



Research article

Accuracy of intraoperative frozen section in surgical staging of endometrial cancer

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ABSTRACT

Objective: This study evaluates the role of frozen section (FS) in determining the extent of disease during surgery.

Materials and methods: This study retrospectively analyzed a cohort of patients diagnosed with endometrioid-type endometrial cancer between 2019 and 2022 who underwent surgical intervention. The frozen section (FS) results were compared with the final pathology reports, focusing on tumor grade, depth of myometrial invasion, cervical involvement, and tumor diameter.

Results: The final analysis included 187 patients. The predictive accuracy of FS in determining PS results was 85.6 % for endometrioid histology, 95.7 % for grade 3 tumors, 90.2 % for depth of myometrial invasion, 89.7 % for cervical involvement, and 95.9 % for tumor diameter. Notably, 9.8 % of cases initially classified as grade 1 intraoperatively were upgraded with the final pathology. Similarly, 6.3 % of grade II cases were upgraded, while 60.4 % were downgraded.

Conclusion: Our study highlights the effectiveness of FS as a dependable tool for assessing endometrial carcinomas and guiding surgical staging decisions. By utilizing FS, the risk of unnecessary surgeries and associated morbidity in patients can be reduced.

1. Introduction

Endometrial cancer is the sixth most commonly diagnosed cancer and the 14th leading cause of cancer death among women worldwide [1]. The majority of patients (71 %) present with disease localized to the uterus, classified as stage I by the International Federation of Gynecology and Obstetrics (FIGO) staging system [2,3]. Endometrial cancer predominantly affects postmenopausal women. Studies indicate that 3–20 % of women with postmenopausal bleeding are diagnosed with endometrial cancer, while 5–15 % are found to have endometrial hyperplasia [4,5].

The most prevalent type of endometrial cancer is endometrioid adenocarcinoma [6]. The most crucial prognostic factors for endometrial cancer include myometrial invasion (MI), lymphovascular space invasion, lymph node involvement, and recurrence [7]. While comprehensive surgical staging is widely accepted as essential for high-risk endometrial cancer due to the significant risk of cancer spreading to nearby lymph nodes, the necessity of pelvic and paraaortic lymph node resection in the complete surgical staging of low-risk endometrial cancer remains controversial [8–12].

The likelihood of lymph node involvement increases with factors such as higher tumor grade, deeper myometrial invasion, cervical

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involvement, adnexal metastasis, presence of lymphovascular invasion, and the presence of a histological subtype associated with a poor prognosis [8]. The reported prevalence of pelvic and para-aortic lymph node metastases ranges from 5 % to 34 % and 5 %–25 %, respectively [13].

This study aims to evaluate the concordance between frozen section (FS) and permanent section (PS) in assessing tumor grade, depth of myometrial invasion, and cervical involvement.

2. Materials and methods

This retrospective study included 187 patients who underwent surgical staging for endometrioid-type endometrial cancer at the gynecological oncology department of Mersin University Hospital between 2019 and 2022. Upon admission, patients were asked for their consent to participate in retrospective data research, and written authorization was obtained from those who agreed. The study was approved by the Mersin University Clinical Research Ethics Committee (number: October 04, 2023/668).

All study participants had a preoperative diagnosis of endometrioid-type endometrial cancer established through either endometrial biopsy or curettage. During the specified timeframe, 235 individuals received a clinical diagnosis of endometrial cancer based on histological examination. The final analysis included 187 patients after excluding 48 individuals who were found to have non-endometrioid endometrial cancer, carcinosarcoma, or leiomyosarcoma on endometrial biopsy.

Patient data, including age, stage, grade, depth of myometrial invasion, cervical involvement, and tumor size, were extracted from medical records. The initial surgical intervention consisted of a hysterectomy and bilateral salpingo-oophorectomy, followed by FS analysis of the specimen. Lymph node dissection was performed in cases where the FS revealed high-risk features. In some instances, lymphadenectomy was also carried out in select low-risk cases based on the attending physician's clinical judgment. The study included patients with a preoperative endometrial biopsy confirming endometrioid-type endometrial cancer and an intraoperative frozen section analysis. Patients with intraoperative FS findings indicative of specific histological types, such as carcinosarcoma or leiomyosarcoma, were excluded from the study. Additionally, individuals with concurrent primary ovarian cancers were excluded. In certain cases, intraoperative frozen section analyses yielded results that fell within a range, such as Grade 1–2 or Grade 2–3. In these instances, where a definitive grade could not be assigned, the clinical decision-making process erred on the side of caution, and the higher grade within the reported range was assumed for subsequent management and treatment planning. This approach prioritizes patient safety and ensures that potentially more aggressive therapeutic interventions are not overlooked due to an ambiguous initial assessment. The FS results were compared with the final PS findings. The accurate diagnosis provided by an experienced pathologist was considered the gold standard.

The study analyzed age and various pathological factors, including histopathologic type, tumor diameter, grade, myometrial invasion, and cervical involvement, as assessed by both FS and PS. The sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and accuracy of FS in predicting PS outcomes were evaluated for each parameter.

Statistical analysis was performed using SPSS (Armonk, NY, USA: IBM, demo 22 version). Categorical variables were summarized using counts and percentages, while continuous variables were summarized using means and standard deviations. The chi-square test was employed to analyze the association between categorical variables. The sensitivity, specificity, PPV, NPV, and accuracy of FS findings in predicting PS outcomes were calculated. A significance level of 0.05 was used for all statistical tests.

3. Results

During this period, our clinic examined 894 frozen sections, of which 235 (26.3 %) were for endometrial cancer. The patients' average age was 59.73 ± 9.29 years (range 33–84) (Table 1). Of the 187 patients, 124 (66.3 %) underwent laparotomy, and 63 (33.7 %) underwent laparoscopy. Among the laparotomy group, 13 (10.5 %) patients received only hysterectomy and bilateral salpingo-oophorectomy. Pelvic lymph node dissection was performed in 43 (34.7 %) patients along with hysterectomy. In 68 (54.8 %) patients, both pelvic and para-aortic lymph node dissection were performed in conjunction with hysterectomy. In the laparoscopy group, 24 (38.1 %) patients underwent only hysterectomy and bilateral salpingo-oophorectomy. Pelvic lymph node dissection was performed in 32 (50.8 %) patients along with hysterectomy, while 7 (11.1 %) patients underwent both pelvic and para-aortic lymph node dissection in addition to hysterectomy.

Table 1
The mean age of patients and FIGO stages.

Age (mean \pm SD)	59.73 \pm 9.29
FIGO Stage n (%)	
IA	122 (66.7)
IB	32 (17.5)
II	10 (5.5)
IIIA	2 (1.1)
IIIB	1 (0.5)
IIIC1	9 (4.9)
IIIC2	5 (2.7)
IVA	1 (0.5)
IVB	1 (0.5)

The FS examination identified 179 (95.7 %) patients as malignant and 8 (4.3 %) as benign. The PS results diagnosed 183 (97.9 %) patients as malignant and 4 (2.1 %) as benign (Table 2).

In the entire study population, 176 patients (84.1 %) were diagnosed with endometrioid-type endometrial cancer during the initial frozen section analysis. Similarly, 163 patients (87.2 %) were identified as having endometrioid-type endometrial cancer in the subsequent permanent section analysis (Table 2). The sensitivity and specificity of frozen section analysis in predicting permanent section results were 95.7 % and 16.7 %, respectively. The PPV was 88.6 %, and the NPV was 36.4 %. The overall accuracy of frozen section analysis in detecting endometrioid-type histology was 85.6 % (Table 3).

The average tumor diameter was 3.68 ± 1.67 cm on FS reports and 3.66 ± 1.73 cm on PS reports (Table 2). Tumor size was not specified in two patients despite an FS result of endometrioid endometrial cancer. When classifying tumor diameter as <2 cm or ≥ 2 cm, the sensitivity and specificity of FS were 97.4 % and 83.3 %, respectively (Table 3).

The sensitivity and specificity of FS for assessing myometrial invasion (MI) were 81.6 % and 93.7 %, respectively. The PPV was 83.3 %, and the NPV was 92.9 % (Table 3). In one patient, MI could not be determined by FS.

The study revealed that cervical involvement was reported in 7.3 % of patients at FS and 13.7 % at PS (Table 2).

The grade was not reported in the FS results of four patients, and the PS grade was not reported in 12 patients. The accuracy rates for tumors classified as grade 1, grade 2, and grade 3 were 75.0 %, 73.2 %, and 95.7 %, respectively (Table 3).

4. Discussion

The management of low-risk endometrial cancer remains a subject of considerable debate, particularly regarding the use of lymphadenectomy, postoperative chemotherapy, and postoperative radiation therapy. The decision to perform lymphadenectomy is influenced by various factors, with tumor grade, diameter, and MI being particularly significant. Endometrioid endometrial cancer is categorized into three risk groups: low, intermediate, and high. The low-risk group includes tumors with grade 1 or 2 and superficial MI (<50 %). The intermediate-risk group encompasses tumors with deep MI (≥ 50 %) or grade 3 tumors with superficial MI (<50 %). The high-risk group consists of tumors with grade 3 and deep MI (≥ 50 %). These risk categories are defined based on MI and tumor grade. Lymphadenectomy is generally not recommended for low-risk patients, may be considered for intermediate-risk cases, and is recommended for high-risk cases [14].

The typical age of onset for endometrial cancer is between 50 and 65 years, with an average age at diagnosis of 60 years [15]. In our study, the average age of patients diagnosed with endometrial cancer was 59.73 ± 9.29 years.

The primary objective of this study was to establish a correlation between the grade and myometrial invasion assessed by frozen section analysis and permanent pathology assessment. Our investigation revealed that 9.8 % of cases initially classified as grade I intraoperatively were subsequently upgraded with the PS. Similarly, 6.3 % of grade II cases were upgraded, while 60.4 % were downgraded. The clinical implications of grade upgrading in endometrial cancer were effectively demonstrated by Creasman et al. [8]. Their study showed that a transition from grade I to grade II doubled the likelihood of myometrial invasion into the middle and outer thirds of the uterus. These findings suggest a higher recurrence rate, poorer prognosis, and the potential need for adjuvant radiation therapy [16,17].

The FS demonstrated a sensitivity of 85 % and a specificity of 97 % in predicting myometrial invasion in cases with endometrial

Table 2
FS and PS results of tumor grade, MI, histological type, tumor diameter, and cervical involvement.

	FS n (%)	PS n (%)
Benign	8 (4.3)	4 (2.1)
Malign	179 (95.7)	183 (97.9)
Histologic type		
Endometrioid	176 (94.1)	163 (87.2)
Non Endometrioid	3 (1.6)	11 (5.9)
Mix	0	6 (3.2)
Carcinosarcoma	0	3 (1.6)
Endometrial Hyperplasia	3 (1.6)	3 (1.6)
Other Benign results	5 (2.7)	1 (0.5)
Tumor diameter		
<2 cm	21 (11.9)	24 (13.1)
≥ 2 cm	156 (88.1)	159 (86.9)
Diameter (mean \pm SD)	3.68 ± 1.67	3.66 ± 1.73
Myometrial invasion		
<50 %	130 (73.0)	133 (72.7)
≥ 50 %	48 (27.0)	50 (27.3)
Cervical involvement		
No Cervical involvement	166 (92.7)	158 (86.3)
Cervical involvement	13 (7.3)	25 (13.7)
Tumor grade		
Grade 1	104 (59.4)	130 (76.0)
Grade 2	51 (29.1)	28 (16.4)
Grade 3	20 (11.4)	13 (7.6)

Table 3

The precision of frozen section analysis in forecasting paraffin section outcomes.

	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Accuracy (%)
Malign-Benign Differentiation	96.2	25.0	98.3	12.5	94.65
Endometrioid Type Histology	95.7	16.7	88.6	36.4	85.6
Tumor Diameter	97.4	83.3	98.1	78.9	95.9
MI (50 %)	81.6	93.7	83.3	92.9	90.2
Cervical Involvement	40.0	98.0	76.9	90.8	89.7
Grade 1	74.8	75.6	90.2	50	75.0
Grade 2	57.1	76.5	33.3	89.7	73.2
Grade 3	76.9	97.4	71.4	98.0	95.7

MI: Myometrial invasion.

cancer [18]. Another research investigation observed that the FS exhibited a sensitivity and specificity of 92 % in predicting myometrial infiltration [19]. The current investigation assessed the sensitivity and specificity of frozen sections in predicting myometrial invasion, yielding values of 81.6 % and 93.7 %, respectively.

In the study by Kumar et al., 31 out of 784 examined cases (4 %) were identified as histologically discordant [20]. In contrast, the present investigation observed a higher prevalence of histological discordance, with 23 cases (12.7 %) out of the total sample size of 187. The predominant histopathological presentation in our cases was endometrioid tumors. Santoro et al. also examined the histopathological concordance rates, finding them to be 97.2 % for endometrioid cancer and 59 % for non-endometrioid cancer in their cohort of 202 individuals, of which 180 had endometrioid-type cancer [21]. Mandato et al. reported histopathological accuracy rates of 95 % and 76 % for type 1 and type 2 endometrial cancer, respectively [22]. In our study, based on the endometrioid-type histopathological assessment, the diagnostic accuracy of FS in predicting PS outcomes was 85.6 %. The sensitivity and specificity of FS were 95.7 % and 16.7 %, respectively.

The study found that the sensitivity and specificity of FS in predicting PS outcomes were 97.4 % and 83.3 %, respectively, when tumor diameter was categorized as either less than 2 cm or 2 cm or greater. Moreover, our accuracy findings are consistent with the previously reported range of 95.5 %–99.6 % [20,23].

Accurate molecular classification of endometrial cancer is essential for predicting prognosis and making treatment decisions. The 2023 FIGO staging revision now incorporates molecular subtypes, recognizing their significant impact on patient outcomes [24–26]. Our study was unable to incorporate molecular classification due to the timing of patient surgeries. However, future research should prioritize molecular profiling to optimize treatment strategies and enhance personalized care for endometrial cancer patients. While the 2023 FIGO staging highlights the importance of molecular classification, our study's primary aim was to assess the accuracy of frozen section diagnosis in predicting final pathology results, essential for informing surgical decision-making regardless of the molecular subtype.

The study's retrospective nature presents challenges in controlling for potential confounding factors and establishing causal relationships. Future validation of the results will require prospective studies. Due to being limited to a single center and having a relatively small sample size, the study's findings may have limited applicability to other populations and settings. Consequently, larger, multicenter studies are necessary to confirm the results. The absence of complete FS data for certain parameters in some cases serves as a limitation that could impact the analysis's accuracy, emphasizing the importance of prioritizing complete data collection in future studies. Moreover, focusing exclusively on endometrioid-type endometrial cancer limits the generalizability of the findings to other histological subtypes, indicating a need for further research to explore the role of FS in non-endometrioid endometrial cancers.

The research specifically delves into endometrioid-type endometrial cancer, which is the most prevalent subtype, thereby increasing the significance and relevance of the findings for this particular group of patients. The study assessed the agreement between FS and PS for various crucial parameters, offering a thorough insight into the precision and dependability of FS in surgical staging. The participation of experienced gynecopathologists in the examination of FS and PS samples bolsters the internal validity of the study by reducing potential bias in the assessment process.

Ethics committee approval

The Mersin University Clinical Research Ethics Committee approved the study on October 04, 2023 with the board decision numbered 668.

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Data availability statement

The authors do not have permission to share data.

CRedit authorship contribution statement

Sevki G. Gokulu: Visualization, Supervision, Project administration, Conceptualization. **Tolgay T. Ilhan:** Validation, Formal analysis. **Gorkem Ulger:** Writing – review & editing, Writing – original draft, Resources. **Ali Yildizbakan:** Resources, Investigation. **Murside Cevikoglu-Killi:** Software, Methodology. **Ayse Turkmen:** Resources.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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