

## EVALUATION OF MYOMETRIAL INVASION AND CERVICAL INVOLVEMENT IN TYPE I ENDOMETRIAL CANCER USING DIFFUSION-WEIGHTED MAGNETIC RESONANCE IMAGING

HARIYONO WINARTO<sup>1\*</sup>, BRIAN PRIMA ARTHA<sup>1</sup>, SAHAT B. MATONDANG<sup>2</sup>, TANTRI HELLYANTI<sup>3</sup>, ARIA KEKALIH<sup>4</sup>

<sup>1</sup>Division of Gynecologic Oncology, Department of Obstetrics and Gynecology, Dr. Cipto Mangunkusumo Hospital, Jakarta, Indonesia,

<sup>2</sup>Department of Radiology, Dr. Cipto Mangunkusumo Hospital, Jakarta, Indonesia, <sup>3</sup>Department of Pathological Anatomy, Dr. Cipto Mangunkusumo Hospital, Jakarta, Indonesia, <sup>4</sup>Division of Epidemiology and Biostatistics, Department of Community Medicine, Faculty of Medicine, Universitas Indonesia, Jakarta, Indonesia  
Email: hariyono.winarto@ui.ac.id

Received: 22 Oct 2019, Revised and Accepted: 25 Mar 2020

### ABSTRACT

**Objective:** Surgical procedure and adjuvant treatment of type I endometrial cancer were affected by some variables assessed preoperatively. Diffusion-weighted magnetic resonance imaging (DWI) is a promising modality in evaluating myometrial invasion and cervical involvement, investigating the diagnostic values of DWI in assessing myometrial invasion and cervical involvement.

**Methods:** A cross-sectional study was conducted. This study involved all type I endometrial cancer patients in Dr. Cipto Mangunkusumo Hospital from April 2016 until April 2019. The depth of myometrial invasion and cervical involvement was examined using 1.5-T MR unit. The result was compared to the surgical pathologic findings as the reference standard.

**Results:** 34 types I endometrial cancer patients were enrolled in this study. The sensitivity of DWI in evaluating myometrial invasion and cervical involvement in type I endometrial cancer was 94.12% and 57.14%, while the specificity was 64.71% and 92.59%, respectively.

**Conclusion:** DWI can provide reliable prognostic variable information about the myometrial invasion and cervical involvement in the preoperative preparation of endometrial cancer patients.

**Keywords:** Diffusion-weighted magnetic resonance imaging, Endometrial cancer, Myometrial invasion, Cervical involvement

© 2020 The Authors. Published by Innovare Academic Sciences Pvt Ltd. This is an open access article under the CC BY license (<http://creativecommons.org/licenses/by/4.0/>)  
DOI: <http://dx.doi.org/10.22159/ijap.2020.v12s3.39452>

### INTRODUCTION

As the second most common of female genital organ cancer after cervical cancer, about 382,069 cases on 2018, endometrial cancer is very crucial to be managed [1]. The most common type of endometrial cancer is type I endometrial cancer, which is an estrogen-dependent carcinoma characterized with endometrioid adenocarcinoma in histopathology examination. The main treatment for endometrial cancer is surgery. Surgical procedure and adjuvant treatment of type I endometrial cancer were affected by some variables assessed preoperatively. Stage, myometrial invasion, grade histology, LVSI status, tumor size are important variables that may be assessed preoperatively.

Magnetic resonance imaging (MRI) has shown its superiority in evaluating endometrial cancer cases. Diffusion-weighted magnetic resonance imaging (DWI) is a functional imaging technique that displays information about water mobility, tissue cellularity, and integrity of the cellular membranes. Endometrial tumors exhibit restricted diffusion compared with surrounding tissue, demonstrated as the high signal intensity at DWI [2]. DWI offers promising preoperative examination in evaluating endometrial cancer. This study will be focused to evaluate the diagnostic capacity of magnetic resonance diffusion imaging in predicting myometrial invasion and cervical involvement of type I endometrial cancer.

Table 1: Characteristic of patients with type I endometrial cancer

Characteristic	Patients	%
Parity		
Nulliparous	18	52.9 %
Primiparous	2	5.9 %
Multiparous	14	41.2 %
BMI		
Underweight (<18.5)	0	0
Normal (18.5-22.9)	7	20.6 %
Overweight (23-24.9)	5	14.7 %
Obesity I (25-29.9)	12	35.3 %
Obesity II (≥30)	10	29.4 %
Hypertension		
Yes	13	38.2 %
No	21	61.8 %
Diabetes Mellitus		
Yes	3	8.8 %
No	31	91.2 %
Grade histology		
1	17	50 %
2	10	29.4 %
3	7	11.6 %

Myometrial invasion and cervical involvement were evaluated preoperatively using DWI. Histopathology examination was done postoperatively as a gold standard. The result was shown in table 2-5.

## MATERIALS AND METHODS

This study compared DWI assessment in predicting myometrial invasion and cervical involvement in type I endometrial cancer to the postoperative histopathology results. We included all type I endometrial carcinoma patients in Dr. Cipto Mangunkusumo General Hospital from April 2016 to April 2019 with available preoperative DWI. Data were collected from medical records. Institutional review board approval was obtained in this retrospective study.

DWI examination was performed using 1.5-T MRI scanner. Imaging data were retrieved from the picture archiving and communication system (PACS) and reviewed by the experts. Histopathology analysis was done by section along the longitudinal plane of the uterus. Assessment was estimated grossly and confirmed microscopically

without knowledge of the MR findings. Myometrial invasion and cervical involvement were evaluated in this study. Myometrial invasion was categorized into two levels: 1) invasion less than 50% of the myometrial thickness (including tumor confined to the endometrium only), 2) invasion 50% or more of myometrial thickness. Cervical involvement was categorized as tumor invasion of cervical stroma and no tumor invasion of the cervical stroma.

## RESULTS

A total of 67 endometrial cancer patients had surgery in our hospital. Histology result of type I endometrial cancer was found in 50 patients with 34 preoperative DWI available. Patients' age ranged from 22 to 73 y old, with a median of 55 y old. Characteristics of patients are shown in table 1.

**Table 2: DWI myometrial invasion findings compared to the histopathology examination**

		Histopathology		Total
		≥ 50% invasion	< 50% invasion	
MR-DWI	≥ 50% invasion	16	6	22
	< 50% invasion	1	11	12
	Total	17	17	34

**Table 3: Diagnostic values of DWI compared to the gold standard**

Parameter	Estimate	Lower-upper 95% CI
Sensitivity	94.12%	(73.02-98.95)
Specificity	64.71%	(41.3-82.69)
Positive predictive value	72.73%	(51.85-86.85)
Negative predictive value	91.67%	(64.61-98.51)
Accuracy	79.41%	(63.2-89.65)
Positive likelihood ratio	2.667	(1.909-3.725)
Negative likelihood ratio	0.09091	(0.01162-0.7113)

**Table 4: DWI findings in evaluating cervical involvement compared to the histopathology examination**

		Histopathology		Total
		Yes	No	
MR-DWI	Yes	4	2	6
	No	3	25	28
Total		7	27	34

**Table 5: Diagnostic values of MR-DWI compared to histological findings in assessing cervical involvement**

Parameter	Estimate	Lower-Upper 95% CI
Sensitivity	57.14%	(25.05-84.18)
Specificity	92.59%	(76.63-97.94)
Positive predictive value	66.67%	(30.0-90.32)
Negative predictive value	89.29%	(72.8-96.29)
Accuracy	85.29%	(69.87-93.55)
Positive likelihood ratio	7.714	(2.005-29.68)
Negative likelihood ratio	0.4629	(0.2393-0.8952)

## DISCUSSION

In our study, we have observed the characteristic of the endometrial carcinoma patient in Dr. Cipto Mangunkusumo General Hospital. More than half of type I endometrial carcinoma patients in our hospital were nulliparous women. Overweight and obesity were found in the majority of patients. These results corresponded with the previous meta-analysis in 2018, which revealed that endometrial carcinoma had a strong association with these factors. Parity reduced risk of disease (RR 0.66; 95%CI 0.60-0.74). Body mass index was strongly associated with increased overall cancer risk in premenopausal women (RR per 5 kg/m<sup>2</sup> 1.49; 95%CI 1.39-1.61), while the waist-to-hip ratio was associated with total endometrial cancer (RR per 0.1 unit 1.21; 95%CI 1.13-1.29) [3]. Despite the slow progression in type I endometrial cancer, most of our patients were diagnosed with low-grade endometrial cancer. This condition might

be caused by the patient's tendency to go to the doctor immediately when there was vaginal bleeding.

Sensitivity of DWI in assessing myometrial invasion in this study was good. It showed that DWI was good in identifying patients with deep myometrial invasion. Specificity of DWI in assessing myometrial invasion was moderate. It correlates with low positive predictive value. These values may lead to overtreatment in some low-risk endometrial cancer patients. However, it is clinically acceptable due to the difference in management guidelines. NCCN recommends surgical staging in almost all endometrial cancer, except patients with low risk for nodal metastases (less than 50% myometrial invasion, tumor less than 2 cm, well or moderately differentiated histology). Sentinel lymph node mapping may be considered in selected patients [4]. Lymphadenectomy is not recommended by ESGO in low-risk endometrial cancer and only

considered in intermediate risk endometrial cancer. Data has not shown survival benefit but may be considered for staging purpose [5]. Adjuvant treatment is affected by prior surgery management. Incomplete surgical procedure will cause additional adjuvant treatment. Risk and complication of surgical staging is more tolerable than adjuvant treatment.

Six patients were identified having deep myometrial invasion with DWI, whereas the histopathology result was a superficial myometrial invasion. This result might contribute to the low specificity and positive predictive value of DWI in evaluating myometrial invasion. Four out of six patients had other pathological conditions besides endometrial cancer. Adenomyosis, leiomyoma, and other pathological condition may affect the interpretation of DWI. This pitfall has been identified in the Guideline of The European Society of Urogenital Radiology 2019 [6]. Large tumor size, thin myometrium, uterine atrophy, isointense endometrial tumor, uterine body involvement, and other anatomical distortion may interfere with the interpretation.

DWI is usually performed after the diagnosis of endometrial cancer established. Diagnosis of endometrial cancer should be based on histopathology result. Therefore, endometrial sampling usually performed prior DWI. Bleeding and inflammation in the uterine cavity may lead to misinterpretation in DWI. However, more than one-week time interval will mostly diminish misinterpretation in evaluation myometrial invasion. The data about the time interval between endometrial sampling and DWI examination was not available in this study. This limitation should be considered when interpreting the results.

Apparent diffusion coefficient as a quantitative analysis may improve the result in evaluating the myometrial invasion of endometrial cancer. Endometrial cancer tends to show a lower apparent diffusion coefficient compared to normal tissue or benign lesion. This study was using ADC value cutoff  $1 \times 10^{-3} \text{ mm}^2/\text{s}$ . In the study of Takeuchi *et al.*, the mean ADC value was  $0.84 \pm 0.19 \times 10^{-3} \text{ mm}^2/\text{s}$  and  $1.58 \pm 0.36 \times 10^{-3} \text{ mm}^2/\text{s}$  for endometrial cancer and normal tissue, respectively. Using ADC value cutoff  $1.2 \times 10^{-3} \text{ mm}^2/\text{s}$  will result sensitivity 96% and specificity 95% [7]. Meta-analysis study in 2019 showed the result of sensitivity, specificity, and area under the curve of ADC to evaluate myometrial invasion were 71%, 67%, and 77%, respectively. It should be noticed that the ADC value cutoff in this meta-analysis varied from 0.75 to 0.77 [8]. The ideal ADC value cutoff was still disputable.

There was a limited reference of cervical involvement evaluation using DWI. In this study, there is a disproportion and lack of sample size in the cervical involvement of endometrial cancer patients. Only seven patients (20.5%) were positive for cervical involvement among 34 patients in this study. Sensitivity of DWI in evaluating cervical involvement was 57.14% (CI 25.05-84.18). Wide confidence interval corresponds to the small number of sample. Though, there was a study in 2016 showed similar sensitivity in the evaluation of cervical involvement using dynamic contrast-enhanced (58.3% and 50%) [9]. High specificity result of cervical involvement evaluation in this study showed that DWI is able to exclude cervical involvement in endometrial cancer. Misinterpretation in cervical involvement may be caused by several factors such as: the extreme angle between uterus and cervix, minimal slices in DWI. Despite of these results, there is no difference on hysterectomy procedure type related to cervical involvement (except for parametrium involvement). Low sensitivity of DWI can also be tolerated due to the rarity of cervical

involvement in low-risk endometrial cancer or superficial myometrial invasion.

We recognize that there are some limitations in this study. Even though we have included all of endometrial cancer in our institution, only a few were included due to the limited number of patients. Further study with a larger sample should be performed to improve the result. Second, the variability of the time interval between DWI and surgery procedure may affect the disease progression, which may interfere the interpretation. The last limitation was we only used single-axis image analysis due to the limited resources. It should be considered to use a multiple slice and axis to avoid misinterpretation. Quantitative evaluation in DWI using apparent diffusion coefficient may improve the result.

## CONCLUSION

This study demonstrated the usefulness of magnetic resonance diffusion imaging in evaluating myometrial invasion and cervical involvement for type I endometrial cancer. Some factors were recognized in misinterpretation of diffusion-weighted imaging, such as: cornual involvement, tumor size, uterine atrophy, anatomical factors, and multislice imaging. Those factors should be noticed to obtain a better result.

## FUNDING

Nil

## AUTHORS CONTRIBUTIONS

All authors have contributed equally.

## CONFLICT OF INTERESTS

All authors have none to declare.

## REFERENCES

1. Bray F. Global cancer statistics globocan estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA: Cancer J Clin* 2018;68:394-424.
2. Beddy P. Evaluation of the depth of myometrial invasion and overall staging in endometrial cancer: comparison of diffusion weighted and dynamic contrast-enhanced MR imaging. *Radiology* 2012;262:530-7.
3. Raglan O. Risk factors for endometrial cancer: an umbrella review of the literature. *Int J Cancer* 2019;145:1719-30.
4. McMillian N, Scavone J. Uterine neoplasms. *NCCN Guidelines* 2017;2:UN1-MS56.
5. Colombo N. ESMO-ESGO-ESTRO consensus conference on endometrial cancer. *Int J Gynecol Cancer* 2016;26:2-30.
6. Nougaret S. Endometrial cancer MRI staging: updated guidelines of the European society of urogenital radiology. *Eur Radiol* 2019;29:792-805.
7. Takeuchi M. Diffusion-weighted magnetic resonance imaging of endometrial cancer: differentiation from benign endometrial lesions and preoperative assessment of myometrial invasion. *Acta Radiol* 2009;50:947.
8. Yan BC. The diagnostic performance of ADC value for tumor grade, deep myometrial invasion and lymphovascular space invasion in endometrial cancer: a meta-analysis. *Acta Radiol* 2019;1-10. DOI:10.1177/0284185119841988
9. Lin G. Endometrial cancer with cervical stromal invasion: diagnostic accuracy of diffusion-weighted and dynamic contrast-enhanced MR imaging at 3T. *Eur Radiol* 2017;27:1867-76.