Preoperative Pelvic MRI and Serum Cancer Antigen–125: Selecting Women With Grade 1 Endometrial Cancer for Lymphadenectomy

Elizabeth A. Sadowski[1,2]
Jessica B. Robbins[1]
Kristie Guite[1]
Krupa Patel-Lippmann[1]
Alejandro Munoz del Rio[1]
David M. Kushner[2]
Ahmed Al-Niaimi[2]

OBJECTIVE. The objective of our study was to determine the predictive value of preoperative pelvic MRI and serum cancer antigen–125 (CA-125) evaluation in selecting women with grade 1 endometrial cancer for lymphadenectomy as part of the cancer staging operation.

MATERIALS AND METHODS. A new preoperative clinical protocol including MRI and CA-125 evaluation was adopted at our institution in patients with grade 1 endometrioid adenocarcinoma. Lymphadenectomy was considered as part of the surgical staging operation if there was an elevated CA-125 value or a positive MRI finding (≥ 50% myometrial invasion, cervical invasion, abnormal lymph nodes, extrauterine disease, or tumor index ≥ 36 cm). From January 2012 through May 2013, a retrospective analysis was performed of 100 women who underwent preoperative MRI and CA-125 evaluation; we refer to this cohort as the "preoperative study cohort." The sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) were calculated using final surgical pathology and CA-125 results as the reference standard. The rate of metastatic lymph nodes in the preoperative study cohort was determined. From May 2009 through January 2011, a retrospective analysis of a cohort who did not undergo preoperative MRI and CA-125 evaluation was undertaken to compare lymphadenectomy and lymph node metastasis rates before and after implementation of the new protocol; we refer to this cohort as the "historical cohort."

RESULTS. The new clinical protocol had sensitivity of 94%, specificity of 91%, PPV of 84%, and NPV of 97%. When histologic grade alone was considered, positive lymph node rates in the preoperative study cohort was 4.0% versus 4.2% in the historical cohort. In the preoperative study cohort, the lymph node metastasis rate increased to 11.1% with a positive MRI finding or elevated CA-125 value.

CONCLUSION. Preoperative MRI and CA-125 evaluation identified women for lymphadenectomy with a high NPV.

Keywords: DWI, endometrial cancer, MRI

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[1]Department of Radiology, University of Wisconsin School of Medicine and Public Health, Clinical Science Center, 600 Highland Ave, E3, Madison, WI 53792-3252. Address correspondence to E. A. Sadowski (esadowski@uwhealth.org).

[2]Department of Obstetrics and Gynecology, University of Wisconsin School of Medicine and Public Health, Madison, WI.

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Endometrial cancer is a common gynecologic malignancy, and the endometrioid adenocarcinoma subtype accounts for nearly 75–90% of cases, of which grade 1 tumors comprise up to 58% [1–10]. Currently, endometrial cancer is surgically staged, which includes evaluating the status of the pelvic and paraaortic lymph nodes according to the 2009 FIGO system [2]. Nodal status is an important factor in the staging of endometrial cancer because it dictates the need for adjunct therapy and influences prognosis [1–8]. Early-stage disease, which is defined as disease confined to the uterine corpus without lymph node metastasis, has a 5-year disease-free survival approaching 90% [4–8]. In the presence of positive paraaortic lymph node metastasis, the 5-year disease-free survival decreases to 47% [7].

When histologic grade alone is considered, the overall risk of lymph node metastasis in grade 1 endometrioid adenocarcinoma ranges from 0% to 5% [5–12]. However, when deep myometrial invasion is present in women with grade 1 endometrioid adenocarcinoma, the risk of lymph node metastasis increases to 11–25% [5, 10]. Studies have also shown an increased risk of lymph node metastasis with increasing tumor size and the presence of cervical invasion and extrauterine spread [2, 3, 13, 14]. Whether to perform lymphadenectomy differs somewhat on the basis of regional guidelines and local expertise; however, in the absence of any of the mentioned risk factors, most surgeons believe that lymphadenectomy can be avoided [2, 3].

Despite the well-defined criteria for surgical staging in endometrial cancer, controver-

sy still exists regarding the need for lymphadenectomy. Implementation of a preoperative algorithm could avoid the risks and complications from lymphadenectomy in women at low risk of lymph node metastasis. Some centers choose intraoperative frozen section to determine tumor size and the presence of myometrial invasion and cervical invasion. However, obtaining intraoperative samples for frozen section has the limitations of variable reproducibility among pathologists and among institutions. Preoperative MRI is being increasingly used to evaluate key factors in predicting lymph node metastasis because MRI provides accurate information about the tumor size and spread [1–4, 13–36].

A preoperative algorithm that detects the subgroup of women who would benefit most from lymphadenectomy and that identifies women at low risk of lymph node metastasis who can avoid lymphadenectomy and the associated risks would be beneficial in clinical practice [13–18, 34]. At our center, a new preoperative clinical protocol including preoperative MRI and CA-125 evaluation was adopted in patients with grade 1 endometrioid adenocarcinoma based on a low-risk assessment regimen published in the literature [13–15]. The impetus for this clinical change was to use MRI preoperatively in place of intraoperative frozen section because of the inconsistent accuracy of frozen section [35, 36]. Furthermore, the preoperative protocol was proposed to improve patient care by allowing preoperative patient counseling and appropriate resource allocation, such as reservation of the appropriate operating room time. The goals of our study were to determine the sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) of the new preoperative clinical protocol using the final surgical pathology result and CA-125 level as the reference standard. In addition, we calculated the rate of lymphadenectomy and the positive lymph node metastasis rate in women who underwent preoperative MRI and compared these values with those of a historical cohort who did not undergo preoperative MRI and CA-125 evaluation.

Materials and Methods

Study Population

After we received approval from the institutional review board, we performed a retrospective analysis to determine the predictive value of preoperative serum CA-125 evaluation and pelvic MRI in 100 consecutive women diagnosed with grade 1 endometrioid adenocarcinoma and treated at our institution from January 2012 through May 2013. We refer to this group as the "preoperative study cohort." An analysis of a cohort of 95 women with grade 1 endometrioid adenocarcinoma who did not undergo preoperative CA-125 evaluation and pelvic MRI (May 2009–January 2011) was undertaken. We refer to this group as the "historical cohort." We compared lymphadenectomy and lymph node metastasis rates in women before the implementation of the new protocol (i.e., historical cohort) and after the implementation of the new protocol (i.e., preoperative study cohort).

Preoperative Study Cohort

All patients underwent endometrial biopsy to determine the grade and histology of the tumor before referral to the gynecologic oncologists for

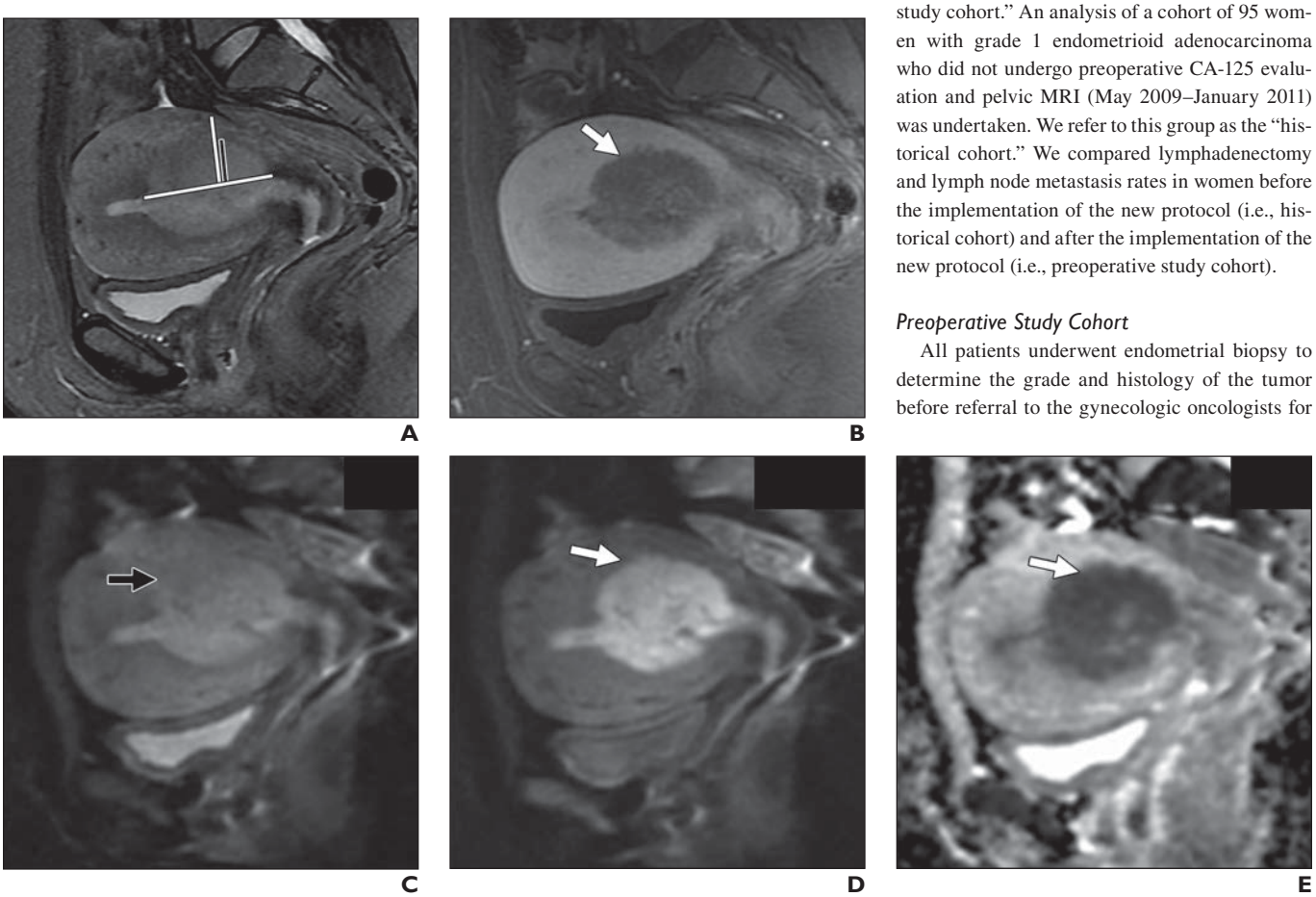

Fig. 1—55-year-old woman with grade 1 endometrioid adenocarcinoma.
A, Sagittal T2-weighted image depicts deepest extent of myometrial invasion. Measuring depth of myometrial invasion was performed by drawing line along expected inner edge of myometrium (*white horizontal line*); then, lines perpendicular to first line were drawn to measure thickness of entire myometrium (*white vertical line*) and extent of tumor invasion into myometrium (*black line*). Ratio of tumor invasion over myometrial thickness was determined to be < 50% or ≥ 50% myometrial invasion.
B, Sagittal contrast-enhanced T1-weighted image depicts deep myometrial invasion (*arrow*).
C–E, Sagittal DW image obtained with b value of 0 s/mm^2 (**C**), sagittal DW image obtained with b value of 500 s/mm^2 (**D**), and apparent diffusion coefficient (ADC) map (**E**) depict tumor. Note tumor edge (*arrows*) is less obvious on DW image obtained with b value of 0 s/mm^2 (**C**) than on DW image obtained with b value of 500 s/mm^2 (**D**) and on ADC map (**E**). Appearance of tumor on DW image obtained with b value of 0 s/mm^2 (**C**) corresponds to tumor's appearance on T2-weighted image (**A**).

TABLE 1: MRI Sequences and Parameters for Imaging Women With Grade 1 Endometrial Cancer

MRI Parameters	MRI Sequences								
	Axial T1	Axial Fat-Saturated T1	Axial Fat-Saturated T2	Axial Fat-Saturated T2	Optional[a] Axial Fat-Saturated T2	Axial DWI	Sagittal Fat-Saturated T2	Sagittal DWI	Sagittal Fat-Saturated T1
Time after injection of contrast material (s)		180							40, 90
MR sequence	FSE	FSE	FR FSE	FR FSE	FR FSE	EPI	FR FSE	EPI	Spoiled GRE
No. of dimensions	2	2	2	2	2	2	2	2	3
TE (ms)	9	9	86	90	90	65	90	65	1.8
TR (ms)	600	600	3400	3800	RT	10,000	3800	6000	3.8
Echo-train length	4	4	21	21	21	NA	21	NA	IP[b]
Flip angle (°)	90	90	90	90	90	90	90	90	12
No. of signals acquired	4	2	3	2	2	8	2	8	1
Bandwidth (kHz)	27	27	31.25	31.25	31.25	NA	31.25	NA	62
FOV (cm)	26	32	26	34	34	34	32	32	28
Slice thickness (mm)	5	6	5	6	6	4	5	4	4.6
Slice interval (mm)	1.5	1	1.5	1	1	0.5	1.5	0.5	
Matrix size	256 × 224	256 × 192	320 × 256	320 × 256	320 × 256	160 × 160	256 × 224	160 × 192	256 × 192
b Value (s/mm^2)						0, 500		0, 500	
Acquisition time (min:s)	3:36	4:32	3:30	4:11	RT	2:50	4:10	5:25	0:27
Scanning coverage	SP to top of sacrum	Below SP to mid kidneys	SP to top of sacrum	Below SP to mid kidneys[c]	Below SP to mid kidneys[c]	Pubic bone to iliac crest	Entire uterus	Entire uterus	Entire pelvis

Note—FSE = fast spin-echo, FR = fast recovery, EPI = echo-planar imaging, GRE = gradient-recalled echo, RT = respiratory triggered, NA = not applicable, IP = inversion preparation, SP = symphysis.

[a]The optional respiratory-triggered fat-saturated T2-weighted sequence is used when there is motion artifact on the non–respiratory-triggered axial fat-saturated T2-weighted images.

[b]Inversion time = 20 ms.

[c]Axial T2-weighted images are obtained to include the retroperitoneum to the level of the mid kidneys.

definitive treatment at our institution. According to clinical protocol, all women with grade 1 endometrioid adenocarcinoma had a serum CA-125 level drawn and underwent preoperative pelvic MRI at our institution. Although all women with grade 1 endometrioid adenocarcinoma were eligible for MRI, women with a body mass index (BMI) of greater than 45 and medical comorbidities may not have been considered for lymphadenectomy at the surgeon's discretion. All women underwent total hysterectomy with bilateral oophorectomy and pelvic washings. According to the clinical protocol, the decision to also perform pelvic and paraaortic lymphadenectomy was based on MRI risk criteria and CA-125 level. The indications for incorporating lymphadenectomy were either a CA-125 value of at least 30 IU/mL or any one of the following MRI risk factors: at least 50% myometrial invasion, cervical invasion, extrauterine disease, abnormal lymph nodes, or tumor index (length × width × height) of at least 36 cm. These criteria were chosen by our gynecologic oncology surgeons after a review of the published literature on CA-125 level and MRI findings for risk assessment of lymph node metastasis [13–15]. The decision to not use the Mayo criterion [16] of a maximum tumor diameter of more than 2 cm was made by the gynecologic oncology section physicians. Our gynecologic oncology surgeons decided to use the tumor index on the basis of validation studies in the literature showing a lymph node metastasis rate of 3.3% using a tumor index cutoff of 36 cm [15]. Furthermore, our gynecologic oncology group was interested in implementing a preoperative protocol for improved patient counseling and appropriate resource allocation, and the Mayo criterion is based on tumor size determined at intraoperative frozen section [16].

Historical Cohort

All patients underwent endometrial biopsy to determine the grade and histology of the tumor before referral to the gynecologic oncologists for definitive treatment at our institution. Preoperative MRI was not performed when these patients presented (May 2009–January 2011). All women with grade 1 endometrioid adenocarcinoma in this time period underwent total hysterectomy with bilateral oophorectomy and pelvic washings and pelvic and paraaortic lymphadenectomy. This group serves as a historical control to compare lymphadenectomy rates and rates of lymph node metastasis in women with grade 1 endometrioid adenocarcinoma treated at our institution before and after implementation of a new preoperative clinical protocol, which included MRI and CA-125 evaluation.

Imaging Protocol

The MRI examinations were performed on a 1.5-T scanner (Signa or Optima, GE Healthcare) or a 3-T scanner (Discovery 750, GE Healthcare) using a body torso or cardiac coil. A standard MRI protocol that has previously been published in the literature [2, 3] was used. The details of the MRI protocol are given in Table 1. Women were asked to refrain from eating or drinking for 4 hours before imaging. No antiperistaltic agents were administered before the MRI examinations. Axial and sagittal DW images and T2-weighted images through the pelvis were obtained first. The axial T2-weighted images were extended to include the renal veins to assess for lymphadenopathy. Sagit-

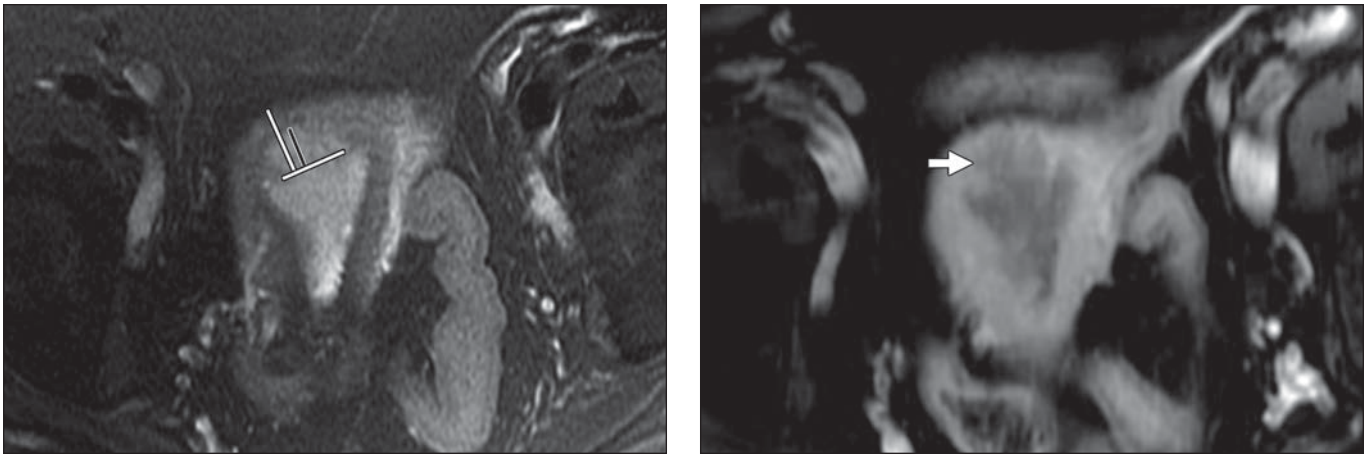

Fig. 2—65-year-old woman with grade 1 endometrioid adenocarcinoma.
A, Axial T2-weighted image depicts deepest extent of myometrial invasion. Measuring depth of myometrial invasion was performed by drawing line along expected inner edge of myometrium (*white horizontal line*); then, lines perpendicular to first line were drawn to measure thickness of entire myometrium (*white vertical line*) and extent of tumor invasion into myometrium (*black line*). Ratio of tumor invasion over myometrial thickness was determined to be < 50% or ≥ 50% myometrial invasion.
B, Axial contrast-enhanced T1-weighted image depicts deep myometrial invasion (*arrow*).

tal and axial contrast-enhanced T1-weighted images were obtained also.

MRI and Surgical Pathology Report Analyses

All MRI examinations were interpreted by an abdominal radiologist on the day of the examination. The clinical radiology reports that were generated included the following information: tumor location, tumor index (length × height × width [in centimeters]), the extent of myometrial invasion, extent of cervical invasion, presence of extrauterine spread, and presence of abnormal lymph nodes (enlarged lymph nodes [> 1 cm] or lymph nodes that appeared round without a fatty hilum or a necrotic center). Myometrial invasion was measured as described previously by Lin et al. [25]: The myometrium was measured at its deepest point on either axial or sagittal images (Figs. 1 and 2). Eleven abdominal radiologists were involved in interpreting the clinical MRI examinations. Three of the 11 abdominal radiologists specialize in women's imaging, and the remaining abdominal radiologists specialize in renal or hepatobiliary imaging.

All surgical pathology specimens were interpreted by gynecologic pathologists. The surgical pathology reports that were generated included the following: tumor histology, tumor grade, tumor location, tumor size in one or two dimensions (tumor index was not reported on surgical pathology because measurements in three dimensions were not obtained), extent of myometrial invasion, presence of cervical invasion, presence of extrauterine spread, and status of lymph nodes if lymphadenectomy was performed. All cases included in the analysis were evaluated for macroscopic and microscopic disease. Retrospectively, final radiology reports were compared with the final surgical pathology results.

Medical Record Data Review and Analysis

In both patient cohorts, clinical information including patient age and BMI were recorded, and averages were calculated. The CA-125 levels were recorded for the preoperative study cohort. For the historical cohort, the pathology reports were reviewed in a similar fashion to the review of the pathology reports of the preoperative study cohort.

Statistical Analysis

All clinical data, including the rate of metastatic lymph nodes, for the preoperative study cohort and the historical cohort were compared using the Fisher exact test for categoric tests.

In the preoperative study cohort, the sensitivity, specificity, PPV, and NPV of MRI and CA-125 evaluation for predicting the need for lymphadenectomy were calculated. True-negative (TN), true-positive (TP), false-negative (FN), and false-positive (FP) rates were determined by comparing the need for lymphadenectomy based on preoperative MRI findings and CA-125 level with the reference standard of final surgical pathology result and CA-125 level. Patients were considered to need lymphadenectomy based on preoperative MRI and CA-125 evaluation if any of the following criteria were met: CA-125 value of at least 30 IU/mL, at least 50% myometrial invasion on MRI, suspected cervical involvement on MRI, abnormal lymph nodes, or extauterine spread on MRI, or tumor index of at least 36 cm. Patients were considered in need of lymphadenectomy by final surgical pathology and CA-125 level if any of the following criteria were met: CA-125 value of at least 30 IU/mL, at least 50% myometrial invasion, cervical involvement, extrauterine spread, or lymph node metastasis. The tumor index was not determined by surgical pathology and could not be used as part of this analysis.

In the preoperative study cohort, a subanalysis was performed comparing the rate of metastatic lymph nodes in the women with an elevated CA-125 value and the various MRI risk criteria—that is, tumor index, extent of myometrial invasion, presence of cervical invasion, and lymph node status.

Results

The preoperative study cohort was composed of 100 women who were imaged with preoperative MRI and treated at our institution from January 2012 through May 2013. The mean period between surgery and serum CA-125 evaluation was 24.1 ± 13.6 (SD) days. The mean period between MRI and surgery was 21.1 ± 15.8 days. One patient was excluded from the final analysis because blood obscured the tumor on the MRI study. MRI examinations of the remaining 99 patients were of diagnostic quality and were included in the final analysis. In the historical cohort, 95 women treated at our institution for endometrial cancer from May 2009 through January 2011 were included in the analysis.

The demographic data, including age and BMI, and lymph node metastatic rates were statistically similar for the two cohorts during the two time periods studied (Table 2). The lymphadenectomy rate significantly decreased from 100% in the historical cohort to 36.4% in the preoperative study cohort ($p < 0.001$).

When MRI and CA-125 results were compared with surgical pathology and CA-125 results, there were 59 TN, 32 TP, 2 FN, and

TABLE 2: Demographic and Clinical Characteristics of Patients With Grade 1 Endometrial Adenocarcinoma During the Two Time Periods Studied

Characteristics	Preoperative Study Cohort[a]	Historical Cohort[b]	*p*
Total no. of patients	99	95	
No. (%) of patients who met clinical protocol criteria for lymphadenectomy	38 (38.4)	Not applicable	
No. (%) of patients who underwent lymphadenectomy	36 (36.4)	95 (100)	< 0.001
Age (y)			0.324
Average ± SD	60 ± 11	59 ± 12	
Range	28–83	29–88	
Body mass index			0.870
Average ± SD	35.0 ± 8.2	35.4 ± 8.6	
Range	21.5–59.8	19.9–55.9	
CA-125 at surgery (IU/mL)			
Average ± SD	18.5 ± 16.4	Not obtained	
Range	3–109	Not obtained	
Stage[c], no. (%) of patients			0.57
IA	68 (68.7)	71 (74.7)	
IB	14 (14.1)	11 (11.6)	
II	4 (4.0)	9 (9.5)	
III or IV	4 (4.0)	4 (4.2)	
Myometrial invasion on pathology, no. (%) of patients			0.39
< 50%	75 (75.8)	77 (81.1)	
≥ 50%	24 (24.2)	18 (18.9)	
Cervical invasion on pathology, no. (%) of patients	7 (7.1)	8 (8.4)	0.805
Lymph node metastasis, no. (%) of patients	4 (4.0)	4 (4.2)	1

Note—CA-125 = cancer antigen–125.
[a]January 2012–May 2013.
[b]May 2009–January 2011.
[c]According to the 2009 criteria of the International Federation of Gynecology and Obstetrics [2].

6 FP results, which yielded a calculated sensitivity of 94% (32/34), specificity of 91% (59/65), PPV of 84% (32/38), and NPV of 97% (59/61). The FN and FP cases were retrospectively reviewed, and a brief summary is provided here.

The two FN cases were in patients whom our protocol failed to classify as at high risk for lymph node metastasis on MRI. Both of these patients had at least 50% myometrial invasion on final pathology (myometrial invasion of 9/17 mm in the first patient and 7/12 mm in the second patient) that was not prospectively identified on MRI. In one of these patients, the margins of the tumor were not well seen on the T2-weighted or T1-weighted contrast-enhanced images; however, the DW images accurately delineated the tumor, and at least 50% myometrial invasion was identified by the authors on retrospective review (Fig. 3). Recognition of myometrial invasion may be improved by using orthogonal views to the sagittal plane of the uterus.

There were six FP cases that were retrospectively reviewed. In three of the six cases more than 50% myometrial invasion was prospectively identified on MRI; however, on final pathology there was less than 50% myometrial invasion (4/12 mm in the first patient, 3/8 mm in the second patient, and 3/12 in the third patient). One of the six patients was reported to have cervical invasion on MRI that was not called on final pathology because the edge of the tumor was 1 mm from the cervix. In two of the six patients, lymph nodes that were considered to appear suspicious on MRI were negative for metastasis on surgical pathology. In all six patients, lymphadenectomy was performed because of the MRI findings and all lymph nodes were negative.

When histologic grade alone was considered, the number of women with positive lymph nodes in the preoperative study cohort was 4.0% (4/99) (Table 1). Table 3 presents the rate of lymph node metastasis based on risk factors (i.e., MRI findings and CA-125 level). The rate of lymph node metastasis was 11.1% (4/36) when any one of the MRI risk factors was positive or the CA-125 value was elevated in the women who underwent lymphadenectomy.

Table 4 presents the clinical and MRI findings in the four patients with pathologically positive lymph node metastases. All four patients had a large tumor index (> 36 cm) and deep myometrial invasion (> 50%) on MRI.

Discussion

The risk of lymph node metastasis in grade 1 endometrial adenocarcinoma cancer is low, ranging from 0% to 5% [5–12], and the benefits of lymphadenectomy are debated [1–10, 13–18, 34–37]. Despite the controversies about the role of lymphadenectomy and the varying approaches that exist across institu-

TABLE 3: Rate of Lymph Node Metastasis by MRI Findings and Cancer Antigen–125 (CA-125) Level in the Preoperative Study Cohort: January 2012–May 2013

Risk Factors	Percentage of Patients With Lymph Node Metastasis (No. of Patients With Lymph Node Metastasis/Total No. of Patients With Risk Factor)
MRI findings	
Tumor index[a] ≥ 36 cm	30.8 (4/13)
≥ 50% myometrial invasion or cervical invasion present	13.3 (4/30)
Abnormal lymph nodes[b]	22.2 (2/9)
CA-125 level	
≥ 30 IU/mL	15.4 (2/13)
MRI finding of ≥ 50% myometrial invasion, cervical invasion present, tumor index[a] ≥ 36 cm, or suspicious lymph nodes[b] or CA-125 level of ≥ 30 IU/mL	11.1 (4/36)

[a]Length × width × height.
[b]Defined as enlarged lymph nodes (> 1 cm) or lymph nodes that appeared round without a fatty hilum or a necrotic center.

tions and regions, women with low-risk endometrial cancer may undergo lymphadenectomy to identify patients with lymph node metastasis [38]. Positive lymph nodes lead to upstaging of cancer because of the increased risk of recurrence and dramatically decreased survival rate [4–8]. Women with advanced disease are treated with adjunct therapy to improve survival. A preoperative algorithm that detects the subgroup of women at increased risk of lymph node metastasis who would benefit most from lymphadenectomy and that allows lymphadenectomy to be avoided in women at low risk of lymph node metastasis would be beneficial in clinical practice [13–18, 34].

MRI is used to assess patients with endometrial cancer because of its reported excellent accuracy in determining the extent of disease, including myometrial invasion and cervical invasion [2–4, 13–24, 26, 27, 34]. Furthermore, several European countries routinely use preoperative MRI to triage patients to tertiary care centers if lymphadenectomy is deemed necessary [33, 39]. This strategy is particularly critical in countries with capitated health care plans because avoiding lymphadenectomy in women at low risk of lymph node metastasis avoids the risk of the possible complications of lymph node dissection, increased anesthesia and operating room times, and the need for a specialized oncologic surgeon at a tertiary care center [39, 40]. At our center, a new preoperative clinical protocol based on a low-risk assessment regimen published in the literature [13–15] was implemented. This protocol includes preoperative MRI and serum CA-125 evaluation in women diagnosed with grade 1 endometrioid carcinoma. The goals of our study were to determine the sensitivity, specificity, PPV, and NPV of the new preoperative clinical protocol [41].

The results of our study show that our preoperative clinical protocol, which included preoperative MRI and serum CA-125 evaluation, has a calculated sensitivity of 94%, specificity of 91%, PPV of 84%, and NPV of 97% in predicting women in need of lymphadenectomy when final surgical pathology and serum CA-125 results were used as the reference standard. Of the 99 patients, there were only two FNs, indicating that the new clinical protocol is a good risk assessment model [34].

When histologic grade alone was considered, the overall rate of lymph node metastasis in women with grade 1 endometrioid adenocarcinoma in the preoperative study cohort was 4.0% (4/99). This rate is not statistically different from the rate of lymph node metastasis of 4.2% (4/95) in the historical cohort who did not undergo preoperative MRI or CA-125 evaluation to determine the need for lymphadenectomy. Only 36.4% (36/99) of the women in the preoperative study cohort underwent lymphadenectomy, compared with 100% (95/95) of the women in the historical cohort who underwent lymphadenectomy. The similar rate of metastasis between the two groups studied is reassuring that our protocol is not missing a large number of women with lymph node metastasis while decreasing the lymphadenectomy rate, although the true rate of lymph node metastasis in the preoperative study cohort will be realized only on follow-up of the women who did not undergo lymphadenectomy.

In our study, the presence of any one of the following findings increased the incidence of lymph node metastasis to 11.1% (4/36): at least 50% myometrial invasion on MRI, evidence of cervical invasion on MRI, tumor index of at least 36 cm on MRI, abnormal lymph nodes on MRI, or an elevated CA-125 value of at least 30 IU/mL. Similar studies calculating lymph node metastasis rates have been performed using the Korean gynecologic oncology group criteria [17]. Investigators noted a

TABLE 4: MRI Findings and Cancer Antigen–125 (CA-125) Level of Patients With Pathologically Proven Metastatic Lymph Nodes

Patient No.	MRI Findings				CA-125 Level (IU/mL)
	Tumor Index[a] (cm)	Myometrial Invasion	Cervical Invasion	Suspicious Lymph Nodes[b]	
1	46	≥ 50%	No	Yes[c]	50
2	> 36[d]	≥ 50%	No	No	26
3	104	≥ 50%	No	Yes[e]	15
4	137	≥ 50%	Yes	No	109

[a]Length × width × height.
[b]Defined as enlarged lymph nodes (> 1 cm) or lymph nodes that appeared round without a fatty hilum or a necrotic center.
[c]Pelvic lymph nodes only.
[d]Tumor was too large and too ill defined to obtain an exact value.
[e]Pelvic and paraaortic lymph nodes.

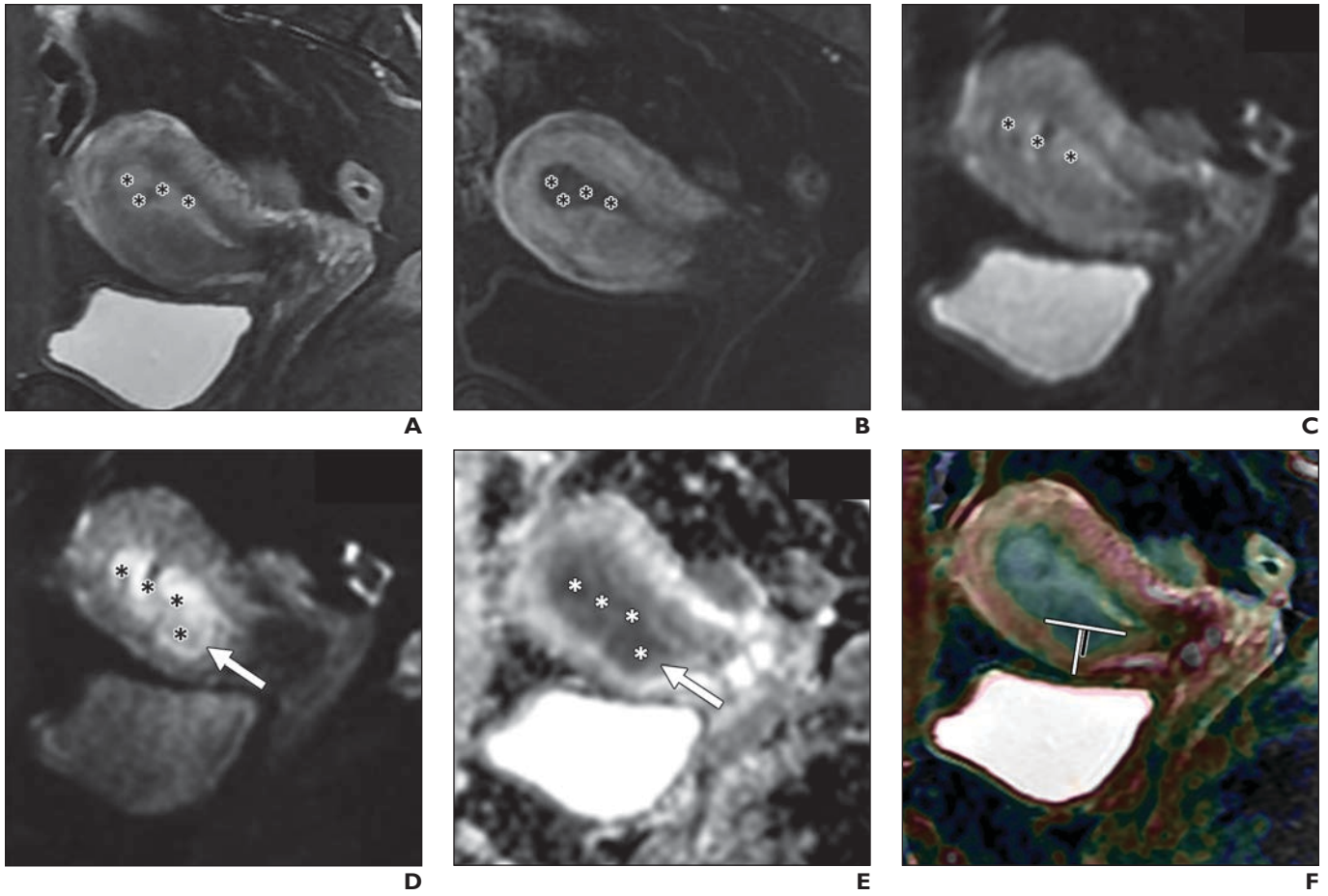

Fig. 3—63-year-old woman with grade 1 endometrioid adenocarcinoma. Myometrial invasion was interpreted as being < 50% on initial radiology report. Pathology determined myometrial invasion was 9/17 mm, or > 50%, so imaging finding was false-negative. On retrospective review of MR examination, endometrial tumor did appear to have ≥ 50% myometrial invasion on DW images.

A, Sagittal T2-weighted image shows abnormal signal intensity (*asterisks*), which indicates presence of tumor in endometrial canal. There is no obvious myometrial invasion.

B, Sagittal T1-weighted image obtained 90 seconds after contrast injection shows very mild enhancement of endometrial tumor (*asterisks*) in endometrial canal. There is no obvious myometrial invasion.

C, On sagittal DW image obtained with b value of 0 s/mm^2, endometrial tumor is seen as mildly hyperintense tissue in endometrial canal (*asterisks*).

D, On sagittal DW image obtained with b value of 500 s/mm^2, endometrial tumor tissue (*asterisks*) is more hyperintense than on **C**, and it is apparent that tumor extends into myometrium (*arrow*).

E, Apparent diffusion coefficient (ADC) map shows that endometrial tumor in endometrial canal (*asterisks*) is dark and restricting diffusion and that tumor extends into myometrium (*arrow*).

F, To determine level of myometrial invasion, measurements can be made on fusion image of sagittal ADC map on top of sagittal T2-weighted image. First, line along expected inner edge of myometrium (*white horizontal line*) is drawn; then, lines perpendicular to first line can be drawn to measure thickness of entire myometrium (*white vertical line*) and extent of tumor invasion into myometrium (*black line*).

0% lymph node metastasis rate in women with grade 1 endometrioid adenocarcinoma when there was less than 50% myometrial invasion, no extension beyond the corpus (no cervical invasion), no enlarged lymph nodes on MRI, and a CA-125 level that was not elevated; however, if any of these parameters were positive, the lymph node metastasis rate increased to 22% [17]. Investigators of another study noted a lymph node metastasis rate of 15.3% when any of the following high-risk factors was present: grade 3 endometrioid or serous papillary tumor, tumor index of at least 36 cm, and high CA-125 level [15].

Alternative methods in the decision analysis for performing lymphadenectomy need to be mentioned including the use of frozen section at surgery. The ability to perform accurate frozen-section analyses is variable from institution to institution and is based on local expertise and equipment availability. The accuracy of frozen-section analyses for assessing low-risk patients significantly varies among centers, with some reporting inaccurate frozen-section results compared with final pathology results in up to 16% of cases [42]. Investigators have also noted that frozen-section FN rates result in suboptimal surgical treatment of 13% of stage IA patients [43]. Furthermore, frozen section can provide information only at the time of surgery and may increase operating room time. The preoperative information gained from the MRI and CA-125 evaluation was thought to be an added benefit from the standpoints of resource allocation, patient counseling, and decision making by referring clinicians and patients.

There are a few limitations of our study. It is a retrospective review of radiology reports at a single academic referral center for gynecologic malignancies. These results may differ with the inclusion of multiple centers.

We also use a single MRI scanner vendor; therefore, results may differ on the basis of vendor differences. Other limitations include the possibility of overestimating the amount of myometrial invasion in patients with large tumors that expanded the endometrial cavity and thinned the myometrium. This limitation is one that may be mitigated by the fact that a larger tumor would potentially have a large tumor index, and therefore the overestimation of the myometrial invasion would be noncontributory to the decision to perform lymphadenectomy given that the tumor index could be at least 36 cm. There is also the possibility that the lack of CA-125 data in the historical cohort would influence the final outcomes if CA-125 levels between cohorts were statistically different. Finally, because of the retrospective nature of this study, we were unable to use the surgical pathology tumor index because three measurements were not included in the surgical pathology reports. This limits our ability to compare MRI size with pathologic size. However, our criterion of tumor index is based on the work of several other investigators who have validated the use of tumor index in assessing lymph node metastasis risk [13–15].

In conclusion, the detection of lymph node metastasis changes the clinical treatment and course in women with grade 1 endometrial adenocarcinoma. Detecting the subgroup of women who may be at increased risk for potential lymph node metastasis is important both to identify the women with positive lymph node metastasis and to avoid the risks of unnecessary lymphadenectomy in women at low risk of lymph node metastasis. In our study, women with grade 1 endometrioid adenocarcinoma and an elevated CA-125 level or an MRI finding of a tumor index of at least 36, myometrial invasion of at least 50%, cervical invasion, or abnormal lymph nodes (defined as enlarged lymph nodes [> 1 cm] or lymph nodes that appeared round without a fatty hilum or a necrotic center) had an increased rate of lymph node metastasis of 11.1% (4/36). Our preoperative protocol had an excellent NPV of 97% when final surgical pathology and CA-125 results were used as the reference standard.

The results of this study support the use of preoperative MRI and CA-125 evaluation to identify women with grade 1 endometrioid carcinoma who are at higher risk of lymph node metastasis while avoiding unnecessary surgery in those with a low risk of lymph node metastasis. A larger prospective clinical trial is needed to validate our results, determine if this protocol could be applied across centers, and allow acceptance among our gynecologic oncology colleagues as a valid protocol for predicting the need for lymphadenectomy.

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