Accuracy of frozen-section examination for myometrial invasion and grade in endometrial cancer

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ABSTRACT

Objective: To evaluate the accuracy of frozen section (FS) analysis in endometrial cancer.
Study design: The medical records of 816 patients with stage IA–IVB endometrial carcinoma were evaluated. Concordance of the frozen section examination and postoperative evaluation in terms of the depth of myometrial invasion (MI) and grade was assessed.
Results: The mean age of the patients was 58.1 years. Postoperative pathology revealed endometrioid type tumor in 756 patients. Concordance of intraoperative and postoperative pathology results in terms of grade was 89%. This rate was 96.8% for grade 1, 86% for grade 2 and 91.3% for grade 3 tumors. Sensitivity and specificity of intraoperative evaluation for grade 1, grade 2 and grade 3 were 89.3%, 91.2%, 77.8% and 93.1%, 96.1%, 99.5%, respectively. Intraoperative and postoperative determination of MI was consistent in 85.4% of patients. MI was assessed accurately in 78.5% of patients with no involvement of myometrium and in 90.5% and 95.3% of patients with myometrial invasion $<1/2$ and $\geq 1/2$, respectively. Sensitivity and specificity of FS in prediction of the absence of MI, MI $< 1/2$ and $\geq 1/2$ were 60%, 91.5%, 88.8% and 96.6%, 88.3%, 98.3%, respectively. The accuracy of myometrial invasion was affected by the postoperative grade. Concordance was higher in grade 2 and 3 than grade 1 tumors.
Conclusion: The accuracy of intraoperative pathologic evaluation in endometrial cancer is reasonably high. For that reason, results of the intraoperative pathologic examination should be taken into consideration primarily in the management for lymphadenectomy.

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1. Introduction

Intraoperative evaluation of the specimen with frozen section (FS) is very important in determining the type and extent of the surgery in gynecologic oncology. Other than its primary use in ovarian and endometrial cancer, it is feasible to use FS in all genital cancers [1,2].

Endometrial cancer has been proposed to be surgically staged by the FIGO since 1988, but the extent of the surgery for endometrial cancer is controversial and there is discussion on whether lymphadenectomy should be performed in the routine surgical procedure. Nonetheless, pelvic and para-aortic lymphadenectomy increases morbidity [3–5]. Also, addition of lymphadenectomy to the staging surgery of early stage endometrial cancer has been proven not to improve the survival [6]. In view of that, performing lymphadenectomy in all patients with endometrial cancer will result in overtreatment and an increase in morbidity. Detection of the risk factors predicting the lymph node involvement and performing lymphadenectomy in the patients with these risk factors will be the appropriate surgical treatment option. These risk factors are cell type, tumor size, presence of cervical invasion, grade and depth of myometrial invasion. These could be determined preoperatively or intraoperatively with different degrees of accuracy [7–13]. In terms of grade, concordance between the results of endometrial curettage and paraffin sections ranges from 36% to 96% [14–18]. Regarding the detection of the depth of myometrial invasion, magnetic resonance imaging, transvaginal ultrasonography and intraoperative macroscopic examination reveal varying degrees of concordance with postoperative pathology, respectively 70–95%, 78–85% and 81–91% [14,17,19–27]. Additionally, depth of myometrial invasion and grade can be detected with high accuracy with FS. Conversely, there are also studies showing quite low

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accuracy rates. The rates of accuracy reported with this method vary from 58% to 98% for the grade and 54% to 95% for the depth of myometrial invasion [14–17,26,28–36].

In this study, the efficiency of FS in determining the grade and depth of myometrial invasion in endometrial cancer was evaluated.

2. Materials and methods

Data of 816 endometrial cancer patients diagnosed and treated between 1993 and 2009 were analyzed. Staging surgery was performed according to the criteria of FIGO 1988. Endometrial curettage specimens that were pathologically diagnosed as complex atypical hyperplasia or endometrial cancer in other hospitals were assessed again. Hysterectomy materials of patients with the preoperative diagnosis of complex atypical hyperplasia or endometrial cancer were evaluated by FS intraoperatively. In evaluation of FS, the uterus was opened, the cavity was inspected for irregularities of contour and color, and 2–5 full-thickness slices were made through the wall of the uterus. The area of deepest myometrial invasion was selected for FS examination. If no tumor was apparent on gross examination, at least five random sections were performed. After all the samples were frozen at −25 °C, they were sliced in 8 μm thickness and stained with hematoxylin–eosin manually. They were evaluated for grade, depth of myometrial invasion, lymphovascular space invasion and size of the tumor.

Staging surgery was performed in patients whose FS analysis was reported as all cell types except endometrioid adenocarcinoma, grade 2–3 tumor, myometrial invasion of tumor $\geq 1/2$ and tumor size above 2 cm. Also, patients with a preoperative pathological diagnosis of high risk cell type or grade 3 tumors were staged directly. Although FS was performed in some of these patients, who were assessed as having high risk in the preoperative period, the decision of staging was not affected by the results of FS. All these patients underwent staging surgery regardless of the result of FS. We performed FS in these patients because of the academic studies done before.

The concordance between the results of FS and the results of paraffin sections was analyzed in terms of the presence of myometrial invasion and the tumor grade. Descriptive statistics were calculated by using the SPSS (Statistical Package for Social Sciences) 17.0 package program. Chi-square test was used for nominal variables and kappa test was used for dependent variables. The cut-off value for statistical significance was set at $p < 0.05$.

3. Results

The mean age of the patients was 58.1 years (29–93, median 59). The stage of the tumor was IB in 433 patients. The postoperative pathologic diagnosis of 756 patients was endometrioid type tumor in paraffin section analysis. For 22 patients in whom no tumor was detected at paraffin section, endometrial cancer had been reported in the preoperative endometrial curettage materials and these patients were accepted as stage IA. Intraoperative and postoperative pathological results of the patients are shown in Table 1.

3.1. Grade

Out of 64 patients whose FS analysis did not reveal malignancy, 44 patients (68.8%) were diagnosed as having endometrial cancer according to the results of paraffin section analysis (Table 2). Tumor was grade 1 in 43 of these 44 patients and grade 3 in one patient. Tumor was limited to the endometrium in 34 patients and myometrial invasion was reported in 10 patients but it was <1/2 of

Table 1
Surgical-pathologic factors.

Parameter	n	%
Stage		
IA	158	19.4
IB	433	53.1
IC	103	12.6
IIA	14	1.7
IIB	20	2.5
IIIA	17	2.1
IIIB	2	0.2
IIIC	51	6.3
IVA	2	0.2
IVB	16	2
Cell type in paraffin section		
Benign	22	2.7
Endometrioid	756	92.6
Clear cell	14	1.7
Serous	8	1
Mucinous	5	0.6
Squamous	1	0.1
Carcinosarcoma	1	0.1
Mixed type	9	1.1
Grade		
Frozen/section		
No tumor[a]	64	7.8
Grade 1	527	64.6
Grade 2	179	21.9
Grade 3	46	5.6
Paraffin section		
No tumor[a]	22	2.7
Grade 1	571	70
Grade 2	169	20.7
Grade 3	54	6.6
Myometrial invasion		
Frozen/section		
No tumor[a]	64	7.8
No myometrial invasion	107	13.1
<1/2	454	55.6
≥1/2	191	23.4
Paraffin section		
No tumor[a]	22	2.7
No myometrial invasion	140	17.2
<1/2	449	55
≥1/2	205	25.1

[a] Benign or hyperplasia.

the myometrium. Concordance between FS and paraffin section in terms of grade was 96.8%, 86% and 91.3% for grade 1, grade 2 and grade 3 tumor, respectively (Tables 2 and 3). While the concordance for all grades was 89% ($n = 756$), overestimation and underestimation of the grade were 2.8% ($n = 23$) and 8.2% ($n = 67$), respectively. When the level of grade increased, the probability of accurate determination of grade by FS decreased. While the sensitivity of FS for the tumor-free group was 94.5%, it decreased to 77.8% for patients with grade 3 tumor (Table 3). Additionally, tumor was not detected later in paraffin sections of 31.3% of patients who were reported to be tumor-free in FS (PPV). Nevertheless, out of cases wherein no tumor was identified in paraffin sections, 90.5% had been detected by FS intraoperatively (specificity).

3.2. Myometrial invasion

The concordance between paraffin section and FS in patients who were found to have tumors limited to the endometrium was 78.5%. This ratio was 90.5% and 95.3% for myometrial invasion <1/2 and $\geq 1/2$, respectively (Tables 2 and 3). For all patients, the concordance was 85.4% ($n = 597$) for myometrial invasion, and overestimation and underestimation of it were 4% ($n = 33$) and 10.6% ($n = 86$), respectively. FS could detect correctly only 60% of the patients with tumor localized in the endometrium that was