Preoperative imaging of primary intra-abdominal gynaecological malignancies. Diagnostic accuracy of CT-scan and MRI. A Greek cohort study

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Summary

Objectives: To determine the radiological modalities that provide at the initial workout the most accurate information regarding the operability and the type of operation for patients with primary cervical, endometrial, and ovarian carcinomas.

Patients and Methods: The medical records of 611 patients with gynaecological cancer were reviewed. The preoperative radio-logical findings were compared with the intraoperative and pathological ones. The diagnostic accuracy of CT and MRI at various sites was evaluated for all three kinds of carcinoma in combination.

Results: MRI was more accurate than CT in determining cervical enlargement (82% vs 73%), parametrial invasion (91% vs 74%) and the only examination that could evaluate cervical tumour size as well as cervical stromal and myometrial infiltration. Regarding lymph node involvement their results were similar (86% vs 88%). Both methods were comparably accurate in evaluating ovarian tumours (82% vs 84%), ascites (82% vs 81%), omental (73% vs 77%) and mesenterial infiltration (88% vs 93%). They also proved to be highly accurate (100% vs 98%) in the evaluation of solid abdominal organs.

Conclusions: Non-enchanced MRI should only be used for the preoperative evaluation of a patient with cervical carcinoma, while CT with intravenous and per os contrast media for one with ovarian cancer. Regarding patients with endometrial cancer, no high-resolution method is required for endometrioid grade I tumours, while contrast-enchanced MRI should be employed for all other cases.

Key words: CT-scan; MRI; Preoperative evaluation; Cervical; Endometrial; Ovarian carcinoma.

Introduction

In the therapeutic workout of gynaecological malignancies, the initial evaluation of the extent of disease is essential in order to choose the best treatment modality.

The International Federation of Gynaecology and Obstetrics (FIGO) staging system [1], incorporates various parameters, but yet fails to include important others, such as tumour volume and lymph node involvement. Additionally, significant rates of inaccuracy have been reported when clinical examination, classic radiological studies (IVP, barium enema), cystoscopy and sigmoidoscopy are only used [2-5].

One must not forget that accurate staging alters the treatment choice, from radical surgery to radiotherapy or concurrent chemo-radiotherapy for cervical cancer, or changes the type of surgery from simple total abdominal hysterectomy to hysterectomy plus pelvic and/or paraaortic selective lympadenectomy for endometrial cancer.

Part of the present data, regarding operable cervical carcinoma, were presented in the 12th International Meeting of the European Society of Gynaecological Oncology (ESGO 12), 21-24 April 2001, Venice (Italy).

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Regarding ovarian carcinoma, although surgically obtained information is required for a correct staging, and additionally, advanced stage does not preclude surgical intervention, there is several information that may modify or postpone surgery, such as paraaortic lymph node involvement, parenchymatic liver metastasis, or even an overall estimation of bulky tumour that cannot be optimally removed, and therefore requires neoadjuvant chemotherapy before surgery.

Computerised tomography scan (CT) and magnetic resonance imaging (MRI) are the two newest imaging modalities that have significantly improved the accuracy of pretreatment evaluation, especially regarding the parametrial, pelvic side-wall, uterine corpus, lymph node (pelvic and paraaortic) metastasis, as well as the tumour size. Unfortunately, a number of studies have shown that considerable limitations or discrepancies still exist between the radiological findings and the intraoperative or pathological ones [6-11].

We conducted the present retrospective study to assess the accuracy of preoperative staging with CT and MRI, and their capability to determine the operability and the type of operation needed, in a large series of patients suffering from the three main intra-abdominal carcinomas (cervix, endometrium, ovary), by comparing the radiological findings with our intraoperative and pathological ones.

Patients and Methods

In this retrospective study we reviewed the records of 611 patients who were admitted and operated on at the Department of Gynaecology of Metaxa Memorial Cancer Hospital from January 1990 until December 1999 for primary carcinomas of the uterine cervix, endometrium, and ovaries. Patients who, due to the advanced stage of their disease or any other reason (i.e. refusal, other serious medical problems), had not been operated on, were excluded from this study. We also excluded patients with microinvasive carcinomas, recurrent disease, or those who had received any kind of neoadjuvant therapy. In detail we included: 189 patients with cervical cancer diagnosed from colposcopically directed or cone biopsies, 228 with endometrial cancer whose diagnosis was set from curettage, and 194 women with ovarian tumours which proved to be carcinomas postoperatively.

Regarding our methodology, we reviewed the reports of CT and MRI studies we had performed preoperatively, and compared them with our records of intraoperative findings and the reports from pathology.

All CT-scans had been performed using per os (gastrografin®: Schering; Germany) and intravenous (ultravist®: Schering; Germany) contrast media, while no contrast enhancement had been used for MRI scans.

CT scans were performed with third-generation scanners (LX, Philips, The Netherlands; 120kV, 200 mAs) until 1998, and a spiral tomographer (Tomoscan AV, Philips, The Netherlands; 120 kV, 320 mAs) afterwards. Consecutive 5-10 mm thick sections from the diaphragm to the inferior ramus of the symphysis pubis were obtained.

MRIs were performed using a 1.0 T magnet (Magnitom-impact, Siemens, Germany). Consecutive 5-10 mm thick T1-weighted images (SE, TR=480 msec, TE=15 msec) and T2-weighted ones (SE, TR=3000 msec, TE=90 msec) were obtained in both the transverse and sagittal axis, from the diaphragm to the vaginal introitus, without intrinsic gap.

No clinical information was provided to the radiologist, apart from what kind of primary carcinoma the patient was suffering from.

All possible information regarding the intra-abdominal extent of the disease was collected. In detail we looked for: cervical enlargement/tumour size, cervical stromal invasion, parametrial invasion, lymph node enlargement at various anatomic sites, depth of myometrial invasion, bladder invasion, rectal invasion, hydronephrosis, ureter dilation, superficial and/or parenchymatic liver metastasis, characteristics of adnexal tumours (solid, cystic, mixed), ascites, omental infiltration, mesenterium infiltration, large (> 2 cm) peritoneal implantations and spleen metastasis.

For each diagnostic test we calculated: its sensitivity (ability to detect disease), its specificity (ability to exclude disease), its positive predictive value (likehood of disease in a patient with a positive test result), its negative predictive value (likehood of no disease in a patient with a negative test result), and its accuracy.

Tests for statistical significance were performed using x^2 test with Yates' correction and the McNemar's test.

Results

All 611 patients had undergone preoperative CT of the whole abdomen, while MRI had also been performed in 45 cases of cervical carcinoma, 42 of endometrial carcinoma, and 34 patients with ovarian tumours.

Positive findings of the preoperative radiological evaluation of the patients with cervical cancer, as well as their intraoperative-pathological findings are shown in Table 1. Table 2 summarises the results of the patients with endometrial carcinoma, and Table 3 those of the patients with ovarian cancer. Finally, Table 4 summarises

Table 1 — Positive CT-scan, MRI, and intraoperative-pathological findings of cervical cancer patients

	CT-scan	MRI	Surgical-Pathological
Cervical enlargement	45%	56%	63%
Tumour size ²	ND	2.5 (1.2-5.1) cm	2.3 (0.9-5.2) cm
Cervical stroma invasion			
no invasion	ND	14%	19%
<1/2	ND	42%	43%
>1/2	ND	44%	38%
Parametrial invasion	28%	21%	14%
Lymphadenopathy ³ (pelvic)	26%	23%	20%
Lymphadenopathy ³ (paraaortic)	15%	9%	6%

n=189; 'maximum diameter > 4 cm (usually antero-posterior); 'median (range); 'lymph nodes > 1.5 cm; ND: not detectable.

Table 2 — Positive CT-scan, MRI, and intraoperative-pathological findings of endometrial cancer patients

	CT-scan	MRI	Surgical-Pathological
Uterine enlargement	57%	61%	65%
Myometrial invasion			
<1/2	ND	48%	62%
>1/2	27%	52%	38%
Cervical involvement	17%	10%	12%
Cervical stroma invasion	ND	8%	6%
Adnexal tumour	7%	5%	8%
Lymphadenopathy ² (pelvic)	24%	21%	19%
Lymphadenopathy ² (paraaortic)	11%	9%	6%

n=228; 'uterine corpus > 9 cm; 'lymph nodes > 1.5 cm; ND: not detectable.

Table 3 — Positive CT-scan, MRI, and intraoperative-pathological findings of ovarian cancer patients

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	CT-scan	MRI	Surgical-Pathological
Ovarian tumour (overall)	96%	89%	100%
cystic	18%	21%	12%
solid	25%	24%	25%
mixed	57%	55%	63%
Ascites	53%	53%	58%
Omental infiltration	36%	27%	43%
Peritoneal implants	16%	20%	28%
Lymphadenopathy (pelvic)	5%	3%	2%
Lymphadenopathy (paraaortic)	10%	7%	5%
Mesenterial infiltration	7%	6%	12%
Liver metastasis			
superficial	0%	22%	40%
parenchymatic	6%	6%	-
Splenic metastasis	5%	6%	6%
Hydronephrosis	5%	-	7%
Hydroureter	9%		10%

n=194; 'lymph nodes > 1.5 cm.

	CT-scan		MRI		p-value	
	Sensitivity	Accuracy	Sensitivity	Accuracy	S	À
Cervical enlargement	60	73	75	82	< 0.0001	0.002
Uterine enlargement	62	71	68	74	NS	NS
Parametrial invasion	60	74	100	91	< 0.0001	0.085
Lympadenopathy	69	88	70	86	0.041	NS
Ovarian tumour (overall)	91	84	94	82	0.066	NS
Ascites	80	81	81	82	NS	NS
Omental infiltration	69	77	66	73	NS	0.052
Peritoneal implants	57	86	60	91	NS	NS
Mesenterial infiltration	52	93	45	88	NS	NS
Liver metastasis	94	98	100	100	< 0.0001	0.002
Splenic metastasis	94	98	100	100	< 0.0001	0.002
Hydronephrosis	75	96	75	96	NS	NS
Hydroureter	75	96	75	96	NS	NS

Table 4 — Sensitivity(%) and accuracy(%) of CT-scan and MRI in tumour detection at various anatomic sites §

§: Only data and statistical comparisons of sites/organs that both CT-scan and MRI could evaluate are shown; n=121; (S): sensitivity rates; (A): accuracy rates; NS: not significant.

the sensitivity and accuracy rates of CT and MRI in detecting tumour locations at specific sites as well as their statistical significance.

In the evaluation of cervical enlargement (> 4 cm) indicating either large cervical tumour or extension of endometrial carcinoma to the uterine cervix - the sensitivity, specificity, positive predictive value (ppv), negative predictive value (npv), and accuracy of CT were respectively, 60%, 81%, 50%, 81%, 73%, while of MRI they were 75%, 92%, 88%, 90%, 82%.

Uterine corpus enlargement (> 9 cm) was quite accurately evaluated by both imaging modalities (CT-73%; MRI-74%), due mainly, to their high specificity [85%] and 88%), although they were relatively less sensitive (62% and 68%).

Regarding tumour size (for cervical cancer patients), MRI was the only radiological examination that could accurately evaluate it preoperatively. As shown in Table 1, MRI measurements were within 0.3 cm of those determined pathologically.

In the determination of cervical stromal invasion (for patients with cervical or endometrial carcinomas) as well as the depth of myometrial invasion (for patients with endometrial cancer), MRI was practically the only modality that could provide us with safe evaluations. CT was unable to determine invasion of < 1/2, and could only demonstrate a small percentage of full thickness invasion. In detail, sensitivity, specificity, ppv, npv, and accuracy of MRI imaging were 88%, 82%, 85%, 77%, 86%, respectively. In general, we must point out a trend in radiological reports to overestimate the depth of invasion.

Regarding the locoregional extent of disease (cervical or endometrial) to the parametria, MRI was again found to be more accurate than CT (although not significantly). The sensitivity, specificity, ppv, npv, and accuracy of MRI imaging were 100%, 90%, 63%, 100%, 91%, respectively, compared with 60%, 77%, 30%, 92%, 74% of CT.

Lymph node involvement in the pelvis and the paraaortic area was very satisfactorily evaluated by both MRI

and CT imaging. Node size larger than 1.5 cm was considered positive in all cases. Obviously, there was an overestimation of lymph nodes suspected of being infiltrated since in about 22-30% of the resected nodes reactive lymphadenopathy or hyperplasia was only proven to exist. Sensitivity, specificity, ppv, npv, and accuracy of the two imaging methods were 70%, 92%, 76%, 91%, 86%, respectively for MRI, and 69%, 92%, 71%, 95%, 88% for CT.

Both CT and MRI proved to be very accurate in evaluating cystic or solid adnexal tumours, as shown in Table 3. On the other hand, there was an overestimation of mixed tumours, with a corresponding underestimation of cystic tumours. These confounding results were obviously due to the surprojection of the intestine. Overall, the sensitivity of the radiological methods ranged from 67% for cystic tumours to 100% for solid, the specificity from 83-100%, the ppv from 65-100%, the npv from 71-100%, while the accuracy ranged from 82-100%.

CT and MRI were comparably sensitive, specific and accurate in the diagnosis of malignant ascites. The sensitivity was 80% and 81%, the specificity 83%, and the accuracy 81% and 82%, respectively.

Omental infiltration (for ovarian cancer patients) was preoperatively diagnosed with a sensitivity, specificity, ppv, npv, and accuracy of respectively, 69%, 86%, 86%, 66%, 77% using CT, and 66%, 82%, 78%, 65%, 73% with MRI.

The evaluation of mesenterial infiltration resulted to be inadequate by both CT and MRI. Although the accuracy of both method, was high, 93% and 88% respectively, it was due to their high specificity 99% and 92% rates, while, unfortunately, sensitivity was low 52% and 45%, respectively. Therefore, the results in the preoperative evaluation of the mesenterium cannot be considered satisfactory.

Relevant to the above findings were the results regarding the presence of peritoneal implants. High accuracy rates were found for both CT and MRI (86% and 91%, respectively) due to high specificity of both tests (100%), but yet relatively low sensitivity (57% and 60%, respectively). One point that should be emphasized is that CT detected implants ≥2 cm, while MRI was able to detect nodules 1-2 cm.

Regarding liver and splenic parenchymatic metastasis, both methods were highly sensitive (94% and 100%, respectively) and extremely accurate (98%, 100%). Nevertheless, we must not forget that there was no histological confirmation of the radiological findings in any case of liver disease and therefore our conclusions are indirectly based on the findings of splenic metastasis, where histological confirmation existed (similar structure of the two organs), and the very bad course of these patients. On the contrary, superficial liver metastases were undetectable with CT. Only MRI detected 55% of them (sensitivity), being once again highly accurate (93%) and specific (96%).

Finally, both methods proved to be very good in the diagnosis of hydronephrosis and hydroureter (although radiological findings were surgically confirmed only in patients with ovarian cancer). Sensitivity, specificity, ppv, npv, and accuracy were similar (75%, 99%, 90%, 97%, 96%, respectively).

Discussion

Accurate staging of primary gynaecological malignancies is critical for treatment planning and prognosis. Although surgery is the best first-line therapeutic approach, it is not always feasible, depending on the stage of the disease.

During the past decade, a large number of studies were published, validating the contribution of CT and MRI in the correct, non-invasive evaluation of the extent of disease. Although the majority of them included a relatively small number of patients, advantages but also limitations and/or discrepancies between radiological and surgical/pathological findings have been underlined [2-11].

In the present study we attempted to further evaluate the accuracy and clinical value of high-resolution radiological tests, and hence to propose guidelines for the initial workout of all primary intra-abdominal gynaecological malignancies.

For cervical carcinoma, we found MRI to be generally more accurate and informative compared to CT. Due to its excellent soft tissue contrast, MRI could very well distinguish cancer from the surrounding normal cervical tissue, thus give accurate evaluation of tumour size. As was shown before, MRI measurements were within 0.3 cm of those determined pathologically. Furthermore, its discrimination accuracy could help to evaluate preoperatively the depth of cervical stroma invasion and thus identify a group of patients that would require more aggressive treatment. CT on the other hand, could not to provide such information, and only indirect data could be collected from the evaluation of cervical size.

Parametrial invasion, which is decisively important for treatment planning, was significantly better evaluated with MRI than with CT (Tables 1, 4). MRI was found to be an absolutely sensitive (100%) method, highly speci-

fic (90%), and accurate (91%). In comparison CT presented lower figures, 60%, 77%, 74%, respectively. Our findings are similar to those reported in the literature and emphasize the high predictive value of MRI in determining a patient's operability [3, 9, 12, 13].

Lymphatic involvement was similarly assessed by both imaging methods, Since size criteria is used to consider lymph node metastasis (node >1.5 cm is reported positive), a radiological disease overestimation was recorded, compared to pathological findings, as expected. On the other hand, imaging techniques missed a number of cases with lymph node microinfiltration but no enlargement. Overall, the accuracy of our radiological reports for lymph node involvement was 86% for MRI versus 88% for CT, and lay within those reported internationally [3, 5, 9, 12-14].

Additionally, and although beyond the inclusion criteria of this study (inoperable patients), CT and MRI were found to be highly reliable (data not shown here) in the evaluation of bladder invasion. Both of them were 100% sensitive, 92% specific and 94% accurate. Focal loss of the perivesical fat plane, asymmetrical bladder wall thickening or nodular indentations were the common radiological findings that indicated further evaluation with cystoscopy. Relevant, although somewhat inferior were the radiological results for rectal involvement. In general, we can say that CT and MRI could safely indicate the "suspect" patients needing further evaluation (high ppv), but especially those in whom bladder or rectal invasion could be ruled out (decisively high npv), and therefore save them the discomfort and cost of performing cystoscopy or sigmoidoscopy [15].

Regarding endometrial carcinoma, our results showed that only MRI could evaluate preoperatively the depth of myometrial invasion and the possibility of cervical involvement, thus in concord to those reported internationally [2, 16-18]. These two factors together with histological type and tumour grade, which are usually known for the earlier performed curettage biopsy, as well as lymph node involvement, constitute the prognostic parameters that determine the type of operation that is required, but also the prognosis [2, 19, 20]. The practical advantage of such knowledge before surgery (since incision of the uterus intraoperatively can grossly provide this information), is that by identifying the group of patients with advanced disease who require extensive surgery, they can be referred to a tertiary oncology centre in order to undergo pelvic and/or paraaortic selective lymphadenectomy.

Our MRI results, although better than CT, were inferior to those reported by other authors because no contrast enhancement had been used in our series.

Finally, regarding cases of ovarian carcinoma, our data suggested that both CT and MRI are comparably good for the preoperative evaluation of these patients. Adnexal tumours, ascites, omental infiltration and lymph node involvement were quite satisfactorily evaluated by both CT and MRI. Unexpectedly, the statistical analysis revealed that in our series, MRI imaging of the omentum was inferior compared to CT (p = 0.052). This finding may be attributed to the respiratory artefact, which affects the

upper abdomen. On the other hand, mesenteric infiltration and peritoneal implants were relatively poorly evaluated by all imaging modalities [10, 21-25]. Both CT and MRI were comparably efficient in excluding disease (high specificity rates), but not good in detecting it (low sensitivity rates). Of course one must not disregard the fact that MRI detected smaller (1-2 cm) peritoneal implants compared to CT (≥ 2 cm), and detected superficial liver metastases as well as metastases on the hemidiaphragms while CT did not.

And last but not least, CT and MRI were decisively good in detecting parenchymatic disease in the liver and the spleen. At the above sites, radiological methods were both highly sensitive 94% and 100% respectively, specific 99% and 100%, and therefore accurate 98% and 100% and reliable in their evaluations. Despite the proximity of the figures, the statistical comparison disclosed a significant superiority of MRI over CT, which was due to the absolute (100%) sensitivity and accuracy rates of MRI. Thus finding obviously lacks of clinical importance.

The above findings of ours are in accord with the reports of other authors, and a very recent publication of the Radiological Diagnostic Oncology Group [26], and underline the comparability of CT and MRI imaging in staging ovarian carcinomas.

Although the present study is one of the largest published thus far, and the only one that combines data regarding all three kinds of gynaecological carcinomas, thus providing more spherical conclusions, we must point out some bias in that only a part of the patients had undergone both radiological studies. This bias limits the statistical significance of the comparisons performed, but yet describes the true characteristics of our cohort in a country where MRI has not been widely available within the National Health Service.

Hence, based on our findings and the review of the past decade's international literature we can propose the following guidelines: (1) for cervical cancer, since evaluation of the pelvic extent of disease is critical in order to decide the operability of a patient, lower abdomen nonenchanced MRI should always and only be performed. Chest X-ray and a sonogram of the upper abdomen should complete the evaluation in order to detect any possible extrapelvic metastasis. (2) For endometrial carcinoma, since the tumour histological type, grade and corpus uteri size are usually known from the preceding curettage, we must divide patients into two subgroups. For those with endometrioid grade I tumours and no enlargement of the uterus, no high resolution imaging is required since no deep myometrial invasion nor cervical or nodal involvement are expected in the vast majority of them [2, 19]. Thus a whole abdomen sonogram must be considered adequate. For the rest of the patients, a detailed evaluation of the pelvis is recommended. Contrastenhanced MRI of the lower abdomen should be performed since it seems to be the only method that can at the same time evaluate myometrial, cervical, and nodal involvement. Once again the upper abdominal organs should be examined by a sonogram. (3) For ovarian carcinoma, since exploratory laparotomy will almost in all

cases be carried out for both staging and therapeutic purposes, and since the imaging figures of CT and MRI for the various anatomic sites are comparable, only a CT-scan of the whole abdomen should be performed using per os and intravenous contrast media. The relevant superiority (not significant) of MRI over CT should be reserved for the follow-up of patients with doubtful CT results in order to decide whether or not a second surgical intervention or adjuvant treatment should be performed [23, 26].

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