

The Accuracy of Frozen Section in the Diagnosis of Malignant Adnexal Masses

Malign Adneksiyal Kitlelerin Tanısında Donuk (Frozen) Kesit İncelemesinin Doğruluğu

Nuri Yıldırım¹, Alkım Gülşah Şahingöz Yıldırım², Ahmet Mete Ergenoğlu¹, Ahmet Özgür Yenieli¹, Osman Zekioglu³, Necmettin Özdemir³, M. Coşan Terek¹

ABSTRACT

Objective: To measure the accuracy of the frozen section in the diagnosis of malignant adnexal masses.

Methods: 192 patients who had been operated due to adnexal masses and submitted for intraoperative frozen section were evaluated retrospectively. The results were compared with paraffin section.

Results: In all cases, opinion on frozen section was available. The sensitivity of frozen section through benign, borderline and malignant tumors were 98.8%, 90% and 93.8% respectively, where as the specificity of the latter tumors were 92.3%, 98.9% and 100% respectively. The overall accuracy was 97.9%. Two benign cases were diagnosed as borderline, one borderline as benign and one malignant case as a benign in frozen section. The misdiagnosed malignant case was mucinous and the others were serous type tumors.

Conclusion: Frozen section has high accuracy in the diagnosis of malignant ovarian tumors. Paraffin section is the gold standard method, but because of the need for the quick result in the operation for the surgical management, frozen section must be performed to all suspicious adnexal masses.

Key words: Adnexal mass, frozen section, paraffin section

ÖZET

Amaç: Malign adneksiyal kitlelerin tanısında donuk (frozen) kesit incelemesinin doğruluğunun belirlenmesi

Yöntemler: Adneksiyal kitle nedeniyle opere edilen ve operasyon sırasında donuk kesit incelemesi istenen 192 hasta retrospektif olarak incelenmiştir. Sonuçlar parafin kesit sonuçlarıyla karşılaştırılmıştır.

Bulgular: Tüm olgularda, donuk kesit incelemesine yanıt verilebilmiştir. Donuk kesit incelemesinin, benign kitleleri saptamadaki duyarlılığı, %98,8; borderline (hudut) kitleleri saptamadaki duyarlılığı %90; malign kitleleri saptamadaki duyarlılığı ise %93,8 saptanmıştır. Spesifite sırasıyla %92,3, %98,9 ve %100 saptanmıştır. Toplamda doğruluk oranı ise %97,9 bulunmuştur. Donuk kesitler parafin kesitlerle karşılaştırıldığında, iki benign olguya yanlış olarak borderline, bir borderline olguya benign, bir malign olguya ise benign tanısı konulmuştur. Yanlış tanı konulan malign olgu müsinöz tip, diğer benign ve borderline olgular ise seröz tip over tümörüdür.

Sonuç: Donuk kesit incelemesi, malign adneksiyal kitleleri saptamada yüksek duyarlılığa sahiptir. Parafin kesit altın standart yöntemdir, ancak operasyon sırasında cerrahi müdahalenin şekli için daha hızlı yanıt gereklidir. Bu nedenle, donuk kesit incelemesi şüpheli adneksiyal kitlelerin cerrahi tedavisinde hızlı sonuç verdiği için tüm adneksiyal kitlelere uygulanmalıdır.

Anahtar kelimeler: Adneksiyal kitle, donuk kesit, parafin kesit

INTRODUCTION

Malignant ovarian neoplasm is the most common cause of death among gynecological cancers [1]. It is very important to differentiate malignant adnexal masses from benign and borderline tumors.

Borderline tumors are important because they are characterized by some histologic features of malignancy (epithelial cell stratification, increased mitotic activity, nuclear atypia) but lack of stromal invasion. In order to this, they don't have meta-

¹ Ege University Faculty of Medicine, Department of Obstetrics and Gynecology, Izmir, Turkey

² Tepecik Maternity and Research Hospital, Izmir, Turkey

³ Ege University Faculty of Medicine, Department of Pathology, Izmir, Turkey

Yazışma Adresi /Correspondence: Nuri Yıldırım,

Ege Üniversitesi Tıp Fakültesi Kadın Hastalıkları ve Doğum AD, Izmir, Turkey Email: nuri-yildirim@hotmail.com

Geliş Tarihi / Received: 23.09.2015, Kabul Tarihi / Accepted: 04.01.2016

Copyright © Dicle Tıp Dergisi 2016, Her hakkı saklıdır / All rights reserved

static activity. They have good long-term outcome after conservative surgery. Pathologic examination is necessary to diagnose malignant tumors. During surgery, surgeon must have opinion about the tumor to extent the surgery if the tumor is malignant. For this reason, section intra-operatively is a very useful method for extension or conservative management. In this study, we wanted to measure the accuracy of frozen section for diagnosing the feature of the tumor by comparing with the gold standard paraffin section. We also looked for the relationship between the volume of the tumor and the feature of them as benign, borderline or malignant.

METHODS

IN this study, 192 women operated for adnexal masses between 2005-2008 and underwent frozen section were retrospectively reviewed. The criteria for frozen section intra-operatively were:

- Clinically suspicious tumors (by imaging techniques or intraoperative inspection)
- Elevated CA125
- Family history
- Young patients who are planned to have conservative surgery for fertility preservation

After resection, tumor was immediately sent to the pathology laboratory without fixation. The frozen and the paraffin sections were reported by two experienced gynecological pathologists (N.O. and O.Z.) After macroscopic examination, the sections were obtained from the most suspicious regions by cryostat instrument and stained with hematoxylin-eosin. They were reported as benign, borderline or malignant approximately 15 minutes after the resection of the tumor. Later, frozen sections were compared with the paraffin sections.

For the statistical analysis, the final paraffin sections were assumed gold standard. For the comparison between the frozen and the paraffin section kappa value is used for measure of agreement; for sensitivity, specificity and predictive values, standard 2x2 tables were used. For the relationship between the tumor size and the malignancy feature of the tumor, Kruskal-Wallis test is used.

RESULTS

One hundred and ninety-two women who were operated for adnexal masses underwent frozen section to determine the malignancy potential of the tumor. Median age of the women was 45.5 (15-81 ages). Out of 192 patients, 188 were agreed with the final paraffin section and 4 were disagreed. The overall accuracy was 97,9% with kappa level 0,914. Two benign tumors are misdiagnosed as borderline, one borderline as benign and one malignant as benign in the frozen section. The misdiagnosed malign case was Krukenberg (mucinous) and the others were serous type tumors. The comparison between the results of frozen and the paraffin section are shown in the table 1 and the sensitivity, specificity and predictive values are shown in the table 2.

Out of 192 patients, 110 were premenopausal and the rest were postmenopausal. In 11 of the patients, tumor was bilateral, the frozen and the final paraffin section were all agreed in these patients. According to the data, tumor volume was significantly higher in malign cases according to the benign cases ($p=0.0001$) (Figure 1), but we could not found any statistically significant relationship between the CA125 level and the final paraffin section ($p=0.214$).

Table 1. The comparison between the results of frozen and the paraffin section

Frozen	Histopathology			Total
	Benign	Borderline	Malignant	
Benign, n	164	1	1	166
%within frozen	98.8	0.6	0.6	100
%within pathology	98.8	10	6.3	86.5
Borderline, n	2	9	0	11
%within frozen	18.2	81.8	0	100
%within pathology	1.2	90	0	5.7
Malignant, n	0	0	15	15
%within frozen	0	0	100	100
%within pathology	0	0	93.8	7.8
Total, n	166	10	16	192
%within frozen	86.5	5.2	8.3	100
%within pathology	100	100	100	100

Table 2. Sensitivity, specificity and predictive values of frozen section (CI 95%)

	Benign	Borderline	Malignant
Sensitivity, %	98.8 (0.97-1)	90 (0.71-1)	93.8 (0.81-1)
Specificity, %	92.3 (0.82-1)	98.9 (0.97-1)	100 (1-1)
PPV*, %	98.8 (0.97-1)	81.8 (0.59-1)	100 (1-1)
NPV**, %	92.3 (0.82-1)	99.4 (0.98-1)	99.4 (0.98-1)

*positive predictive value, **negative predictive value, CI: Confidence interval

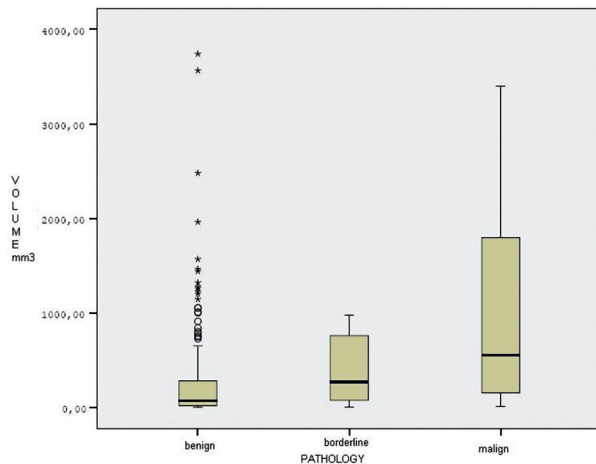


Figure 1. Relationship between the volume and the malignancy potential of the tumor (Tumor volume is significantly higher in malignant group according to benign group (p=0.0001)).

DISCUSSION

Malignant ovarian neoplasms are the most common cause of death among gynecological cancers [1] and preoperative diagnosis is limited [2,3]. It is necessary to know the behavior of the tumor intra-operatively, since the malignant tumor needs a greater resection such as hysterectomy, bilateral salpingo-oophorectomy, omentectomy and regional lymph node dissection. But in the benign or borderline tumor, there is no need to radical surgery; instead excision of the tumor is enough mostly. This distinction is very important especially for the young women at the reproductive ages for fertility preservation. Therefore, correct intraoperative histologic assessment is of the essence to avoid under or over treatment.

Frozen section is a very useful method for diagnosing the behavior of the tumor intra-operatively as benign, borderline or malignant, with a higher accuracy. Most studies have reported the accuracy of

frozen section from 90% to 97% [3-7]. In the present study, the overall accuracy is 97.9%.

In the literature, the reported frozen section utilization ratios for ovarian lesions range from 7.4% to 47% [8-10]. For endometriotic cysts and simple pure cystic lesions, surgeons do not prefer frozen section. Suspicious appearances, solid components, the older the age of the patient are providers for frozen section.

The sensitivity rates for benign and malignant tumors for frozen section are 98.8% and 93.8% respectively in our study and it is correlated with others [7,11,12]. The sensitivity rate for the borderline ovarian tumors is 90% similar to the study of Ilvan et al. with 87% [7]. But there are studies in which the sensitivity rate of the borderline tumors is lower that changes from 45% to 78% [4,12-15]. Positive predictive value of frozen section for malignant ovarian tumors is 100% in our study like many other studies [3-5,8,13]. This result indicates that any over-treatment or extensive unwarranted surgery was not performed to any patient.

In the present study, two benign tumors according to the final paraffin section were diagnosed as borderline and one borderline tumor diagnosed as benign in the frozen section. Although these results were wrong, the management for patients did not change at all. Only a patient whose final pathology result was Krukenberg (mucinous adenocarcinoma metastasis to ovary) tumor was diagnosed as benign in the frozen section. In the literature, there are these kinds of mistakes. In cases where the signet-ring cells are sparse, the stroma of Krukenberg tumor may mimic fibroma or fibro-thecoma in frozen sections [7,16].

In conclusion, the frozen section of the adnexal masses intra-operatively has high accuracy in the diagnosis of the behavior of the tumor. It is a very helpful method for surgeon in planning the management of the operation. The surgeon and the pathologist must be in a close contact and all clinical knowledge about the patient should be reported to the pathologist.

Declaration of Conflicting Interests: The authors declare that they have no conflict of interest.

Financial Disclosure: No financial support was received.

REFERENCES

1. Yancik R. Ovarian cancer. Age contrasts in incidence, histology, disease stage at diagnosis, and mortality. *Cancer* 1993;71:517-523.
2. Wakahara F, Kikkawa F, Nawa A, et al. Diagnostic efficacy of tumor markers, sonography and intraoperative frozen section for ovarian tumors. *Gynecol Obstet Invest* 2001;52:147-152.
3. Lim FK, Yeoh CL, Chong SM, et al. Pre and intraoperative diagnosis of ovarian tumours: how accurate are we? *Aust NZ J Obstet Gynaecol* 1997;37:223-227.
4. Rose PG, Rubin RB, Nelson BE, et al. Accuracy of frozen-section (intraoperative consultation) diagnosis of ovarian tumors. *Am J Obstet Gynecol* 1994;171:823-826.
5. Kudela M, Marek R, Pilka R, et al. Benefits and the accuracy of the intra-operative frozen section at suspected ovarian tumours. *Ceska Gynekol* 2015;80:250-255.
6. Alabalık U, Avcı Y, Keleş AN, et al. Five year evaluation of intraoperative pathology consultations in a university hospital. *Dicle Med J* 2013;40:207-211.
7. İlvan S, Ramazanoglu R, Ulker Akyıldız E, et al. The accuracy of frozen section (intraoperative consultation) in the diagnosis of ovarian masses. *Gynecol Oncol* 2005;97:395-399.
8. Twaalfhoven FC, Peters AA, Trimboş JB, et al. The accuracy of frozen section diagnosis of ovarian tumors. *Gynecol Oncol* 1991;41:189-192.
9. Maiman M, Seltzer V, Boyce J. Laparoscopic excision of ovarian neoplasms subsequently found to be malignant. *Obstet Gynecol* 1991;77:563-565.
10. Puls L, Heidtman E, Hunter JE, et al. The accuracy of frozen section by tumor weight for ovarian epithelial neoplasms. *Gynecol Oncol* 1997;67:16-19.
11. Usubutun A, Altınok G, Kucukali T. The value of intraoperative consultation (frozen section) in the diagnosis of ovarian neoplasms. *Acta Obstet Gynecol Scand* 1998;77:1013-1016.
12. Yeo EL, Yu KM, Poddar NC, et al. The accuracy of intraoperative frozen section in the diagnosis of ovarian tumors. *J Obstet Gynaecol Res* 1998;24:189-195.
13. Wang KG, Chen TC, Wang TY, et al. Accuracy of frozen section diagnosis in gynecology. *Gynecol Oncol* 1998;70:105-110.
14. Gol M, Baloglu A, Yigit S, et al. Accuracy of frozen section diagnosis in ovarian tumors: is there a change in the course of time? *Int J Gynecol Cancer* 2003;13:593-597.
15. Medeiros LR, Rosa DD, Edelweiss MI, et al. Accuracy of frozen-section analysis in the diagnosis of ovarian tumors: a systematic quantitative review. *In J Gynecol Oncol* 2005;15:192-202.
16. Acs G. Intraoperative consultation in gynecologic pathology. *Semin Diagn Pathol* 2002;19:237-254.