Usefulness of MRI for evaluation of neoadjuvant chemotherapy effectiveness and preoperative staging of cervical cancer

Poster No.: C-1595
Congress: ECR 2011
Type: Scientific Paper
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Keywords: Oncology, Genital / Reproductive system female, Pelvis, MR, Chemoembolisation, Staging, Surgery, Neoplasia, Pathology
DOI: 10.1594/ecr2011/C-1595

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Purpose

Uterine cervical cancer is the third most common gynaecological malignancy after endometrial and ovarian cancers. Standard treatment for patients with locally advanced cervical cancer is chemoradiotherapy.

MRI is the imaging modality of choice for preoperative staging and follow-up in patients with cervical cancer. The purpose of this study was to investigate diagnostic capabilities of MRI for evaluation of effectiveness of neoadjuvant chemotherapy (NACT) with uterine arteries chemoembolization (UACE) and for preoperative staging of cervical cancer.

Methods and Materials

40 consecutive patients aged 25-63 y. o. with clinical stage IIB-IIIB uterine cervical cancer were included in this study approved by institutional board. Informed consent was obtained in all cases.

Treatment consisted of one courses of systemic chemotherapy and one course of bilateral UACE with gemcitabine plus lipiodol followed by hysterectomy with pelvic lymphadenectomy.

Pelvic MRI was performed before start of treatment and repeated before surgery. Maximal tumor diameter was measured and tumor response evaluated using RECIST criteria [1]. Criterion for partial response was decrease of tumor by more than 30%. If tumor decreased by less than 30% or increased by no more than 20% stabilization was reported.

International Federation of Obstetrics and Gynecology (FIGO) classification was used for preoperative MRI staging [2] (Fig. 1 on page 2). Complete replacement of hypointense cervical stroma ring with tumor nodular protrusion or low-intensity bunds extending to parametrium were considered parametrial invasion signs [3-6] (Fig. 2 on page 3). Pelvic lymph nodes measured 1 cm or more in short axis were considered enlarged [7]. Preoperative MRI findings were correlated with surgical pathologic examination.

Images for this section:
Fig. 1: FIGO classification for cervical carcinoma.

Stage I: The carcinoma is strictly confined to the cervix (extension to the corpus would be disregarded)
  IA Invasive carcinoma which can be diagnosed only by microscopy, with deepest invasion ≤5 mm and largest extension ≥7 mm
  IA1 Measured stromal invasion of ≤3.0 mm in depth and extension of ≤7.0 mm
  IA2 Measured stromal invasion of >3.0 mm and not >5.0 mm with an extension of not >7.0 mm
  IB Clinically visible lesions limited to the cervix uteri or pre-clinical cancers greater than stage IA
  IB1 Clinically visible lesion ≤4.0 cm in greatest dimension
  IB2 Clinically visible lesion >4.0 cm in greatest dimension
Stage II: Cervical carcinoma invades beyond the uterus, but not to the pelvic wall or to the lower third of the vagina
  IIA Without parametrial invasion
  IIA1 Clinically visible lesion ≤4.0 cm in greatest dimension
  IIA2 Clinically visible lesion >4 cm in greatest dimension
  IIB With obvious parametrial invasion
Stage III: The tumor extends to the pelvic wall and/or involves lower third of the vagina and/or causes hydrenephrosis or non-functioning kidney
  IIIA Tumor involves lower third of the vagina, with no extension to the pelvic wall
  IIIB Extension to the pelvic wall and/or hydrenephrosis or non-functioning kidney
Stage IV: The carcinoma has extended beyond the true pelvis or has involved (biopsy proven) the mucosa of the bladder or rectum. A bullous edema, as such, does not permit a case to be allotted to Stage IV
  IVA Spread of the growth to adjacent organs
  IVB Spread to distant organs

Fig. 1: FIGO classification for cervical carcinoma.

Fig. 2: MRI signs of parametrial invasion in two different patients with cervical cancer. (A) Complete disruption of hypointense cervical stroma on the right side with nodular tumor protrusion to the parametrium is present. Note preservation of hypointense stroma ring along the left contour of the cervix what excludes invasion. (B) In the different
patient tumor replaces cervix with low-intensity bundles extending to left parametrium. Hypointense cervical stroma ring along the right contour of the cervix is preserved on bough transversal and coronal T2W images.
Results

Oil emboli deposition in the tumor after UACE was clearly seen on CT images as zones of high density (about 150 Hounsfield units) while MRI was not able to demonstrate this (Fig. 3 on page 7).

Based on preoperative MRI data complete tumor response after NACT was observed in 7 of 40 (18%) patients. In those patients increased signal intensity zone corresponding to tumor was not visualized on T2W images any more with complete or partial recovery of hypointense cervical stroma (Fig. 4 on page 7). Deficit of cervical tissues occurred after tumor resorption in some patients (Fig. 5 on page 7). Pathomorphological examination revealed no residual tumor cells in 1 of those 7 cases, isolated cancer cells - in 5 (Figs. 4 on page 7 and 5 on page 7) and microinvasive cancer (stage IA) - in 1 (Fig. 6 on page 8).

In the remaining 33 (83%) patients residual tumor was present on preoperative MRI and was confirmed on pathology. Sensitivity, specificity and accuracy of MRI in the detection of stage IA or greater residual tumor were 97%, 100% and 98% respectively.

Partial tumor response (Fig. 7 on page 8) or tumor stabilization (Fig. 8 on page 9) were achieved in 21 and 12 patients respectively. According to pathomorphological study tumor invasion to parametrium (stage IIB) was detected in 11 of 33 (33%) patients, to pelvic wall (stage IIIB) - in 2 (6%) and to the bladder (stage IVA) - in 1 (3%). Preoperative MRI and pathomorphology findings coincided in 23 of 33 (70%) cases (Fig. 7 on page 8), MRI stage was overestimated in 6 (18%) and underestimated in 4 (12%) (Fig. 9 on page 9). Sensitivity, specificity and accuracy of MRI in the evaluation of parametrial tumor invasion were 73%, 77% and 76% respectively.

Pelvic lymph nodes metastases were confirmed on pathology in 9 of 40 (23%) patients. MRI diagnosis was true positive in 4 patients (lymph nodes measured 1.4-2.7 cm in short axis on MRI), false positive - in 3 (1.1-1.2 cm) and false negative - in 5 (5-8 mm). Sensitivity, specificity and accuracy of MRI for lymph nodes metastases detection were 44%, 90% and 85% respectively.

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**Fig. 3:** CT (A) and T2W (B) images of pelvis after UACE. Deposition of lipiodol oil in the tumor is clearly defined by CT as an area of increased density but is not appreciated on MRI.

**Fig. 4:** Sagittal T2W images before (A) and after NACT (B). There is complete regression of the tumor with restoration of signal intensity and normal structure of the cervix. Isolated dystrophic cancer cells were revealed in the cervix on pathology. Note several Nabothian cysts in the cervix.
Fig. 5: Sagittal T2W images before (A) and after NACT (B). There is complete regression of the tumor with restoration of normal structure of the anterior lip of the cervix and marked thinning of the posterior lip. Isolated dystrophic cancer cells were revealed in the cervix on pathology. Uterine leiomyomas notably decreased in size after UACE as well.

Fig. 6: Sagittal T2W images before (A) and after NACT (B). No obvious tumor was present on MRI scan after NACT (complete regression). Residual microinvasive cancer (stage IA) was revealed in the cervix on pathology however.
**Fig. 7:** T2W image before treatment (A) shows cervical cancer invading to left parametrium (stage IIB). After NACT (B) tumor size decreased by 49% (partial response). Thin rim of hypointense stroma appeared along left contour of the cervix indicating parametrial invasion regression. Tumor downstaging to IB was confirmed on pathology.

**Fig. 8:** T2W images before (A) and after NACT (B) show no tumor size change indicating stabilization.
Fig. 9. Accuracy of MRI in preoperative staging of cervical cancer treated with neoadjuvant chemotherapy with uterine arteries chemoembolization.

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Fig. 9: Accuracy of MRI in preoperative staging of cervical cancer treated with neoadjuvant chemotherapy with uterine arteries chemoembolization.
Conclusion

In patients with uterine cervix cancer treated with neoadjuvant chemotherapy with uterine arteries chemoembolization the overall tumor response rate (complete response + partial response) was 70% (28/40). In 5 of 7 complete MRI responses isolated cancer cells were revealed on pathology. Residual stage IA tumor was not detected by MRI in another 1 patient. Sensitivity, specificity and accuracy of MRI in the detection of stage IA or greater residual tumor were 97%, 100% and 98% respectively.

Sensitivity, specificity and accuracy of MRI in the detection of parametrial tumor invasion and pelvic lymph nodes metastases were 73%, 77%, 76% and 44%, 90%, 85% respectively. Sensitivity of size criterion of 1 cm in a short axis for pelvic lymph nodes metastases detection is low as smaller lymph nodes may be malignant.

MRI has a high accuracy in the preoperative staging of the cervical cancer and in the diagnosis of residual tumor after neoadjuvant chemotherapy.

References


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