



ORIGINAL RESEARCH PAPER

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ROLE OF MRI IN PRE OPERATIVE STAGING OF CARCINOMA ENDOMETRIUM

KEY WORDS: carcinoma endometrium, MRI, myometrial invasion, lymph node metastasis

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ABSTRACT

According to current consensus, early stage endometrial cancer does not require nodal dissection. The key factor is proper selection of cases with early stage carcinoma pre-operatively to avoid extensive surgery. Aim-Aim of the study is to find accuracy of MRI in pre-operative staging of carcinoma endometrium. Materials and methods-The study is done in a tertiary care hospital on 42 patients. Information regarding the age, complaints, comorbidities and histological type of the tumour were taken. The findings between pre-operative MRI and the post-operative histopathology report with respect to deep myometrial invasion and lymph node metastasis were thoroughly analysed and accuracy of MRI was assessed. Results-The sensitivity, specificity, PPV, NPV and diagnostic accuracy of MRI for diagnosing deep myometrial invasion are 82.35%, 100%, 100%, 89.3% and 92.86% respectively. The sensitivity, specificity, PPV, NPV and diagnostic accuracy of MRI for diagnosing lymph node invasion are 80%, 94.6%, 66.7%, 97.2% and 92.86%. Conclusion-MRI has good diagnostic accuracy to detect deep myometrial invasion and there by detecting the subset of patients who needs proper lymph node dissection.

Endometrial cancer is the most common gynaecological cancer(1,2,3,4) and the fourth common cancer in female in the western world(1). It is the sixth leading cause of death in females and the five-year relative survival risk is around 82% (1). It usually occurs in perimenopausal or postmenopausal women, with a peak incidence at age 55–66 years. It is rare in patients under 40 years old, in whom it may be associated with Stein-Leventhal syndrome (5) or Lynch Syndrome(1). The common risk factors include obesity, chronic estrogen exposure in the form of exogenous estrogen, late menopause, infertility, tamoxifen use; diabetes and hypertension(1,6). Abnormal uterine bleeding or postmenopausal bleeding is a frequent early sign. There is no standard or routine screening test for women at average risk. 67% are diagnosed in the early stages of the disease because of symptomatic abnormal bleeding (1,7). The most common histologic type is Adenocarcinoma, accounting for 60%–70% of endometrial tumors. Adenoacanthoma and adenosquamous carcinoma account for 20%–30%. Less common histologic types include clear cell, mucinous, secretory, and papillary serous (8).

Prognosis and treatment are based mainly on three factors: histologic grading of the neoplasm, the presence of nodal metastasis, and the extent of myometrial invasion (9,10,11). The grade of the tumour can be found out by pre-operative endometrial sampling and higher grade tumours can be planned for lymphadenectomy by an expert. The depth of myometrial invasion correlates to the risk of lymph node metastasis and 5-year survival (11).

Endometrial cancer is surgically staged. Patients with greater than 50% myometrial invasion have a six- to seven fold higher prevalence of pelvic and para-aortic lymph node metastasis and advanced surgical stage when compared to patients with less than 50% myometrial invasion. Patients with deep myometrial invasion should therefore be considered for more aggressive surgical staging, including pelvic and para-aortic lymphadenectomy (12), and therefore need specialist referral or a gynaecologic oncologist. Myometrial invasion can be found by 3 ways - pre-op imaging, intra op gross inspection of specimen and intra-op frozen section. Even though the latter two help in preventing unnecessary lymphadenectomies they doesn't help in pre-op planning. Hence centres where on call expert is not available will not be able to do these cases and in turn will increase the burden on higher centres. Here comes the role of pre op imaging. Thus, a reliable method of preoperative staging is essential to find patients who need lymph node sampling. Patients with lymph node metastasis require adjuvant radiotherapy, hormonal therapy or chemotherapy. Patients who undergo pelvic

and para-aortic lymphadenectomy have risks of morbidity, including increased time under general anaesthesia, increased blood loss, and longer postoperative hospitalization (13). Failure to perform lymph node sampling in patients who are at risk for lymph node metastasis may result in understaging and inadequate therapy (14) and may require re-operation.

Several imaging modalities like magnetic resonance imaging (MRI), computed tomography (CT) and transvaginal sonography (TVS) have been studied as tools for preoperative staging of endometrial carcinoma. In a large-scale meta-analysis (15), contrast-enhanced dynamic MRI was found to be slightly more accurate than ultrasound imaging and CT in preoperative assessment of the depth of myometrial invasion. This study is done to know the accuracy of MRI in predicting deep myometrial invasion in patients with endometrial cancer and thus to find out patients who need lymph node sampling and referral to a higher centre.

MATERIALS AND METHODS

The aim of the study is to assess role of MRI in pre operative staging of carcinoma endometrium. This is a diagnostic test evaluation study where test is MRI and the gold standard test is histopathological examination of the specimen. The study is done in Amala Institute of Medical Sciences, a tertiary care hospital in South India. A total of 101 endometrial carcinoma patients who were operated at this institute from January 2017 to December 2018 were considered for the study. Those who did not have a pre-operative assessment with magnetic resonance imaging (MRI) were excluded from the study. After exclusion, a total of 42 confirmed cases of endometrial carcinoma were included. Basic information regarding the age, presenting complaint; history of diabetes, hypertension and dyslipidemia and histological type of the tumour were taken into consideration. The findings between pre-operative MRI and the post-operative histopathology report with respect to deep myometrial invasion and lymph node metastasis were thoroughly analysed. The accuracy of MRI in predicting depth of myometrial invasion and lymph node involvement was assessed in terms of sensitivity, specificity, positive predictive value, negative predictive value and diagnostic accuracy.

RESULTS

The youngest patient with carcinoma endometrium in the study sample was 38 years old and the oldest was 81 years old. The mean age of the group was 59.4±10.2 years. Patients presented with three major complaints - 81% had post-menopausal bleeding, 14.3% had menorrhagia and 4.8% had discharge pervaginum.

Medical co-morbidities like hypertension, diabetes and dyslipidemia were taken into consideration. 50% had hypertension, 38.1% had diabetes and 26.2% had dyslipidemia. 85.7% had endometrioid adenocarcinoma, 7.1% had papillary adenocarcinoma, 4.8% had carcinosarcoma and 2.4% had mixed high grade endometrioid + serous adenocarcinoma.

1 out of 25 (4%) patients without deep myometrial invasion had lymph node metastasis; whereas 4 out of 17 (23.5%) patients with more than 50% myometrial invasion had lymph node metastasis. The histological type of the tumour of the patient with less than 50% myometrial invasion and lymph node positivity is papillary adenocarcinoma.

The role of MRI in predicting myometrial invasion was studied (Table 1). Among the 17 patients with deep invasion, MRI couldn't diagnose 3 patients, ie; the false negative value was 17.6%. The sensitivity, specificity, positive predictive value, negative predictive value and diagnostic accuracy of MRI for diagnosing deep myometrial invasion are 82.35%, 100%, 100%, 89.3% and 92.86% respectively.

Table 1. Relation of MRI with histopathology report in detecting myometrial invasion

Myometrial involvement as per MRI	Histopathological report		Total
	More than half	Less than half	
More than half	14	0	14
Less than half	3	25	28
Total	17	25	42

Comparing the accuracy of MRI in detecting lymph node positivity (Table 2), there were only 2 false positive and 1 false negative cases. The sensitivity, specificity, positive predictive value, negative predictive value and diagnostic accuracy of MRI for diagnosing lymph node invasion are 80%, 94.6%, 66.7%, 97.2% and 92.86% respectively.

Table 2. Relation of MRI with histopathology in detecting lymph node metastasis.

Lymph node status as per MRI	Histopathological report		Total
	Positive	Negative	
Positive	4	2	6
Negative	1	35	36
Total	5	37	42

DISCUSSION

In our study, the maximum number of patients who had endometrial carcinoma were between the age group 50-70 years and more than 80% were postmenopausal. All cases of postmenopausal bleeding and abnormal uterine bleeding in the perimenopausal age group should be thoroughly investigated. Endometrial sampling is advised if the scan shows a thick endometrium. Early diagnosis and prompt treatment increases the survival rate of these patients.

The most common histological type of tumour was endometrioid carcinoma (85.7%). Among these patients, lymph node metastasis was seen in 11.1% only (4 out of 36 patients). But, among the 3 patients with papillary carcinoma 1 patient had lymph node positivity (33.3%). These patients have poor prognosis.

Lymph node positivity was seen in 4% of patients without deep myometrial invasion and in 23.5% of patients with deep invasion. A study done by Creasman which included 180 women with grade 1 cancers, reported the incidence of pelvic node positivity as 0%, 3% and 11% in women with no, inner third and outer third myometrial invasion respectively (16). Mariani et al from the Mayo clinic published their study that demonstrated a subset of endometrial cancer with favorable characteristics which included three low-risk features involving tumor size ≤ 2cm, grade 1 or 2 tumors, and depth of invasion ≤ 50%. In their study they

demonstrated a 5% risk for nodal metastasis and 97% cancer-specific survival in this low-risk group (17).

Pre-treatment knowledge of the depth of myometrial invasion or cervical extension influences the decision whether to perform lymphadenectomy or not (9, 12). The role of MRI in the work-up of patients diagnosed with endometrial cancer includes the assessment of the depth of myometrial invasion, the presence of stromal invasion of the cervix, screening for lymphatic or peritoneal metastases in patients with a poorly differentiated carcinoma, and confirmation of Stage III or Stage IV disease. Pre-operative imaging with MRI helps in distinguishing Stage 1a patients from other stages and thus helps the clinician to decide on need for lymphadenectomy.

In our study, the sensitivity, specificity, PPV, NPV and diagnostic accuracy of MRI for diagnosing deep myometrial invasion were 82.35%, 100%, 100%, 89.3% and 92.86% respectively. Many studies in the literature have co-related with our results. The study done by Koplay et al. (18) has also shown that MRI has high sensitivity and specificity in diagnosing deep myometrial invasion. According to their study, the sensitivity, specificity, positive predictive value, negative predictive value and diagnostic accuracy of diffusion weighted MRI for differentiating between superficial myometrial invasion and deep myometrial invasion were 85%, 89%, 81%, 92% and 88%, respectively. Teng F et al (19) studied the diagnostic value and error analysis of MRI in endometrial carcinoma patients. They found that the sensitivity, specificity, diagnostic accuracy, positive predictive values, and negative predictive values of contrast enhanced magnetic resonance imaging were 90.9%, 91.8%, 91.6%, 73.2% and 97.6%, respectively, for identifying deep myometrial invasion. Study done by Dae shik suh et al (20) concluded that MRI had a rather weak predictive value when used to assess absence of myometrial invasion. This should be borne in mind when choosing patients for conservative treatment of endometrial carcinoma. The negative predictive value (probability of absence of myometrial invasion) as per their study was 49.2%. MRI showed an accuracy of 59.2%, a sensitivity of 68.8%, a specificity of 74.4%, and an 86.9% positive predictive value, for myometrial invasion.

In our study, the accuracy of MRI in diagnosing lymph node invasion is also on the higher side. The sensitivity, specificity, positive predictive value, negative predictive value and diagnostic accuracy of MRI for diagnosing lymph node invasion are 80%, 94.6%, 66.7%, 97.2% and 92.86% respectively. The results are in accordance with many other studies. The sensitivity, specificity and diagnostic accuracy rates were 100%, 96% and 96.5% for pelvic lymph node metastasis respectively, in a study done by Koplay, Dogan et al (18). According to a study done by Teng et al (19), the sensitivity, specificity, diagnostic accuracy, positive predictive values, and negative predictive values of contrast enhanced magnetic resonance imaging were 45.0, 91.2, 85.6, 40.9 and 92.4%, respectively, for identifying pelvic lymph node metastasis. They found that the main causes of error in contrast enhanced magnetic resonance imaging were myomas, cornual lesions, deep myometrial invasion, large tumor size, non endometrioid tumor type, and lower tumor grade. Contrast enhanced magnetic resonance imaging has a high accuracy and a low tendency to produce false negative predictive values. Gynecological oncologists should combine the imaging data and clinical information to make therapeutic decisions and avoid diagnostic errors.

CONCLUSION

In the era where need for lymph node dissection is questioned in cases of early stage carcinoma of endometrium, with proper pre-operative evaluation of depth of invasion, lymph node involvement and grade of tumour, a subset of cases may be managed at peripheral centres without burdening higher centre. But unless properly detected, it might end up in incomplete staging. Hence, there is need for proper pre-operative evaluation with MRI to decide on need for lymph node dissection, unless there is availability of sentinel node.

REFERENCES

1. American Cancer Society. Cancer Facts & Figures 2017. Atlanta: American Cancer

- Society;2017.
2. Parkin DM, Bray F, Pisani P, Ferlay J. Global cancer statistics, 2002. *CA Cancer J Clin*2005; 55: 74–108.
 3. Jemal A, Murray T, Ward E, Samuels A, Tiwari RC, Ghafoor A, Feuer EJ, Thun MJ. Cancer statistics 2005. *CA Cancer J Clin*2005; 55: 10–30.
 4. Takahashi S, Murakami T, Narumy Y et al. Preoperative staging of endometrial carcinoma: diagnostic effect of T2-weighted fast spin-echo MR imaging. *Radiology* 1998, 206:539–547.
 5. Saez F, Oleaga L, Astigarraga E et al. Valor de la resonancia magnética en el estadiaje del carcinoma de endometrio. *Radiología* 1994; 36:329–338.
 6. Homesley HD. Revised 1998 International Federation of Gynecology and Obstetrics staging systems for endometrial and vulvar cancer: an assessment. *ClinObstetGynecol* 1992; 35:89–94.
 7. Sironi S, Taccagni G, Garancini P, Belloni C, Del Maschio A. Myometrial invasion by endometrial carcinoma: assessment by MR imaging. *AJR* 1992; 158:565–569.
 8. Outwater E, Kressel HY. Evaluation of gynecologic malignancy by magnetic resonance imaging. *RadiolClin North Am* 1992; 30: 789–806.
 9. Larson DM, Connor GP, Broste SK, Krawisz BR, Johnson KK. Prognostic significance of gross myometrial invasion with endometrial cancer. *ObstetGynecol* 1996; 88: 394–398.
 10. H, Rubinstein L V, Gherman GM, Karstaedt N. MR imaging evaluation of endometrial carcinoma: results of an NCI cooperative study. *Radiology* 1991; 179:829–832.
 11. Del Maschio A, Vanzulli A, Sironi S et al. Estimating the depth of myometrial involvement by endometrial carcinoma: efficacy of transvaginal sonography vs MR imaging. *AJR* 1993; 160:533–538.
 12. Eltabbakh GH, Piver MS, Hempling RE, Shin KH. Excellent long-term survival and absence of vaginal recurrences in 332 patients with low-risk stage I endometrial adenocarcinoma treated with hysterectomy and vaginal brachytherapy without formal staging lymph node sampling: report of a prospective trial. *Int J RadiatOncolBiolPhys*1997; 38: 373–380.
 13. Larson DM, Hohnson K, Olson KA. Pelvic and para-aortic lymphadenectomy for surgical staging of endometrial cancer: morbidity and mortality. *ObstetGynecol*1992; 79:998–1001.
 14. Doering DL, Barnhill DR, Weiser EB, Burke TW, Woodward JE, Park RC. Intraoperative evaluation of depth of myometrial invasion in stage I endometrial adenocarcinoma. *ObstetGynecol*1989; 74:930–933.
 15. Kinkel K, Kaji Y, Yu KK, Segal MR, Powell CB, Hricak H. Radiologic staging in patients with endometrial cancer: a meta-analysis. *Radiology*1999; 212: 711–718.
 16. Creasman WT, Morrow CP, Bundy BN, Homesley HD, Graham JE, Heller PB. Surgical pathologic spread patterns of endometrial cancer. A Gynecologic Oncology Group Study. *Cancer* 1987;60 Suppl S8:2035–41.
 17. Mariani A, Webb MJ, Keeney GL, et al. Low-risk corpus cancer: is lymphadenectomy or radiotherapy necessary? *Am J Obstet Gynecol*. 2000;182:1506–1519.
 18. Koplay, M. , Dogan, N. U., Erdogan, H. , Sivri, M. , Erol, C. , Nayman, A. , Karabagli, P. , Paksoy, Y. and Celik, C. (2014), DW MRI in endometrial carcinoma. *Journal of Medical Imaging and Radiation Oncology*, 58: 538-546. doi:[10.1111/1754-9485.12209](https://doi.org/10.1111/1754-9485.12209)
 19. Teng F, Zhang Y F, Wang Y M, Yu J, Lang X, Tian W Y, Jiang C X, et al. Contrast enhanced MRI in preoperative assessment of myometrial and cervical invasion, and lymph node metastasis: diagnostic value and error analysis in endometrial carcinoma. *Acta Obstet Gynecol Scand* 2015; 94: 266–273.
 20. Suh, D. , Kim, J. K., Kim, K. R., Kim, D. , Kim, J. , Kim, Y. , Kim, Y. and Nam, J. (2009), Reliability of magnetic resonance imaging in assessing myometrial invasion absence in endometrial carcinoma. *Acta Obstetrica et Gynecologica Scandinavica*, 88: 990-993. doi:[10.1080/00016340903141135](https://doi.org/10.1080/00016340903141135)