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RESEARCH PAPER

Diagnostic Performance of Frozen Section in Detecting Myometrial invasion and Cervical extension in Endometrial Carcinoma

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Abstract

Background: Low-risk endometrial cancer is treated with total hysterectomy and bilateral salphingo-oophorectomy. High-risk patients need detailed surgical staging including lymphadenectomy. An accurate preoperative work up and assessment of high-risk features during surgery is essential. So, an intraoperative frozen section is important for guiding surgical decisions by checking for myometrial invasion and cervical extension.

Objective: To assess the diagnostic performance of frozen section in detecting myometrial invasion and cervical extension in endometrial carcinoma.

Methods: This cross-sectional study was conducted at the Department of gynecological oncology at Bangladesh Medical University, Dhaka, from December 2022 to December 2023. We included 31 patients with histo-pathologically confirmed endometrial cancer (by fractional or diagnostic curettage) who underwent surgery. During surgery, frozen section of resected uterus was done and sent to pathology department to comment for deep myometrial invasion (≥50%) and the presence of cervical involvement within one hour. Later on, histopathology was done on the resected uterus. Finally, frozen section report was compared with final histopathology findings.

Results: The mean age of participants was 56.3 years, ranging from 35 to 70. Most were postmenopausal (83.9%) and nearly two-thirds had low parity. Common health issues included obesity (38.7%), diabetes, and hypertension (45.2%). To detect deep myometrial invasion compared to histopathology; the frozen section showed sensitivity 90.0%, specificity 95.2%, and overall accuracy 93.5%. To detected cervical extension compared to histopathology; the frozen section showed sensitivity 77.8%, specificity 95.5%, and accuracy 90.3%, with few false positive and negative results.

Conclusion: Frozen section is a reliable intraoperative method for evaluating myometrial invasion and cervical extension in endometrial cancer. It offers surgeons valuable real-time information, helping to guide surgical staging and treatment plans, for better patient outcomes.

Keywords: Endometrial cancer, frozen section, cervical extension, myometrial invasion.

Introduction

Endometrial carcinoma (EC) is the most frequently occurring gynecological malignant neoplasm in developed countries. In the Global Cancer Statistics, 420,368 new cases and 97,723 deaths occurred in 2022.[1] It represents the sixth most frequently occurring malignant disorder worldwide. The International Agency for Research on Cancer indicates that the incidence of endometrial cancer is rapidly increasing, estimating it will increase more than 50% over the next two decades across the world. Two main risk factors contributing to an increased incidence of endometrial cancer in high resource countries are increasing prevalence of obesity, as well as longer life expectancy. In contrast, the incidence of EC in low resource countries is only 3.3 per 100000 females.[2]

Endometrial carcinoma arises from the epithelial lining of uterine corpus. It is classified into two clinicopathological types (type I and type II). Type I or endometroid type of endometrial carcinoma is the most common subtype, accounting for >80% of endometrial

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carcinomas, and typically has a favorable prognosis. They are usually low-grade, well-differentiated, estrogen dependent, arise from endometrial hyperplasia and have hormone-receptor positivity. However, type II endometrial carcinoma is a less common type of serous or clear cell adenocarcinoma, accounting for only 10% of endometrial carcinomas. They are poorly differentiated, estrogen-independent tumors, associated with atrophic endometrium and have poor prognosis.[3,4] Nearly 85% of cases are diagnosed at an early stage (International Federation of Gynecology and Obstetrics: FIGO I and II) on the other hand 15% are diagnosed in advanced stage (FIGO III and IV).[5] Surgical staging and treatment represent the first approach for the affected patients.

Accurate preoperative staging of the disease is essential in planning the optimal course of treatment. Ability to distinguish between patients with deep or superficial myometrial invasion (FIGO Stage Ia vs. Stage Ib) would select those women who need pelvic lymphadenectomy.[6] Furthermore, tumor extension to the cervical stroma (Stage II) necessitates radical hysterectomy,[6] so knowledge of cervical extension could help in planning the optimal surgery. The surgical staging is considered comprehensive when it includes total hysterectomy, bilateral salpingo-oophorectomy, cytologic washings and pelvic and para-aortic lymphadenectomy.[7] However, the therapeutic value of en bloc lymphadenectomy is still unresolved in low risk endometrial cancers.[8] Risk classification primarily involves tumor histology, tumor grade and myometrial invasion (MI) and cervical extension.[9] Tumor histology and histological grade can be established before surgery with an endometrial biopsy. Consequently, timely diagnosis and accurate pre-operative assessment of MI and cervical extension are critical steps in planning the appropriate surgical treatment and improving prognosis for patients with endometrial carcinoma.[10] It should be noted that MI and the presence of malignancy in the cervical canal cannot be accurately determined with clinical examination alone. Therefore, being able to select low risk cases based on MI and cervical extension intraoperatively may assist in better surgical planning and avoiding unnecessary lymphadenectomy.[11]

Various pre- and peri-operative assessments, including imaging modalities such as magnetic resonance imaging (MRI) and computed tomography (CT)), and transvaginal ultrasound (TVS), may identify myometrial invasion and cervical extension. MRI sensitivity for myometrial invasion and cervical invasion was determined to be between 70% and 72.73%.[12] While MRI is the most sensitive imaging modality, CT is not as sensitive or specific. TVS sensitivity for myometrial invasion was determined to be 53%; and sensitivity for cervical invasion was determined to be 70%.[13] A prior study determined the sensitivity, specificity, positive predictive value, and negative predictive value in frozen section diagnosis of myometrial invasion with respect to early stage endometrial carcinoma to be 98.25%, 89.06%, 88.89%, and 98.28%, respectively.[14]

Endometrial cancer involving cervical stroma changes its staging and change the treatment modality. Therefore, assessment of cervical extent is important to proceed with surgical procedure. Santoro et al.[15] evaluated the use of frozen section in diagnosing cervical invasion, determining a sensitivity of 52.63%, specificity of 100.00%, and an overall diagnostic accuracy of 95.54%. Literature also indicates the need for intraoperative frozen section if patient has associated adenomyosis or leiomyoma when preoperative diagnosis is inconclusive.

In these contexts, the proposed study was done to assess the accuracy of frozen section biopsy in diagnosis of myometrial invasion and cervical extension in endometrial carcinoma.

Materials and Methods

A cross-sectional analytical research was carried out from December 2022 to December 2023 in the department of gynecological oncology in Bangladesh Medical University (BMU), Dhaka. Patients with endometrial carcinoma confirmed histopathologically after a fractional or diagnostic curettage and admitted for surgical management were included. The sample size was determined from the calculation of a diagnostic test. We used a previous study by Alcazar et al, 2016 which showed a frozen section specificity of 97% at a 95% confidence level and 5% error margin to determine our sample size.[16] The estimated sample size using these variables is estimated to be 51. However, frozen section can be done only in fresh specimen during surgery, total sample size included was 31 cases which met the inclusion criteria using a purposive sampling technique during the study period.

Patients with a histological diagnosis of endometrial carcinoma scheduled for surgery were eligible for inclusion, whereas patients who had received preoperative chemotherapy or radiotherapy, patients who had not undergone surgery, and patients who did not consent were excluded. Independent variables included age, parity, menopausal status, socioeconomic status, histological type and grade, FIGO stage, lymphovascular space invasion (LVSI), and lymph node involvement. Dependent variables included deep myometrial invasion (≥50%) and cervical stromal extension.

After obtaining authorization from the institutional review board of BMU, we approached patients with histologically confirmed endometrial cancer admitted to the gynaecological oncology department at BMU for surgical management during the study period and who fit the inclusion criteria, and informed written consent was obtained. Surgical treatment following the institution's standard of care was performed on all of the patients. The request for a frozen section biopsy was sent to the pathology department the day before surgery. Following the removal of the uterus during the surgical procedure, it was sent for frozen section biopsy for evaluation in the pathology department. The pathologist, who was blinded to preoperative imaging, reported the depth of myometrial invasion and cervical extension within one hour. For the low risk group, surgery included total hysterectomy and bilateral salpingo-oophorectomy. For the high-risk group there was comprehensive surgical staging protocol which typically consists of total hysterectomy, bilateral salpingo-oophorectomy, cytologic washing, and complete pelvic and selective para-aortic lymphadenectomy. Frozen section report and final histopathology report for myometrial invasion and cervical extension was noted in the data collection sheet along with the socio-demographic variables. The frozen section report for myometrium invasion and cervical extension was compared to final histopathology.

Following data collection, the data went through checking and clean-up; afterward, the data was edited, coded and categorized in order to check for errors or omissions to ensure consistency and validity. The data was then analyzed using SPSS for Windows (IBM SPSS Statistics for Windows, version 22.0, Armonk, NY: IBM Corp.) software. For descriptive statistics, means, standard deviations & ranges was calculated for numerical data, and frequencies & proportions for categorical data was also calculated wherever required. To compare frozen section with definitive histopathology, McNemar's test was conducted. All p-values less than 0.05 was considered statistically significant. Sensitivity, specificity, positive predictive value and negative predictive value of frozen section was calculated for both myometrial invasion and cervical extension, considering final histological diagnosis as the "gold standard".

Results

The study was conducted among 31 patients diagnosed with endometrial carcinoma. It was found that more than one third (38.7%) subjects were in the age category of 61-70 years. The mean age of study subjects was 56.32±9.92 years, and ranged from 35 to 70 years. One-fourth 15(48.4%) subjects had monthly income 28,811-89,280 Tk. The greatest proportion of study subjects (96.8%) did not take OCP. None of them had a history of HRT. More than one third 11(35.5%) of the study subjects had primary education. Almost two thirds of study subjects 20(64.5%) had low parity (P1-2). The majority of study subjects (83.9%) were post-menopausal. More than one third (38.7%) of study subjects were obese. The mean BMI was 26.6±4.7 kg/m^2, and ranged from 19 to 35.1 kg/m^2 (table-I).

Table I: Distributions of the study subjects by demographic characteristics (N=31)

Demographic Characteristics	Number	Percentage
Age (in years)		
31-40	1	3.2
41-50	8	25.8
51-60	10	32.3
61-70	12	38.7
Mean±SD	56.32±9.92	
Range	35-70	
Monthly Income		
<7,378	2	6.5
7,378-28,810	8	25.8
28,811-89,280	15	48.4
>89,281	6	19.4
Taking of OCP		
Yes	1	3.2
No	30	96.8
History of HRT		
No	31	100.0
Education		
Illiterate	5	16.1
Primary	11	35.5
Secondary	8	25.8
Higher secondary	5	16.1
Graduate and above	2	6.5
Parity		
Nulliparous	1	3.2
P (1-2)	20	64.5
p≥3	10	32.3
Menopausal status		
Pre-menopausal	5	16.1
Post-menopausal	26	83.9
BMI (kg/m^2)		
18.5-24.9	10	32.3
25-29.9	9	29.0
30-34.9	12	38.7
Mean±SD	26.6±4.7	
Range	19-35.1	

Comparison of myometrial invasion by frozen section against post operative histopathology for evaluation

of deep myometrial invasion (≥ 50%) whereby it was found there were 9(90%) cases of deep myometrial invasion were identified by both investigations (true positives) and 20(95.23%) was found to be not having deeper invasion (true negative) by both investigations. One patient was falsely identified as deeper invasion where histopathology was negative and 1(10%) patient was identified as 1(one) false negative by frozen section. The difference was not statistically significant (p=1.000) in the McNemar test. This shows that frozen section has comparable diagnostic performance to final histopathology in detecting deep myometrial invasion(table-II). The diagnostic performance of frozen section for detection of deep myometrial invasion was evaluated considering final histopathology as gold standard. It was found that sensitivity, specificity, accuracy, positive and negative predictive value was 90.0%,95.2%,93.5%,90.0% and 95.2% respectively (table-IV).

The cervical extension by frozen section was compared with final histopathological report. The study revealed that there were true positive 7(87.5%) cases, false positive 1(12.5) case, false negative 2(8.69%) cases and true negative 21(91.3) cases. The difference was statistically not significant (p=1.000) in McNemar test. That means frozen section had almost similar performance like final histopathology in detecting cervical extension (table-III). The diagnostic performance of frozen section for detecting cervical extension was evaluated considering final histopathology as gold standard. In this study the sensitivity, specificity, accuracy, positive and negative predictive value was 77.8%,95.5%,90.3%,87.5% and 91.3% respectively(table-IV)

Table II: Comparison of of frozen section and post-operative histopathology in detecting deep myometrial invasion (N=31).

Myometrial invasion by frozen section	Myometrial invasion by post-operative histopathology		P-value
	Deep invasion (n=10)	Superficial invasion (n=21)	
Deep invasion (n=10)	9(90%)	1(10%)	1.0
Superficial invasion (n=21)	1(4.7%)	20(95.23%)	

Deep invasion: ≥ 50% invasion, Superficial invasion: no or <50% invasion

Table III: Diagnostic performance of frozen section in detecting cervical extension (N=31).

Cervical extensionby frozen section	Cervical extension bypost-operative histopathology		P-value
	Present (n=9)	Absent (n=22)	
Present (n=8)	7(87.5%)	1(12.5%)	1.0
Absent (n=23)	2(8.69%)	21(91.3%)	

Table IV: Diagnostic performance of frozen section in detecting deep myometrial invasion & cervical extension(N=31)

	Sensitivity	Specificity	PPV	NPV	Accuracy
Myometrial invasion	90%	95.2%	90%	95.2%	93.5%
Cervical Extension	77.8%	95.5%	87.5%	91.3%	90.3%

PPV-positive predictive value, NPV-negative predictive value

Discussion

In this study we have assessed how accurately intraoperative frozen section (FS) can assess myometrial invasion and cervical extension in endometrial cancer. It compared FS performance to final histopathology. The average patient age was 56.3 years, which aligns with the global peak incidence of endometrial cancer occurring between ages 50 and 65.[17] Most patients were postmenopausal (83.9%) and obese (38.7%), both established risk factors for this type of cancer[18]. Additionally, 45.2% had diabetes and hypertension, which highlights the strong link between metabolic conditions and cancer risk, as seen in earlier research.[10, 4] The study's pathological findings were consistent with previous literature: 87.1% had endometrioid histology, 61.3% were grade G1 tumors, and 54.8% had tumors larger than 2 cm. Most patients were diagnosed at early FIGO stages, similar to findings reported by Ozgen and Ozgen and Wang et al[18,19]. Lymph vascular space invasion occurred in 19.4% of patients, and pelvic node positivity was noted in 12.9%, indicating the varied prognosis within the group. Assessing myometrial invasion is crucial for surgical staging. In this study, FS showed a high agreement with final histopathology, finding that 32.3% of patients had deep invasion (≥50%). Frozen section had a sensitivity of 90.0%, specificity of 95.2%, accuracy of 93.5%, PPV of 90.0%, and NPV of 95.2%. These figures are similar to previous studies, where sensitivity ranged from 74% to 93% and specificity from 95% to 97%.[20] Although there was one false positive and one false negative case, the overall performance supports FS's usefulness during surgery, especially for decisions about lymphadenectomy.

Frozen section detected cervical extension in 25.8% of patients, while final pathology found it in 29.0%, indicating strong agreement. FS had a sensitivity of 77.8%, specificity of 95.5%, accuracy of 90.3%, PPV of 87.5%, and NPV of 91.3% in detecting cervical extension. While the sensitivity was lower than for myometrial invasion, the specificity remained high. These results are similar to Richardson et al[21]. who reported a sensitivity of 57.1% and a specificity of 100%. The occurrence of two false negatives in this cohort shows the challenges in identifying subtle cervical involvement, but the high specificity indicates FS is trustworthy for ruling out extension during surgery.

Overall, the findings support FS as a useful diagnostic tool in endometrial cancer, especially in areas where advanced preoperative imaging might not be available. Its high specificity and accuracy for myometrial and cervical involvement make it relevant for deciding surgical staging while minimizing the risk of under- or overtreatment. However, there are some problems with false negatives, particularly for cervical extension, which underscores the need for careful histopathological confirmation.

This study had several limitations. First, the relatively small sample size (n=31) could limit the statistical power and generalizability of the results. Second, the interpretation of FS is prone to inter-observer variability, and the accuracy can depend on the pathologist's expertise. Third, sampling errors during intraoperative sectioning might lead to false negatives, especially in cases of focal cervical extension or subtle deep invasion. Additionally, since this was a single-center study, its external applicability may be limited. Future research should include larger multicenter groups to confirm the diagnostic accuracy of FS across different populations. Combining FS with advanced imaging techniques, like MRI or molecular markers, could further improve intraoperative decision-making. Establishing standard protocols for FS processing and interpretation may also help to reduce variability and enhance reproducibility.

Conclusion

The study showed that frozen section was highly comparable with the definitive histopathological examination in detecting myometrial invasion and cervical extension in endometrial cancer. Therefore, frozen section can be considered routine where facilities are available; for management of patients with endometrial cancer by selecting patient for surgical staging including retroperitoneal lymphadenectomy.

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References

1. Filho AM, Laversanne M, Ferlay J, Colombet M, Piñeros M, Znaor A, et al. The globocan 2022 cancer estimates: Data sources, methods, and a snapshot of the cancer burden worldwide. *International Journal of Cancer*. 2024; 156:1336–46. doi:10.1002/ijc.35278
2. Kehoe S, Bhatla N. Figo Cancer Report 2021. *International Journal of Gynecology & Obstetrics.* 2021 ,155:5–6. doi:10.1002/ijgo.13882
3. Qiu M, Bao W, Wang J, Yang T, He X, Liao Y, et al. FOXA1 promotes tumor cell proliferation through ar involving The notch pathway in endometrial cancer. *BMC Cancer.* 2014 ;14. doi:10.1186/1471-2407-14-78
4. Guo Q, Yi H, Chen X, Song J, Chen L, Zheng X. Is routine frozen section analysis necessary in patients with non endometrioid cancer or grade 3 endometrioid cancer? *International Journal of Gynecology & Obstetrics.* 2021; 156:256–61. doi:10.1002/ijgo.13712
5. Murali R, Soslow RA, Weigelt B. Classification of endometrial carcinoma: More than two types. *The Lancet Oncology*. 2014 ;15. doi:10.1016/s1470-2045(13)70591-6
6. Savelli L, Ceccarini M, Ludovisi M, Fruscella E, De Iaco PA, Salizzoni E, et al. Preoperative local staging of endometrial cancer: Transvaginal Sonography vs. Magnetic Resonance Imaging. *Ultrasound in Obstetrics & Gynecology*. 2008; 31:560–66. doi:10.1002/uog.5295
7. Amant F, Moerman P, Neven P, Timmerman D, Van Limbergen E, Vergote I. Endometrial cancer. *The Lancet*. 2005; 366:491–505. doi:10.1016/s0140-6736(05)67063-8
8. Seracchioli R, Solfrini S, Mabrouk M, Facchini C, Di Donato N, Manuzzi L, et al. Controversies in surgical staging of endometrial cancer. *Obstetrics and Gynecology International.* 2010 ;2010(1). doi:10.1155/2010/181963
9. Bogani G, Dowdy SC, Cliby WA, Ghezzi F, Rossetti D, Mariani A. Role of pelvic and para aortic lymphadenectomy in endometrial cancer: Current evidence. *Journal of Obstetrics and Gynaecology Research.* 2014; 40:301–11. doi:10.1111/jog.12344
10. Yang X, Yin J, Fu Y, Shen Y, Zhang C, Yao S, et al. It is not the time to abandon intraoperative frozen section in endometrioid adenocarcinoma: A large scale, multi Center, and Retrospective Study. *Cancer Medicine*. 2023; 12:8897–910. doi:10.1002/cam4.5643
11. Mariani A, Dowdy SC, Cliby WA, Gostout BS, Jones MB, Wilson TO, et al. Prospective assessment of lymphatic dissemination in endometrial cancer: A paradigm shift in surgical staging. *Gynecologic Oncology*. 2008; 109:11–8. doi: 10.1016/j.ygyno.2008.01.023
12. Yin X, Jia H, Shi M, Wu H, Li Y. Magnetic resonance imaging for detection of depth of myometrial invasion and cervical invasion in patients with endometrial carcinoma. *Int J Clin Exp Med*. 2015; 8:19501-19505. Available from: https://pmc.ncbi.nlm.nih.gov/articles/PMC4694500/
13. Khokhani DP. Endometrial thickness by ultrasonography and its correlation with histopathology in abnormal uterine bleeding among peri and post-menopausal women. *Journal of Population Therapeutics and Clinical*. 2021;695–99. doi:10.53555/fg53rx09
14. Gitas G, Proppe L, Alkatout I, Rody A, Kotanidis C, Tsolakidis D, et al. Accuracy of frozen section at early clinical stage of endometrioid endometrial cancer: A retrospective analysis in Germany. *Archives of Gynecology and Obstetrics*. 2019; 300:169–74. doi:10.1007/s00404-019-05158-0
15. Santoro A, Piermattei A, Inzani F, Angelico G, Valente M, Arciuolo D, et al. Frozen section accurately allows pathological characterization of endometrial cancer in patients with a preoperative ambiguous or inconclusive diagnosis: Our experience. *BMC Cancer*. 2019 Nov;19. doi:10.1186/s12885-019-6318-5
16. Alcazar JL, Dominguez-Piriz J, Juez L, Caparros M, Jurado M. Intraoperative gross examination and intraoperative frozen section in patients with endometrial cancer for detecting deep myometrial invasion: a systematic review and meta-analysis. *International Journal of Gynecological Cancer*. 2016; 26:200-7. doi: 10.1097/IGC.0000000000000618.
17. Ravegnini G, Gorini F, De Crescenzo E, De Leo A, De Biase D, Di Stanislao M, et al. Can mirnas be useful biomarkers in improving prognostic stratification in endometrial cancer patients? an update review. *International Journal of Cancer*. 2021; 150:1077–90. doi:10.1002/ijc.33857
18. ÖZGEN L, ÖZGEN G. Comparison of frozen section accuracy with final pathology results in early clinical stage of endometrioid type endometrial cancer. *The European Research Journal.* 2023; 9:1034–39. doi:10.18621/eurj.1307265
19. Wang T, Jiang R, Yao Y, Wang Y, Liu W, Qian L, et al. Endometrial cytology in diagnosis of endometrial cancer: A systematic review and meta-analysis of diagnostic accuracy. *Journal of Clinical Medicine*. 2023; 12:2358. doi:10.3390/jcm12062358
20. Hahn H-S, Song H-S, Lee I-H, Kim T-J, Lee K-H, Shim J-U, et al. Magnetic resonance imaging and intraoperative frozen sectioning for the evaluation of risk factors associated with lymph node metastasis in endometrial cancer. *International Journal of Gynecological Cancer*. 2013; 23:1411–416. doi:10.1097/igc.0b013e3182a580d3
21. Richardson KJ, Soeters R, Whittaker J, Van Wijk R, Dehaeck K. The role of frozen section in the management of early endometrioid endometrial carcinoma. *Southern African Journal of Gynaecological Oncology*. 2011; 3:28–33. doi:10.1080/20742835.2011.11441171