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Study the results of Frozen Section pathology vs. permanent section pathology in lymph nodes

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ABSTRACT

Frozen Section (FS) may significantly assist a surgeon on surgical method decision making. This paper is brought to investigate the liability of FS as an alternative for permanent section pathology in commencing treatment in patients. This is a prospective descriptive-diagnostic study accompalished on 82 choosed specimens from patients who had biopsy of lymph nodes during 2 years. In this study, the demographic data as age, gender and pathological information regarding to the biopsy section, Frozen section pathology results and standard pathology results of patients were recorded. The results achieved from 82 samples with Frozen section and permanent section pathologies are shown in this study. %67.1 of samples are associated with cervical lymph nodes and 23% with axillary ones. The rate of successful permanent section pathology was %71 in comparison to Frozen pathology with %66 and the sensitivity of %93 and specificity of %63.3 were obtained (P<0.001). The sensitivity in axillary and cervical samples was %100 and %89.8 and specificity rate %75 and %50, respectively. The findings of present study imply that Frozen Section is a reliable method to substitute permanent section pathology.

Key words: Frozen Section, section pathology, lymph node

1. INTRODUCTION

Generally most people get affected by lymphadenitis and lymph nodes, which need to be studied for cytological and pathological aspects. Early diagnosis of malignancies in lymph nodes, treatment and surgery method are quiet important (1). Frozen Section (FS) is a putative challenge between surgeons and pathologists (2, 3). FS plays a key role in surgeon decision making and may greatly assist a surgeon to specify a surgery method (4, 5). FS technique is performed as following: subsequent to dissection of tissue by surgery without fixation, it is being frozen in tetrafluoroethane solution and provided with ANCAP manual microtome in 0.5 mm diameter sections. Samples are being placed on glass slides with frozen edges and stained with thionin. These slides are studied by pathologist with a Nikon YS-100 light microscope. The results are recorded and submitted to the operating room at the time of operation. There, the results are transmitted to database computer (6). Whereas, the most problems of the cancer patients are non-permanent diagnosis in metastasing disease, its expansion and simultaneous involvement of lymph nodes in areas around lesion, high expenses of frequent hospitalizations, and anesthesia stress following to repeated surgery operations; therefore, to reduce the costs and stop frequent hospitalizations and operations as well as anesthetic risks in the patients, there is a need for more precise studies on reliability of FS as a substitute for permanent section pathology or at least as an appropriate procedure for commencing the course of treatment (7, 8).

2. MATERIALS AND METHODS

This attempt is a cross-sectional study carried out after verification of Ethic committee of Yazd Shahid Sadoughi University of Medical Science and informed consent permission received from patients from 2012 to 2013 on 82 petients. Target population of study was inclusive of patients who had Excision of lymph nodes samples due to probability of cancer. Considering %95 confidence interval and sensitivity as %85 in Frozen Section method for lymph nodes biopsy and the minimum standard deviation of 0.07, sample size was selected among 82 individuals. Sampling was done using convenience way. In anesthetic situation in

operating room, some samples from lymph nodes tissue were dissected, transferred to laboratory and investigated by a pathologist. A researcher checklist was used in this study. In that inquiry, relevant information such as age, gender, biopsy section, Frozen Section pathology report and standard pathology report were recorded. All acquired data were analyzed by SPSS 15 software. For statistical comparison, T-test and kappa test were used. In all statistical tests, P-value was considered less than 0.05 as the significant level.

3. RESULTS AND DISCUSSION

82 individuals with mean age of 39.35 ± 15.5 were considered in this study. Minimum patient age was 6 and maximum was 79, of which 36 (%43.9) were men and 46 (%56.1) were women. In terms of biopsy location, for the most of patients 55 people (%67.1), was cervical and for 23 of them (%28), in axillary region (Table 1).

Table 1 . Distribution of studied samples based on biopsy position

Biopsy site	*Number(%)*
Neck	55(67.1%)
Axillary	23(28%)
Inguinal	1(1.2%)
Abdomen	3(3.7%)
Total	82(100%)

In the study of 82 samples with Frozen pathology and permanent section pathology, it was shown that in 71 cases yielded positive results of permanent section pathology, 66 cases had also successful results in Frozen pathology (Sen: %93) and following definite indicators have been evaluated that are: Sen= %93, Spe=%63.6, Accuracy=%89.0, NPV=%58.3, and PPV=%94.3 based on permanent section pathology. Further, concerning achieved results and constancy of Frozen test results with gold results via Kappa test, which it was concluded by considering kappa= 0.545 and P value= 0.001, the results of both methods are steady (Table 2).

Table 2 . Results of frozen pathology and standard pathology in samples under study

Gold / *Frozen*	*Positive*	*Negative*	*Total*
Positive	66	4	70
Negative	5	7	12
Total	71	11	82
P value: 0/001	Kappa: 0/545		

The results of these two methods were analyzed separately in men and women and Frozen Section test sensitivity in males was evaluated as %90.3 and in females as %95; the test specificity in men and women had been %80 and %50, respectively (Table 3).

Table 3. results of Frozen pathology and standard pathology in studied samples based on gender

Sex	*Gold* / *Frozen*	*Positive*	*Negative*	*Total*	Spe	Sen	PPV	NPV	ACC
	Positive	28	1	29					
	Negative	3	4	7	80%	93.3%	96.6%	57.1%	88.9%
Male	Total	31	5	36					
	P_Value=0.0001	Kappa: 0.602							
	Positive	38	3	41					
	Negative	2	3	5	50%	95%	92.7%	60%	89.1%
Female	Total	40	6	46					
	P_Value=0.001	Kappa: 0.484							

Moreover, the results of both tests were analyzed according the involved location and Frozen sensitivity was concluded %89.8 in cervical biopsied patient group and %100 for patients who were sampled from their axillary section (Table 4).

Table 4. Results of Frozen and standard pathology in studied samples based on biopsy location

Sex	*Gold* / *Frozen*	*Positive*	*Negative*	*Total*	Spe	Sen	PPV	NPV	ACC
	Positive	44	3	47					
	Negative	5	3	8	50%	89.8%	93.69%	37.5%	85.5%
Neck	Total	49	6	55					
	P_Value=0.009	Kappa: 0.347							

	Positive	19	1	20					
	Negative	0	3	3	75%	100%	95%	100%	82.6%
Axillary	Total	19	4	23					
	P_Value=0.0001	Kappa: 0.832							

It was observed in the study that based on Gold method, in 71 cases out of 82, the permanent pathology result was positive in cases with the mean age of 40.9 ± 15.3, and in 11 cases was negative, whose their mean age was 28.8±12.9, that is statistically significant (Table 5).

Table 5 . Distribution of samples under study based on standard pathology results

standard pathology results	*Number (%)*	*mean±SD*
Yes	71(86.6%)	40.9±15.3
No	11(13.4%)	28.8±12.9
t: 2/498 df: 80 P value: 0/015		

The biopsy in our study was carried out in cervical region of %72.2 men and %63 women. Likewise, %75 of individuals with 6-39 year old and %59.5 of 40-79 year old patients had also biopsy from their cervical area (Table 6).

Table 6 . Distribution of samples based on biopsy location, gender, and individuals' age group

Biopsy site		Abdomen	Inguinal	Axillary	Neck	Total
Sex	Male	1(2.8%)	1(2.8%)	8(22.2%)	26(72.2%)	36(100%)
	Female	2(4.3%)	0(0.0%)	15(32.6%)	29(63%)	46(100%)
	Total	3(3.7%)	1(1.2%)	23(28%)	55(67.1%)	82(100%)
Age (y)	6-39	1(2.7%)	1(2.5%)	8(20%)	30(75%)	40(100%)
	40-79	2(4.5%)	0(0%)	15(35.7%)	25(59.5%)	42(100%)

The results of study shows that sensitivity, specificity and positive and negative predictive value of this study were %93, %63, %94.3, and %58.3 respectively, and with kappa=0.545 and P=0.001, the accuracy of FS was considered as %89. Furthermore, the results of two studies were separately analyzed for both genders and the Frozen test sensitivity was %90.3 for males and %95 for females; the specificity of test has been %80 and %50 for men and women, respectively. The results of two tests were investigated based on the involved location and the sensitivity of Frozen Section test was calculated as %89.8 in patients biopsied from cervical area and %100 in patients in whom the biopsy was conducted from axillary region. According to kappa test results, it was found that the results of two methods in different locations of biopsy are constant. FS method has variable positive and negative predictive value as well as sensitivity in different diseases and different diagnostic accuracy eventually. The results were varied in different studies that one of the reasons may be the accuracy rate of pathologists. So far, numerous studies have been carried out attributed to breast cancer and evaluation of lymph nodes in axillary area (9, 10). Rohanna Ali et al. reported assessment of sentinel lymph nodes of breast cancer patients with using of Frozen Section during surgery, which it means, this method had a high sensitivity in determination of involved lymph nodes and the ability to prevent subsequent surgery in following hospitalizations (11). Shiller et al. in their study in Bayler University Medical Center in Dalas, studied 922 lymph nodes from 488 cases through tI cytology and Frozen Section and investigated the sensitivity and specificity indicators based on breast cancer subgroups and other tumor metastasis and methodology of morphology and relapse, and eventually, it was found that SLN biopsy is the most predictive factor in breast cancer and evaluation of sensitivity and specificity. Of its limitations were pathologic guidelines in classification of tumor appearance in capsule, subcapsule, or surrounding nodes, likewise, measuring tumor cells and their prevalence pattern had been remained dissolvable (10). A research carried out by Horvath et al. on Sentinel L.N Frozen Section in two types of breast cancer ILC and IDC, showed that whereas, accuracy, sensitivity, and positive predictive value among lymph nodes Frozen Section of these two cases have no significant difference, so, the accuracy of FS in IL, may not be lower than IDC, hence, FS in SLN is used as golden standard to reduce repeated surgery operation for discharging of axillary nodes(12). A research carried out by Ameriek J. Jensenet al. in Portland on accuracy of Frozen Section in study of axillary lymph nodes in breast cancer performed on 416 cases from 1999 to 2008 showed that the accuracy of FS is %88, sensitivity %100 and specificity %100 and most of false negative cases were due to malfunction in biopsy; it was concluded that FS is a reliable test in study of axillary lymph nodes in breast cancer, although, it has a less diagnostic value in DCIS (13). A study accomplished by Mark L Mitchell from 1998

to 2004 in the USA on Sentinel L.N Frozen Section of axillary area on 908 cases that had the sensitivity of %93 in diagnosis of malignancy in lymph nodes (14), which the results of above studies were consistent with our study. In present study we were not able to evaluate any of sensitivity, specificity, and positive or negative predictive value indicators in any particular anatomic areas such as abdomen, pelvis, cephalic, cervical, etc., and study of lymph nodes through FS method for axillary and cephalic and cervical areas was more accurate and effective attributed to abdomen and pelvis areas. A study carried out by Ozgur et al. in 2006 on 284 cases of patients with bladder cancer. The results showed that in 36 cases the result of biopsy in pelvis area was positive and only two cases of which were diagnosed before operation by CT scan, whereas, the results of FS in 29 cases were positive. As a result, it is supposed that whenever it is decided to bring out the lymph nodes of pelvis area, previous FS is necessary and just in case of positive result of FS, the discharge of lymph nodes shall be done to avoid postoperative complications. Results of study showed that sensitivity, specificity and predictive value of FS method in diagnosis of lymph nodes are %80.5, %97.2, %100, and %100 respectively, and these indicators were reported as %5.5, %97.1, %22.2, and %87.6 for CT scan respectively (15), that indicates that, FS diagnostic method is more appropriate than CT scan. In present study, only 3 cases (%3.7) of samples were associated with abdominal lymph nodes and we were not able to evaluate sensitivity, specificity, and predictive value indicators due to rareness of samples. Likewise, in cephalic and cervical diseases, the evaluation of lymph nodes is of great importance, because, in many cases, the task of physician to treat patients as infectious, cancerous, or reactive diseases in clinical situation is becoming complicated and it is only made through evaluation of lymph nodes. In a study performed by Chiniforoush et al. in 2009, they analyzed the pathological results of 100 cervical lymphadenectomies in pathology ward of Ardebil hospital. The results showed that in age group from 0 to 15 years old, reactive modifications with frequency of %57, in age group from 16 to 55 years old tuberculosis with frequency of %44.2, and in age group over 55 years old carcinoma metastatic with frequency of %57 were most prevalent causes of cervical lymphadenopathies. In both genders, tuberculosis cervical lymphadenopathy was the most prevalent (1). In certain cases such as thyroid diseases that accessibility to gland is more feasible, the mission is very simple and it is possible to take sample from lymph nodes of this area with no aggressive action and diagnose the disease partially. In a study made by Mirsadraei et al. in 2007 in Mashhad who investigated the diagnostic value of needle aspiration in thyroid nodules, the results showed that indicators of sensitivity, specificity, and negative and positive predictive value are %91.5, 9.5, 5.89, and %95.80 respectively, and as for its feasibility and cost-effectiveness, it is suggested to be carried out in suspicious patients to cancer (16). The results of this study are consistent with Eyel et al. study in 2013. The results of aforesaid study on analysis of SLN FS of thyroid cancer patients lymph nodes showed that %14.3 (300.43) samples had positive pathology and FS was positive in %11 of cases. Analyzing the results of this study showed that sensitivity, specificity, and positive and negative predictive value of this method are %68.8, %100, %100, and %94.4 respectively, and it represents FS method as an accurate and low cost method in diagnosis of thyroid tumors metastasis for cervical lymph nodes (17). Economic value of FS in disease diagnosis has been found in other researches. As, in a study performed by WeesamAlkhatib et al. on 133 patients (271 lymph nodes), permanent section pathology was compared with Frozen Section that is a reliable tool in diagnosis of involved node, false negative %4-8, sensitivity %91, specificity %100, hence, this results in reduction of anesthesia cost and risk in repeated operation (18).

4. CONCLUSION

The findings of present study imply that Frozen Section is a reliable method to substitute permanent section pathology. Evaluation of lymph nodes by frozen section not only can help in early diagnosis of metastasis, but also is more useful than other diagnostic modality such as frequent imaging include in CT scan and clinical findings.

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AUTHORS CONTRIBUTION

This work was carried out in collaboration between all authors.

CONFLICT OF INTEREST

The authors declared no potential conflicts of interests with respect to the authorship and/or publication of this article.

REFERENCES

1. CHINIFOROUSH M, SOTOUDEH M, JAMEEI A, SHAHBAZZADEGAN S. REVIEW OF THE PATHOLOGIC RESULTS OF 100 CERVICAL LYMPHADENOPATHIES AT FATEMI HOSPITAL OF ARDABIL FROM 2001-2005. JOURNAL OF ARDABIL UNIVERSITY OF MEDICAL SCIENCES (JAUMS). 2009.
2. Taxy JB. Frozen section and the surgical pathologist: a point of view. Archives of pathology & laboratory medicine. 2009;133(7):1135-8.
3. Hashmi AA, Faridi N, Khurshid A, Naqvi H, Malik B, Malik FR, et al. Accuracy of frozen section analysis of sentinel lymph nodes for the detection of Asian breast cancer micrometastasis–experience from Pakistan. Asian Pac J Cancer Prev. 2013;14(4):2657-62.
4. Geramizadeh B, Larijani TR, Owji S-M, Attaran SY, Torabinejad S, Aslani FS, et al. Accuracy of intra-operative frozen section consultation in south of Iran during four years. Indian Journal of Pathology and Microbiology. 2010;53(3):414.
5. Langer I, Guller U, Berclaz G, Koechli OR, Moch H, Schaer G, et al. Accuracy of frozen section of sentinel lymph nodes: a prospective analysis of 659 breast cancer patients of the Swiss multicenter study. Breast cancer

research and treatment. 2009;113(1):129-36.
6. Silva RDPd, Souto LRM, Matsushita GdM, Matsushita MdM. Diagnostic accuracy of frozen section tests for surgical diseases. Revista do Colégio Brasileiro de Cirurgiões. 2011;38(3):149-54.
7. McLaughlin SA, Ochoa-Frongia LM, Patil SM, Cody III HS, Sclafani LM. Influence of frozen-section analysis of sentinel lymph node and lumpectomy margin status on reoperation rates in patients undergoing breast-conservation therapy. Journal of the American College of Surgeons. 2008;206(1):76-82.
8. Tille J-C, Egger J-F, Devillaz MC, Vlastos G, Pelte M-F. Frozen section in axillary sentinel lymph nodes for diagnosis of breast cancer micrometastasis. Anticancer research. 2009;29(11):4711-6.
9. Bats A-S, Buénerd A, Querleu D, Leblanc E, Daraï E, Morice P, et al. Diagnostic value of intraoperative examination of sentinel lymph node in early cervical cancer: a prospective, multicenter study. Gynecologic oncology. 2011;123(2):230-5.
10. Shiller SM, Weir R, Pippen J, Punar M, Savino D. The sensitivity and specificity of sentinel lymph node biopsy for breast cancer at Baylor University Medical Center at Dallas: a retrospective review of 488 cases. Proceedings (Baylor University Medical Center). 2011;24(2):81.
11. Ali R, Hanly AM, Naughton P, Castineira CF, Landers R, Cahill RA, et al. Intraoperative frozen section assessment of sentinel lymph nodes in the operative management of women with symptomatic breast cancer. World journal of surgical oncology. 2008;6(1):69.
12. Horvath JW, Barnett GE, Jimenez RE, Young DC, Povoski SP. Comparison of intraoperative frozen section analysis for sentinel lymph node biopsy during breast cancer surgery for invasive lobular carcinoma and invasive ductal carcinoma. World J Surg Oncol. 2009;7(34.2009).
13. Jensen AJ, Naik AM, Pommier RF, Vetto JT, Troxell ML. Factors influencing accuracy of axillary sentinel lymph node frozen section for breast cancer. The American Journal of Surgery. 2010;199(5):629-35.
14. Mitchell ML. Frozen section diagnosis for axillary sentinel lymph nodes: the first six years. Modern pathology. 2004;18(1):58-61.
15. Ugurlu O, Adsan O, Tul M, Kosan M, Inal G, Cetinkaya M. Value of frozen sections of lymph nodes in pelvic lymphadenectomy in patients with invasive bladder tumor. International journal of urology. 2006;13(6):699-702.
16. MIRSADRAEI S, Mousavi Z, Farzadnia M, BAVAFA A, KAKHI S. Evaluation of diagnostic value of fine needle aspiration in thyroid nodules. MEDICAL JOURNAL OF MASHHAD UNIVERSITY OF MEDICAL SCIENCES. 2007.
17. Jozaghi Y, Richardson K, Anand S, Mlynarek A, Hier MP, Forest V-I, et al. Frozen section analysis and sentinel lymph node biopsy in well differentiated thyroid cancer. Journal of Otolaryngology-Head & Neck Surgery. 2013;42(1):48.
18. Alkhatib W, Hertzenberg C, Jewell W, Al-Kasspooles MF, Damjanov I, Cohen MS. Utility of frozen-section analysis of sentinel lymph node biopsy specimens for melanoma in surgical decision making. The American Journal of Surgery. 2008;196(6):827-33.