Original Article

Comparative Evaluation of Preoperative Imaging and Postoperative Histopathology in 108 Patients Who Underwent Laparoscopic- or Robot-Assisted Surgery for Endometrial Cancer

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Abstract

Objectives: The aim of this study was to compare preoperative imaging evaluation results and postoperative histopathology examinations of patients who underwent laparoscopic- or robot-assisted surgery for suspected Stage IA endometrial carcinoma.

Materials and Methods: There were 298 patients diagnosed with endometrial cancer at our institution between April 2014 and March 2019. Preoperative imaging evaluation based on magnetic resonance imaging (MRI) and computed tomography (CT) revealed 180 patients suspected of having Stage IA disease. Of these, 72 underwent open surgery, 12 underwent robot-assisted surgery, and 96 underwent laparoscopic surgery. In this study, preoperative imaging evaluation results and postoperative histopathology examinations of 108 patients who underwent laparoscopic- or robot-assisted surgery were retrospectively compared.

Results: Of the 108 patients, who underwent laparoscopic- or robot-assisted surgery for suspected Stage IA disease, 98 had Stage IA, two had Stage IB, and four had Stages II and III disease. The sensitivity of imaging evaluations based on preoperative MRI and CT was 90.7%.

Conclusion: Utilizing preoperative MRI and CT imaging resulted in a high rate of successful diagnosis of Stage IA endometrial carcinoma.

Keywords: Endometrial cancer, laparoscopic surgery, postoperative histopathology, preoperative imaging, robot-assisted surgery

Introduction

Endometrial cancer is the most common gynecologic malignancy in frequency in developed countries.[1] Risk classification is mainly based on tumor histology, tumor grade, and myometrial invasion.[2] Stage IA endometrial cancer is defined as cases in which cancer invasion into the myometrium is <50%, and there is no lymph node metastasis and distant metastasis.

Preoperative imaging evaluations are important because they are used to determine surgical procedures based on the estimation of stage of disease progression. At our institution, laparoscopic- and robot-assisted surgeries are performed in patients with Grade 1 (G1) or Grade 2 (G2) endometrioid cancer on endometrial histology in patients with suspected Stage IA disease. For more malignant histological types or advanced endometrial cancer, we opt for laparotomy because it requires more reliable lymphadenectomy and tumor reduction. Compared with open surgery, laparoscopic- and robot-assisted surgeries are cosmetically superior and result in less blood loss.[3] In addition, both are excellent in terms of

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early recovery after the surgery. At our institution, the number of patients who request laparoscopic- or robot-assisted surgery regardless of disease has been increasing. Improvements in laparoscopic- and robot-assisted surgery techniques have led to an increase in these procedures in recent years. We consider the accuracy of preoperative evaluations by comparing results from preoperative imaging and postoperative histopathological examinations and conducted if case selection was done appropriately at our institution. Gynecologists who perform minimally invasive surgery need to be aware of the importance of magnetic resonance imaging (MRI) and computed tomography (CT) because upstaging after minimally invasive surgery can affect the patient's prognosis. The prognosis of patients who underwent laparoscopic- or robot-assisted surgery was also studied.

Materials and Methods

Between April 2014 and March 2019, 298 patients were diagnosed with endometrial cancer at our institution. MRI and CT were advised for these patients. The MRI model was 1.5 or 3T, Ingenia, Philips Healthcare, Best, the Netherlands. Patients who were not allergic to contrast agents underwent contrast-enhanced MRI, which included not only T1-weighted and T2-weighted coordinated images but also diffusion-weighted image and apparent diffusion coefficient. Myometrial invasion and cervical invasion were assessed on MRI, whereas the likelihood of distant metastases and lymph node metastases were assessed on CT. Of the 298 patients, 294 underwent surgery. Among the patients, who underwent surgery, 114 patients with suspected Stage IB or higher disease underwent open surgery. There were 180 patients with suspected Stage IA endometrial cancer, of whom 72 underwent laparotomy, 12 underwent robot-assisted surgery, and 96 underwent laparoscopic surgery for endometrial cancer. The reasons for performing laparotomy on the 72 patients suspected of having Stage IA disease included having distinctive histologies, such as serous or clear cell carcinoma, patients in whom retrieval of the uterus from the vagina was considered difficult due to uterine myoma or large tumor volumes, patients in whom severe adhesions were anticipated, and high-grade obesity. In the last few years, we have been performing laparoscopic- and robot-assisted surgeries on our highly obese patients, but around 2014–2016, we were not performing laparoscopic surgeries on our highly obese patients because of the immaturity of laparoscopic technique. The subjects of this study were 108 cases operated by laparoscopy- or robot-assisted surgery (sample size is 108). For the 108 patients, preoperative imaging evaluations with MRI and CT and histopathological examinations after the surgery were compared, and the correct diagnosis rate was evaluated based on the stage of disease progression estimated preoperatively. Candidates for surgery were presented at a preoperative conference at our institution, and all physicians at our department (including gynecologic oncologists and endoscopic technicians) and two or three physicians in the diagnostic radiology department evaluated the images and decided on the surgical procedure based on this information.

The study was conducted in accordance with the Declaration of Hersinki, and the protocol was approved by the Ethics Committee of Sapporo Medical University (approval number: 322–285). Excel was used for statistical analysis.

Results

The mean and standard deviation for age of the 108 patients who underwent laparoscopic or robot-assisted surgery for endometrial cancer was 56.0 ± 13 years (age range, 31–83 years). The mean and standard deviation for body mass index was 27.2 ± 23.6 kg/m^2 (range, 16.0–42.3 kg/m^2). In the 67 patients, who did not undergo lymphadenectomy, the mean and standard deviation for the duration of surgery and mean and standard deviation for blood loss were 140 dtio. 6 min and 29 min ml, respectively. In 41 patients, who underwent lymphadenectomy, the mean and standard deviation for the duration of surgery and mean and standard deviation for blood loss were 167 ± 67 min and 85 ± 131 ml, respectively.

Among the 108 patients suspected of having Stage IA disease, there were 10 patients with Stage IB or higher disease based on postoperative histopathological examinations, two with Stage IB, four with Stage II, and four with Stage III disease [Figure 1]. Among the 98 patients who had Stage IA disease as assessed by preoperative imaging, there were nine patients in whom adjuvant therapy was administered for reasons such as positive lymphovascular invasion and positive washing cytology of the peritoneal cavity.

The results of preoperative evaluations and postoperative histological examinations were compared, and 98 patients out of 108 were confirmed as having Stage IA disease. The sensitivity of the preoperative evaluations was 90.7%.

The 10 patients with Stage IB or higher disease are listed in Table 1. Patient A had pT1bN0M0 and patient B had pT1bNxM0 disease. Patient A [Figure 2A] was not suspected of having myometrial invasion preoperatively. However, when the MRI was re-reviewed postoperatively, although there was no suspicion of myometrial invasion of half or more on T2-weighted images, invasion to half or more of part of the muscle layer on the apparent diffusion coefficient map was also considered a possible finding. Patient B [Figure 2B] was suspected of having Stage IA disease, which was confirmed when imaging was re-reviewed. Patient C had pT2N0M0 disease [Figure 2C] and patient D had pT2NxM0 disease [Figure 2D], but the possibility of cervical invasion

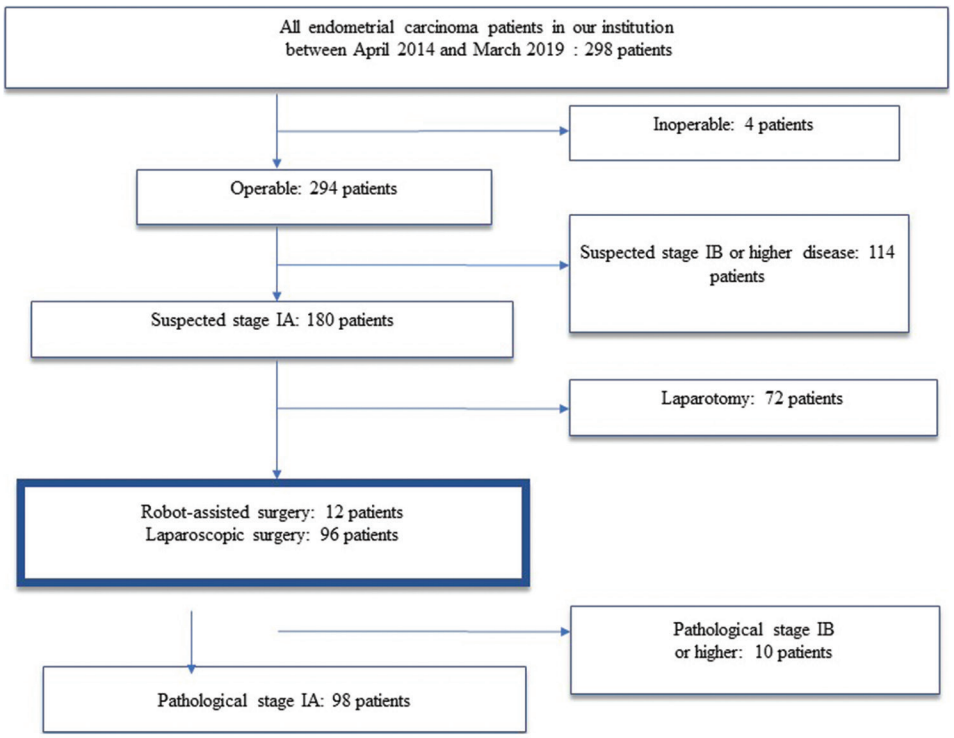

Figure 1: Flow chart for this study

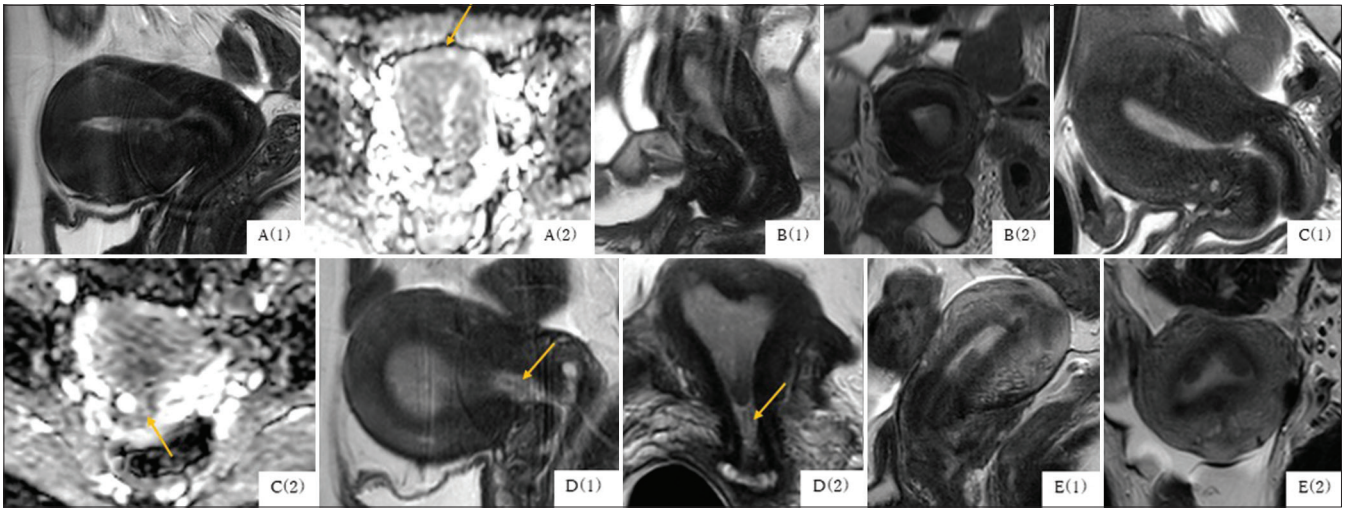

Figure 2: (A) MRI of patient A. (1) T2W sagittal. (2) ADC axial. In the ADC map, there was an area in which myometrial invasion of half or more was suspected when images were re-reviewed postoperatively. (B) MRI of patient B. (1) T2W sagittal. (2) T2W axial. Stage IA disease was suspected even when the images were re-reviewed postoperatively. (C) MRI of patient C. (1) T2W sagittal. (2) ADC axial. When re-reviewed postoperatively, the possibility of cervical invasion was also considered on the ADC. (D) MRI of patient D. (1) T2W sagittal. (2) T2W axial. Although preoperative cervical invasion was not suspected, the possibility of cervical invasion was considered when images were re-reviewed postoperatively. (E) MRI of patient E. (1) T2W sagittal. (2) T2W axial. The possibility of cervical invasion wasn't suspected even when images were re-reviewed postoperatively. MRI: Magnetic resonance imaging, T2W: T2 weighted, ADC: Apparent diffusion coefficient

was also a possible finding when the images were reviewed postoperatively. Patient E had pT2NxM0 disease [Figure 2E]; in this patient, the cervical invasion was not suspected preoperatively, and there was low indication of suspicion of cervical invasion based on the images even when these were re-reviewed postoperatively. Patient F also had pT2NxM0 disease [Figure 3F]; however, cervical invasion was not suspected in this patient even when the images were reviewed after surgery. Patient G had pT2N1M0 disease with left external iliac lymph node (LN) and left obturator LN metastases [Figure 3G]. Although the volume of the tumor was large, preoperatively, it was determined that there were

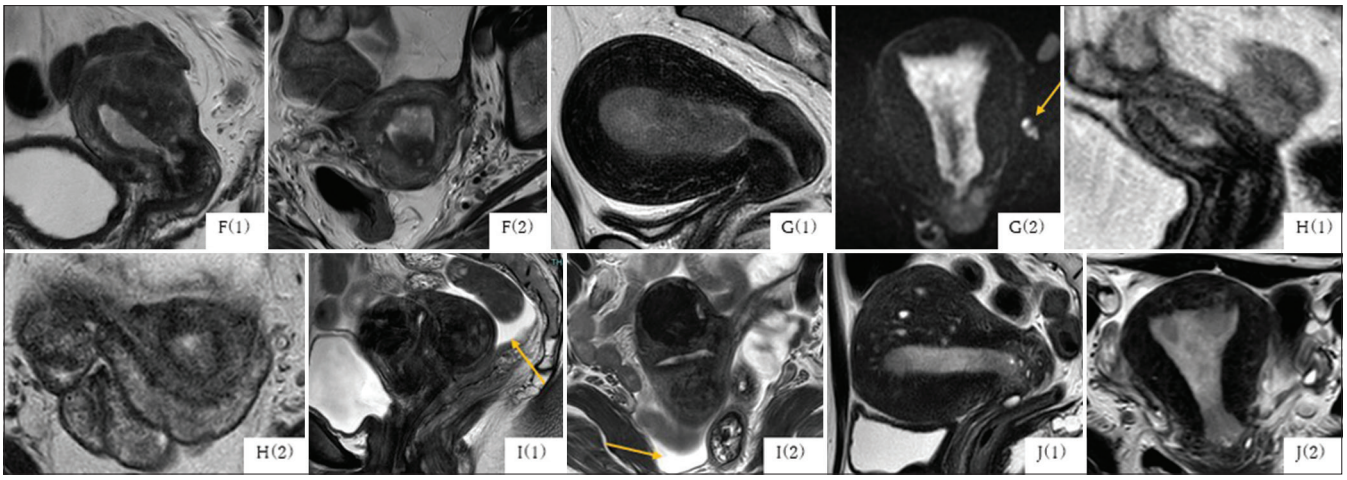

Figure 3: (F) MRI of patient F. (1) T2W sagittal. (2) T2W axial. The possibility of cervical invasion was not suspected even when images were re-reviewed postoperatively. (G) MRI of patient G. (1): T2W sagittal. (2): DWI axial. Although slight enlargement of the left external iliac LN and left obturator LN was observed, when the images were re-reviewed, both were 5 mm or less in the short diameter, and it was difficult to suspect LN metastases preoperatively. (H) MRI of patient H. (1): T2W sagittal. (2): T2W axial. Stage IA disease was suspected even when the images were re-reviewed postoperatively. (I) MRI of patient I. (1) T2W sagittal. (2) T2W axial. When the images were reviewed after surgery, the peritoneal nodules were not evident; however, severe ascites was seen in the 65-year-old patient. (J) MRI of patient J. (1) T2W sagittal. (2) T2W axial. Complications of adenomyosis were observed in this patient. Even when the images were re-reviewed postoperatively, findings that would indicate the possibility of right adnexal invasion and left external iliac LN metastases were scarce. MRI: Magnetic resonance imaging, LN: Lymph node, T2W: T2 weighted, DWI: diffusion weighted image

Table 1: Background of 10 patients who had stage IB or more

	Age	Surgical procedure	Results of postoperative histological examination
Patient A	37	TLH + BSO + PLA	pT1bN0M0
Patient B	62	TLH + BSO	pT1bNxM0
Patient C	47	LAVH + BSO + PLA	pT2N0M0
Patient D	56	TLH + BSO	pT2NxM0
Patient E	40	TLH + BSO	pT2NxM0
Patient F	65	TLH + BSO	pT2NxM0
Patient G	35	TLH + BSO + PLA	pT2N1M0
Patient H	63	TLH + BSO	pT3aNxM0 (tumor in the ovarian vein, T3a)
Patient I	65	RASH + BSO	pT3aNxM0
Patient J	45	TLH + BSO + PLA	pT3aN1M0

TLH: Total laparoscopic hysterectomy, BSO: Bilateral salpingo-oophorectomy, PLA: Pelvic Lymph-adenectomy, LAVH: Laparoscopy-assisted vaginal hysterectomy, RASH: Robot-assisted simple hysterectomy

few findings suggestive of myometrial invasion or cervical invasion or LN metastases. Despite slight enlargement of the left external iliac LN and left obturator LN, when imaging was reviewed postoperatively, both were 5 mm or less in the short diameter, and it was difficult to suspect LN metastases preoperatively. Patient H had a tumor-infiltrating the right and left ovarian veins and was diagnosed with pT3aNxM0 disease [Figure 3H]. The normal muscle layer was thin and myometrial invasion and adnexal invasion were not suspected preoperatively, and the suspicion of Stage IA disease remained even after reviewing the images postoperatively. Patient I had pT3aNxM0 disease with peritoneal dissemination. When the images were reviewed after surgery, the peritoneal nodules were not evident; however, severe ascites was seen for this patient's age [Figure 3I]. Patient J had pT3aN1M0 disease with right adnexal invasion and left external iliac node metastases [Figure 3J]. Although complications of adenomyosis were present, there was low indication of suspect Stage III disease, even when the images were re-reviewed postoperatively.

On the other hand, among the 114 patients with suspected Stage IB or higher disease who underwent surgery, the results of postoperative histological diagnoses were Stage IA in 25 patients, and the specificity was 78.1%. Most of the patients were those for whom myometrial invasion was overestimated due to the large volume of the tumor, and the next most common patients were those with suspected Stage II disease due to observed cervical invasion; however, there was actually no cervical invasion, and many of the patients were those for whom the tumor only hung down to the neck like a polyp.

Recurrence was also evaluated. Of the 98 patients with Stage IA disease, seven had experienced recurrence by the end of October 2020 (recurrence rate of 7.1%). Peritoneal washing cytology at surgery was positive in three patients, the lymphovascular invasion was present in one, and the remaining three patients had no risk factors for recurrence.

Of the 10 patients with Stage IB or higher who underwent laparoscopic or robotic surgery, two (Patient I and J) had recurrence by the end of October 2020. The histological

type of Patient I was serous carcinoma, and the disease-free interval (DFI) was 6 months. Patient J's DFI was 19 months.

Of the 72 patients with Stage IA disease who underwent laparotomy, eight had experienced recurrence by the end of October 2020 (recurrence rate of 11.1%). There were two patients with serous and two with clear cell carcinoma. Besides, two had large tumor volumes and one presented with lymphovascular invasion. No risk factors for recurrence were observed in the remaining one patient.

Discussion

In recent years, with the improvement of laparoscopic and robotic surgery techniques, those surgeries have been increasing. Laparoscopic- and robot-assisted surgeries have been performed for patients with endometrial cancer judged to be appropriate for the procedure based on preoperative evaluations by multiple parties, including radiologists. Preoperative imaging is important in determining the surgical procedure. In this study, we revealed that utilizing preoperative MRI and CT imaging resulted in a high rate of successful diagnosis of Stage IA endometrial carcinoma. Gynecologists who perform minimally invasive surgery need to be aware of the importance of MRI and CT because upstaging after minimally invasive surgery can affect the patient's prognosis.

According to the Guidelines for the Treatment of Endometrial Cancer,[4] myometrial invasion of half or less is defined as low risk. Chi *et al*.[5] reported that the frequency of pelvic LN metastases differed depending on myometrial invasion (none, <1/2, and ≥1/2), with 0%, 0%, and 0% for G1, 4%, 10%, and 17% for G2, and 0%, 7%, and 28%, for Grade 3, respectively, demonstrating higher frequency in patients with a higher degree of myometrial invasion. For advanced endometrial cancer, we opt for laparotomy because it requires more reliable lymphadenectomy and tumor reduction. Thus, preoperative imaging evaluation is important in determining the surgical method.

Horvath *et al*.[6] reported that, in 89 patients with endometrial cancer, 10 out of 60 patients with predicted myometrial invasion of less than half had myometrial invasion of half or more as a result of histopathological examinations (correct diagnosis rate, 83.3%), and four out of 29 patients with suspected myometrial invasion of half or more had myometrial invasion of less than half (correct diagnosis rate, 86.2%). Savelli *et al*.[7] reported that the accuracy of identifying myometrial invasion less or more than half based on MRI was 82%, and Lee *et al*.[8] reported that the accuracy of identifying myometrial invasion was 80% when T2-weighted and gadolinium-enhanced T1-weighted imaging was performed, and the pre- or postmenopausal status of the patient was considered. Yang *et al*.[9] reported a sensitivity of 89.2% and specificity of 89% for identifying myometrial invasion, and sensitivity of 75% and specificity of 92.4% for cervical invasion in preoperative MRI of endometrial cancer. Similarly, Goel *et al*.[10] reported a sensitivity of 75% for myometrial invasion and a sensitivity of 50% for cervical invasion, with a lower sensitivity for cervical invasion. Soneji *et al*.[11] reported that the correct diagnosis rate for myometrial invasion was 73.3% in endometrial cancer and 89.3% for cervical invasion, with 65.6% showing complete agreement between preoperative imaging staging and postoperative histopathological staging from Stage IA to IVB. There was an 86.3% concordance rate between Stages I and IV when stages were not subdivided. Among these, benign findings such as uterine adenomyosis, uterine myoma, and thinning of the myometrium were the most common causes of misinterpretation of the depth of myometrial invasion.

Takeuchi *et al*.[12] noted that reduced field of view (FOV) diffusion-weighted (DW) MRI was able to clearly demonstrate myometrial invasion in two patients with uterine adenomyosis. However, in our institution, we did not perform reduced FOV-DW MRI at this time.

At our institution, 98 of the 108 patients with suspected Stage IA disease were confirmed to have Stage IA disease, resulting in a correct diagnosis rate of 90.7%. This was similar to the findings reported by Horvath *et al*.,[6] Savelli *et al*.,[7] Lee *et al*.,[8] Soneji *et al*.,[11] and Wu *et al*.[13] Similar to the report by Soneji *et al*.,[11] when reviewing our patients with discrepancies between preoperative imaging and postoperative histopathology, there were two patients with benign uterine findings (one with adenomyosis of the uterus and one with thinning of the myometrium). Soneji *et al*.[11] also reported that some patients were suspected of having stage IA disease even after a re-review of the images after surgery. In our study, four out of eight patients, excluding the two with benign uterine findings, were also suspected of having Stage IA disease even after the re-review after surgery.

Todo *et al*.[14] investigated the association between endometrial cancer tumor volume and the presence or absence of LN metastases. The volume index was defined as the product of the major axis (cm), the lateral diameter (cm), and the anteroposterior diameter (cm) of the tumor on MRI and was classified into five groups based on the values. The results showed that LN metastases were observed in 3% of patients in the group with a volume index lower than 8, 9% of patients in the group with an index from 8 to 27, 17% of patients in the group with an index from 27 to 64, 25% of patients in the group with an index from 64 to 125, and 53% of patients in the group with an index of 125 or higher. Among the patients at our institution, both patient G and patient J with LN metastases had a greater volume index (volume index in patient G, 130; volume index in patient J, 30.8). Given these findings, even if

Stage IA is suspected based on preoperative MRI evaluations, the possibility of LN metastases should also be considered if the tumor volume is large. The surgical procedure should be selected accordingly.

Some institutions use intraoperative frozen diagnoses to confirm myometrial invasion. Karatasli *et al*.[15] reported that, in 222 patients with Stage I endometrial cancer, the correct diagnosis rate for myometrial invasion based on MRI was 88.7%, and the rate was 94.4% with intraoperative frozen diagnosis. The correct diagnosis rate reportedly changed to 97.8% on combining MRI and intraoperative frozen diagnosis. Although the estimation of myometrial invasion using intraoperative frozen diagnosis has not been performed at our institution, there seems to be a method to infer myometrial invasion in the intraoperative frozen diagnosis.

The strength of the present study is that CT imaging was performed on all patients, even those who were judged to have no muscle layer invasion, and if enlarged LNs or distant metastasis were suspected, laparotomy was performed which was a more careful examination of the cases. On the other hand, a limitation of this study is that the slice width of the MRI varies from patient to patient. If everyone had had their MRIs taken with a 2 mm slice, the results could have been different.

Conclusion

The results of preoperative evaluations and postoperative histological examinations were compared, and 98 of the 108 patients were confirmed to have Stage IA disease. The sensitivity of preoperative evaluation was 90.7%. Utilizing preoperative MRI and CT imaging resulted in a high rate of successful diagnosis of Stage IA endometrial cancer. To further increase the accuracy rate, a reduction in the slice width of MRI and CT is being considered.

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Conflicts of interest

There are no conflicts of interest.

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