Magnetic resonance imaging in the preoperative staging of endometrial carcinoma

S. Cabrita[1], H. Rodrigues[2], R. Abreu[1], M. Martins[2], L. Teixeira[2], C. Marques[2], F. Mota[1], C. Freire de Oliveira[1]

Departments of Gynecology[1] and Radiology[2], University Hospital of Coimbra (Portugal)

Summary

Purpose of Investigation: Magnetic resonance imaging (MRI) has emerged as an important imaging modality in the evaluation of the extension of endometrial carcinoma which is essential in planning treatment and predicting prognosis. This study aimed to assess the value of MRI in the preoperative staging of endometrial carcinoma. *Methods:* We included in this study 162 patients with a histological diagnosis of endometrial carcinoma who underwent MRI pelvic imaging and surgical staging. MRI images were compared with pathological findings to measure MRI's sensitivity, specificity, positive and negative predictive values and diagnostic accuracy in what concerns myometrial, cervical and lymph node invasion. *Results:* MRI differentiation of deep myometrial invasion from superficial disease agreed with pathological findings in 77% of cases, with a sensitivity of 83%, a specificity of 72% and a diagnostic accuracy of 77%. Concerning cervical invasion, MRI had a sensitivity, specificity and diagnostic accuracy of 42%, 92%, 81% respectively. In assessing lymph node invasion, MRI presented a sensitivity of just 17%, a specificity of 99% and a diagnostic accuracy of 89%. *Conclusion:* Our study confirmed the high accuracy of MRI imaging in assessing myometrial and cervical invasion in endometrial carcinoma. When evaluating lymph node invasion, micrometastases are responsible for the low sensitivy of MRI.

Key words: Magnetic resonance; Endometrial carcinoma; Preoperative staging; Surgical planning.

Introduction

Endometrial carcinoma is the most common gynaecologic cancer and the fourth most frequent malignancy in women [1]. In Portugal, it has an incidence of 17.6/100,000 per year with a mortality rate of 3.4/100,000 per year [2]. Based on the inaccuracy of the clinical staging [3], the International Federation of Gynecology and Obstetrics (FIGO) proposed a surgicopathological staging adopted since 1988 [4]. Besides histological tumor grade, the prognosis is primarily correlated to tumor stage, for which the depth of myometrial and cervical invasion and the presence or not of lymph node metastases are essential [3]. In most institutions, patients with more than 50% of myometrial invasion are offered pelvic and paraaortic lymphadenectomy. Furthermore, cervical invasion also affects the extension of surgery. All these enlarged procedures have risks, namely resulting from increased time of anesthesia and increased blood loss [5]. Preoperative staging seems, therefore, essential in planning treatment, reducing surgery risks and predicting prognosis.

Magnetic resonance imaging (MRI) has emerged as an important imagiologic modality in the evaluation of the extension of endometrial carcinoma [6-9], showing to be important in assessing myometrial and, to a lesser extent, also cervical and lymph node infiltration.

This study aimed to assess the MRI value in the preoperative staging of endometrial carcinoma by comparing MRI to pathological findings concerning myometrial, cervical and lymph node invasion.

Materials and Methods

Population: This study considered 183 women with a histological diagnosis of endometrial carcinoma by endometrial biopsy, who performed preoperative MRI. Given the extent of the disease, nine women were treated with chemotherapy or radiotherapy prior to surgery and were excluded from the study, as were three women with medical contraindications to surgery. Patients whose final histological diagnosis was not endometrial carcinoma were also excluded (3 with carcinosarcoma and 6 with leiomyosarcoma). Our population included, therefore, 162 patients with a mean age of 64.6 years (range 22-94 years), being mostly postmenopausal (91%).

Imagiologic investigation: All patients were imaged with a 1.5-T system prior to surgery. MRI was performed with axial T1-weighted images, axial and sagittal T2-weighted images and also dynamic gadolinium-enhanced T1-weighted imaging. Disease was staged according to imagiologic established criteria.

Surgicopathologic investigation: All women underwent hysterectomy. Lymph node dissection was performed when one of the following was present: histology of serous, clear cell or squamous carcinoma; differentiation grade 3; MRI evidence of cervical of deep myometrial invasion.

Histological examination revealed 146 (90%) endometrioid adenocarcinomas, seven (4.3%) serous carcinomas, four (2.5%) clear cell carcinomas, four (2.5%) adenocarcinomas with squamous differentiation and one (0.7%) mucinous carcinoma. Concerning histological differentiation, 120 (74%) were found to be grade 1, 37 (23%) grade 2 and 5 (3%) grade 3.

Revised manuscript accepted for publication September 24, 2007

Data analysis: Pathology analyzed surgical specimens with no knowledge of MRI results. Both pathology and MRI classified the findings according to the International Federation of Gynecology and Obstetrics staging system for endometrial carcinoma.

MRI findings were compared with pathologic findings (regarded as the gold standard) concerning myometrial, cervical and lymph node invasion. Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and diagnostic accuracy of each of those parameters was calculated.

Results

After comparing MRI findings with pathologic findings of the 162 cases, final results were achieved. Overall staging concordance was 44% (71/162) with 50 cases of understaging and 41 of overstaging. MRI staging of myometrial disease (inner or outer half) accurately assessed 62% of cases (100/162), overestimating 23% (38/162) and underestimating 15% (24/162). From the erroneously staged cases, 57% (35/61) were noted to have leiomyomata or adenomyosis distorting uterine zonal anatomy. MRI differentiation between superficial disease (stages IA and IB) and deep myometrial invasion (IC) agreed with pathological findings in 77% (125/162) of cases, making the correct assessment in 72% of patients with less than half of myometrial infiltration and in 83% of patients with more than half of myometrial infiltration. Regarding this differentiation, MRI showed a sensitivity of 83%, a specificity of 72%, a PPV of 71%, a NPV of 84% and a diagnostic accuracy of 77%. Finally, we found a positive correlation between MRI findings and pathologic findings in characterizing myometrial invasion ($p < 0.001$).

Concerning cervical invasion (Stages IIA and IIB), MRI presented 15 true-positive, 116 true-negative, ten false-positive and 21 false-negative results. Analyzing this parameter, we found a sensitivity of 42%, a specificity of 92%, a diagnostic accuracy of 81%, a PPV of 60% and a NPV of 85%. From the 21 false-negative MRI results, 16 were histologically classified as IIA and only five as IIB, one of which with MRI reference to profuse cervical secretion.

In assessing lymph node invasion, MRI showed two true-positive, 90 true-negative, one false-positive and ten false-negative of the possible 103 comparable results as in 59 cases there was no surgical specimen. All 12 cases of histologic node invasion had a MRI staging with deep myometrial invasion. Considering lymph node invasion, MRI demonstrated a sensitivity of just 17%, a specificity of 99%, a diagnostic accuracy of 89%, a PPV of 66% and a NPV of 90%.

Overall, MRI sensitivity, specificity, diagnostic accuracy, PPV and NPV are depicted in Table 1.

Table 1. — *Overall MRI results concerning deep myometrial, cervical and lymph node invasion.*

	Myometrial (%)	Cervical (%)	Lymph node (%)
Sensitivity	83	42	17
Specificity	72	92	99
Positive Predictive Value	71	60	66
Negative Predictive Value	84	85	90
Diagnostic Accuracy	77	81	89

Discussion

It is well known that treatment and prognosis of endometrial carcinoma depends greatly on tumor staging. Considering endometrial cancer treatment, preoperative knowledge of the depth of myometrial invasion, the presence of cervical infiltration and lymph node invasion or disseminated disease has potential advantages as it should obligate to a pelvic and paraaortic lymphadenectomy, to a radical hysterectomy and eventually to adjuvant treatment. Also, a less invasive surgical technique (i.e., laparoscopy, vaginal approach) represents an option in early endometrial cancer. On the other hand, the prognostic value of tumor size, myometrial infiltration (essentially of the external half), cervical infiltration (cervical stroma) and lymph node metastasis has been established. Better presurgical assessment may contribute to the decreasing endometrial cancer morbidity and mortality by allowing optimization of the primary treatment. For planning treatment and drawing a prognosis, a preoperative work-up with an accurate staging seems fundamental.

In evaluating myometrial invasion, MRI has shown to offer a considerable higher sensitivity and specificity than transvaginal ultrasound or computed tomography, being the only modality to accurately assess cervical involvement. When multifactorial evaluation is required, MRI seems the only modality to accurately estimate myometrial, cervical and lymph node invasion [6, 11, 12]. Further, the accuracy and the cost of MRI have proven to be comparable to surgical staging with intraoperative uterine gross evaluation, also decreasing the number of unnecessary lymphadenectomies [7]. Without this last procedure, a decrease in patient morbidity and mortality should be expected as it is associated, for example, with increased time under general anesthesia or increased blood loss [5].

Our group evaluated the role of MRI in the preoperative staging of endometrial carcinoma by analyzing the results of the institution. Concerning the differentiation between superficial disease (IA, IB) and deep myometrial invasion (IC), our results (Table 1) show an accuracy comparable to those reported in previous literature [9, 11, 13] with more than half of the erroneously staged cases presenting myometrial pathology (i.e., leiomyomata, adenomyosis) distorting uterine zonal anatomy and thus complicating MRI classification. Myometrial compression by an endometrial lesion also biased accurate staging because it produced a distortion of the zonal anatomy difficult to evaluate even with contrast. We also found a positive correlation between MRI and pathologic findings ($p < 0.001$). It is also noteworthy that MRI results present a higher negative than positive predictive value (84% vs 71%) as it contributes to fewer resurgeries.

As for cervical invasion, our results are inferior than those achieved by some centers [9, 14] being comparable to other Portuguese series [16]. A 42% sensitivity, resulting from the 21 false-negative results, may be attributed to the 16 histologically classified IIA cases as they are impossible to categorize by MRI. This results from the difficulty in differentiating cervical secretions from a superficial lesion, because both have the same signal intensity on T2 images. Contrast could have a role in this chapter, producing mucosa enhancement, but this point still has some pitfalls.

Lymph node invasion analysis showed the poorer results of our series as MRI only diagnosed two of 12 cases of ganglionar infiltration. This may be explained by the presence of micrometastases, only histologically detected, as MRI suspicion of lymph node invasion is based on node enlargement (> 1 cm) or central necrosis (more frequent with lymph nodes larger than 2 cm). Nevertheless, it is important to take into account that all 12 cases with histological node invasion, including the ten false-negative MRI cases, showed deep myometrial invasion on MRI. Hence, all patients had indications for lymphadenectomy, which they did.

Conclusion

Our study confirmed the high accuracy of MRI imaging in the locoregional staging of endometrial cancer. Despite the fact that MRI lymph node evaluation has shown a low sensitivity, all cases with histological ganglionar infiltration presented MRI deep myometrial invasion therefore being submitted to an adequate procedure.

Even with the limitations of the technique, MRI has proved to be a valuable contribution in the presurgical assessment of endometrial cancer.

References

[1] Barakat R.R., Park R.C., Grigsby P.W., Muss H.D., Norris H.J.: "Corpus: epithelial tumors". In: Hospins W.J., Perez C.A., Young R.C. (eds.). Principles and Practice of Gynaecologic Oncology. Philadelphia, Lippincott-Raven, 1997, 859.

[2] Pinheiro P.S., Tyczyński J.E., Bray F., Amado J., Matos E.: "Cancer incidence and mortality in Portugal". *Eur. J. Cancer,* 2003, *39,* 2507.

[3] Bonorow R.C., Morrow C.P., Creasman W.T.: "Surgical staging in endometrial cancer: clinical-pathologic findings of a prospective study". *Obstet. Gynecol.,* 1984, *63*, 825.

[4] Shepherd J.H.: "Revised FIGO staging for gynaecological cancer". *Br. J. Obstet. Gynaecol*., 1989, *96,* 889. (Erratum: *Br. J. Obstet. Gynaecol.,* 1992, *99*, 440).

[5] Larson D.M., Johnson K., Olson K.A.: "Pelvic and para-aortic lymphadenectomy for surgical staging of endometrial cancer: morbidity and mortality". *Obstet. Gynecol*., 1992, *79*, 998.

[6] Kinkel K., Kaji Y., Yu K., Segal M., Lu Y., Powell B. *et al*.: "Radiologic staging in patients with endometrial cancer: a meta-analysis". *Radiology,* 1999, *212*, 711.

[7] Hardesty L., Sumkin J., Nath M., Edwards R., Price F., Chang T., *et al*.: "Use of preoperative MR imaging in the management of endometrial carcinoma: cost analysis". *Radiology,* 2000, *215*, 45.

[8] Wiesenfeld U., Cova M., De Lazslo P., Tinelli A., Mangino F., Grimaldi E. *et al*.: "Magnetic resonance (MR) in endometrial carcinoma preoperative evaluation". *Minerva Ginecol*., 2001, *53*, 341.

[9] Manfredi R., Mirk P., Maresca G., Margariti P., Testa A., Zannoni G. et al.: "Local-regional staging of endometrial carcinoma: role of MR imaging in surgical planning". *Radiology,* 2004, *231*, 372.

[10] Hricak H., Stern J.L., Fisher M.R.: "Endometrial carcinoma staging by MR imaging". *Radiology*, 1987, *162,* 297.

[11] Ascher S.M., Reinhold C.: "Imaging of cancer of the endometrium". *Radiol. Clin. North. Am*., 2002, *40*, 563.

[12] Frei K.A., Kink K.: "Staging endometrial cancer: role of magnetic resonance imaging". *J. Magn. Reson. Imaging,* 2001, *13,* 850.

[13] Scoutt L.M., McCarthy S.M., Flynn S.D., Lange R.C., Long F., Smith R.C. *et al*.: "Clinical Stage I endometrial carcinoma: Pitfalls in preoperative assessment with MR imaging". *Radiology,* 1995, *194,* 567.

[15] Taieb S., Ceugnart L., Leblanc E., Chevalier A., Cabaret V., Querleu D.: "IRM des cancer de l'endométre: apports et limites". *Bull. Cancer,* 2002, *89,* 963.

[16] Cunha T.M., Félix A., Cabral I.: "Preoperative assessment of deep myometrial and cervical invasion in endometrial carcinoma: Comparison of magnetic resonance imaging and gross visual inspection". *Int. J. Gynecol. Cancer,* 2001, *11,* 130.

Address reprint requests to:
S. VARGAS CABRITA, M.D.
Rua dos Combatentes, 72, 3 Dto,
3030-181, Coimbra (Portugal)
e-mail: sofiacba@sapo.pt