ J Surg. 2004;74(12):1052-5.
4. Bagis SP, Young JE, Archibald SD, Chen VS. Diagnostic accuracy of fine-needle aspiration biopsy versus frozen section in solitary thyroid nodules. Am J Surg. 1986;152(4):411-6.
5. Shaha AR, DiMaio T, Jaffe BM. Accuracy and pitfalls of frozen section during thyroid surgery. J Surg Oncol. 1990;44(2):84-92.
6. Rosen Y, Rosenblatt P, Saltzman E. Intraoperative pathologic diagnosis of thyroid neoplasms. Report on experience with 504 specimens. Cancer. 1990;66(9):2001-6.
7. Shaha AR, DiMaio T, Webber C, Jaffe BM. Intraoperative decision making during thyroid surgery based on the results of preoperative needle biopsy and frozen section. Surgery. 1990;108(6):964-7.
8. Irish JC, van Nostrand AW, Asa SL, Gullane P, Rotstein L. Accuracy of pathologic diagnosis in thyroid lesions. Arch Otolaryngol Head Neck Surg. 1992;118(9):918-22.
9. Kingston GW, Bugis SP, Davis N. Role of frozen section and clinical parameters in distinguishing benign from malignant follicular neoplasms of the thyroid. Am J Surg. 1992;164(6):603-5.
10. Gibb GK, Pasieka JL. Assessing the need for frozen sections: still a valuable tool in thyroid surgery. Surgery. 1995;118(6):1005-9; discussion 1009-10.
11. McHenry CR, Raeburn C, Strickland T, Mardy JF. The utility of routine frozen section examination for intraoperative diagnosis of thyroid cancer. Am J Surg. 1996;172(6):658-61.
29. Tamimi DM. Value of routine frozen section diagnosis of thyroid lesions. Ann Ital Chir. 2001;72(3):269-6.

30. Lee TJ, Yang HJ, Lin HD, Braverman LE, Tang KT. The accuracy of fine-needle aspiration biopsy and frozen section in patients with thyroid cancer. Thyroid. 2002;12(7):619-26.

31. Abbadou B, Allam S, Chaara LA, Ingea H, Tohme C, Farah P. Use of fine-needle aspiration cytology and frozen section in the management of nodular goiters. Head Neck. 2003;25(1):32-6.

32. Pisanu A, Aste L, Piu S, Cois A, Uccheddu A. [Predictive factors for malignancy in Hurthle-cell thyroid neoplasia. Effect of surgical treatment] Fattori predittivi di malignità nelle neoplasie tiroidee a cellule di Hurthle. Influenza sul trattamento chirurgico. Tumori. 2003;89(4 Suppl):223-5.

33. Pisanu A, Bozorg Grayeli A, Terrada C, Rondini-Gilli E, Mosnier I, Julien N, Bouccara D, Grousard O, Bok B, Sterkers O. [Results of fine needle aspiration biopsy, frozen section diagnosis and definite histological results in thyroid pathology. Report of 163 cases] Analyse des résultats de la cytoponction, de lexamen histologique extemporané et définitif dans le traitement chirurgical de la tumeur de la thyroïde: à propos de 163 cas. Rev Laryngol Otol Rhinol. (Bord) 2003;124(1):59-65.

34. Kesmodel SB, Terhune KP, Canter RJ, Mandel SJ, LiVolsi VA, Baloch ZW, Fraker DL. The diagnostic dilemma of follicular variant of papillary thyroid carcinoma. Surgery. 2003;134(6):1005-12; discussion 1012.

35. Smyrnai L, Kalicoglu MT, Kizilay A, Bozdur MK. [The evaluation of thyroid nodules: is routine use of frozen-section examination necessary following preoperative fine-needle aspiration biopsy?] Tirot nodullerinin dergi-lenderlirilmesi: Ince igne aspirasyon biyopsisinden sonra sonra frozen section incedemisi gerekli midir? Kulak Burun Bogaz Ihtis Derg. 2003;11(3):80-4.

36. Callcut RA, Selvaggi SM, Mack E, Oguz G, Warner T, Chen H. The utility of frozen section evaluation for follicular thyroid lesions. Ann Surg Oncol. 2004;11(1):94-8.

37. Lunachi F, Borsato S, Tregnaghi A, Marino F, Poletti A, Iacobone M, Favia G. Accuracy of fine-needle aspiration cytology and frozen-section examination in patients with thyroid cancer. Biomed Pharmacother. 2004;58(1):56-60.

38. Cetin B, Aslan S, Hatiboglu C, Babacan B, Onder A, Celik A, Getin A. Frozen section in thyroid surgery: is it a necessity? Can J Surg. 2004;47(1):29-33.

39. Ríos Zambudio A, Rodríguez González JM, Sola Pérez J, Soria Cogollos T, Galindo Fernández PJ, Parrilla Paricio P. Utility of frozen-section examination for diagnosis of malignancy associated with multinodular goiter. Thyroid. 2004;14(8):600-4.

40. Pisanu A, Sias I, Uccheddu A. Factors predicting malignancy of Hurthle cell tumors of the thyroid: influence on surgical treatment. World J Surg. 2004;28(8):761-5.

41. Furlan JC, Bedard YC, Rosen IB. Role of fine-needle aspiration biopsy and frozen section in the management of papillary thyroid carcinoma subtypes. World J Surg. 2004;28(9):880-5.

42. Sahin M, Allard BL, Yates M, Powell JG, Wang XL, Hanks JB, Hanks JE, LiVolsi VA. Intraoperative pathologic examination: cost effectiveness and clinical value in patients with cytologic diagnosis of cellular follicular thyroid lesion. Thyroid. 2007;17(6):557-65.