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Imaging diagnostics in ovarian cancer: magnetic resonance imaging and a scoring system guiding choice of primary treatment

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ABSTRACT

Objective: To analyze the ability of magnetic resonance imaging (MRI) and systematic evaluation at surgery to predict optimal cytoreduction in primary advanced ovarian cancer and to develop a preoperative scoring system for cancer staging.

Study design: Preoperative MRI and standard laparotomy were performed in 99 women with either ovarian or primary peritoneal cancer. Using univariate and multivariate logistic regression analysis of a systematic description of the tumor in nine abdominal compartments obtained by MRI and during surgery plus clinical parameters, a scoring system was designed that predicted non-optimal cytoreduction.

Results: Non-optimal cytoreduction at operation was predicted by the following: (A) presence of comorbidities group 3 or 4 (ASA); (B) tumor presence in multiple numbers of different compartments, and (C) numbers of specified sites of organ involvement. The score includes: number of compartments involved (1–9 points), >1 subdiaphragmal location with presence of tumor (1 point); deep organ involvement of liver (1 point), porta hepatis (1 point), spleen (1 point), mesentery/vessel (1 point), cecum/ileocecal (1 point), rectum/vessels (1 point): ASA groups 3 and 4 (2 points). Use of the scoring system based on operative findings gave an area under the curve (AUC) of 91% (85–98%) for patients in whom optimal cytoreduction could not be achieved. The score AUC obtained by MRI was 84% (76–92%), and 43% of non-optimal cytoreduction patients were identified, with only 8% of potentially operable patients being falsely evaluated as suitable for non-optimal cytoreduction at the most optimal cut-off value. Tumor in individual locations did not predict operability.

Conclusion: This systematic scoring system based on operative findings and MRI may predict non-optimal cytoreduction. MRI is able to assess ovarian cancer with peritoneal carcinomatosis with satisfactory concordance with laparotomic findings. This scoring system could be useful as a clinical guideline and should be evaluated and developed further in larger studies.

Introduction

Optimal primary cytoreductive surgery is considered standard treatment of advanced ovarian cancer (OC) [3–5]. Complete resection of all macroscopic disease by primary debulking has been shown to be the single most important independent prognostic factor in the treatment of advanced OC [3,5,6]. However, studies show that primary neoadjuvant chemotherapy combined with interval debulking is not inferior to optimal primary cytoreductive surgery in patients with stage III C or IV OC [3,4,7]. It is important to select those patients who may benefit from primary neoadjuvant chemotherapy.

Perioperative scoring systems have been used for a variety of diagnostic and prognostic purposes, e.g. to determine the quantity

Abbreviations: ASA, American Society of Anesthesiologists. Referring to the co-morbidities scoring index; AUC, area under curve; BMI, body mass index (BMI); Ca125, cancer antigen 125; CT, computed tomography; DWI, diffusion-weighted imaging; FDG-Pet, fluordeoxyglucose-positron emissions topography; LHRs, likelihood ratio; MRI, magnetic resonance imaging; NPV, negative predictive value; OC, ovarian cancer; ORs, odds ratios; PCI, peritoneal cancer index; PPC, primary peritoneal cancer; PPV, positive predictive value.

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and location of peritoneal dissemination [8,9] and to guide optimal primary cytoreductive surgery during colon surgery. The most commonly used prognostic indicator is the peritoneal cancer index (PCI) developed by Sugarbaker [8]. The PCI is based on a comprehensive evaluation of tumor presence (score 1) and tumor size (scores 1–3) in nine abdominal compartments, and is effective for prediction of optimal primary cytoreductive surgery in patients with gastrointestinal cancer, but has not yet been evaluated in OC [10–12]. Whether optimal primary cytoreductive surgery may be performed depends on the tumor load and the localization of metastases.

Imaging diagnostics like CT, FDG-pet/CT and MRI [20–27] provide an architectural drawing that help the surgeon perform optimal primary cytoreductive surgery. The diagnostic efficiency of ultrasound, MRI and CT for prediction of optimal primary cytoreductive surgery and OC stage has been evaluated in a limited number of studies [14–19]. Nevertheless, standard imaging diagnostics have been unable to identify patients in whom adequate debulking is not feasible and who should therefore be offered neoadjuvant therapy [13]. A simplified scoring system applicable to both preoperative MRI and surgical evaluation based on Sugarbaker's PCI [8,28] would be a useful clinical tool in allocating OC patients to either primary surgery or primary neoadjuvant chemotherapy.

The aim of this study was to evaluate the efficacy of MRI for preoperatively predicting the possibility of achieving radical surgery (i.e. no visible tumor left in the abdominal cavity). If radical surgery is not obtainable the woman avoids an unnecessary laparotomy and can be admitted directly to neoadjuvant chemotherapy and interval debulging.

Next, to design a simplified preoperative *scoring system* to stage OC based on Sugerbaker's PCI allocating women to the most optimal form of therapy (either optimal primary cytoreductive surgery or primary neoadjuvant chemotherapy).

Materials and methods

Patients

Ninety-nine women with OC were prospectively included from June 1, 2010 to December 1, 2011. The inclusion criteria were patients with OC verified by biopsy and histology selected for primary radical surgery. We included all FIGO stages originally with the purpose of evaluating the lymph nodes and their resectability. The early stages were not evaluated concerning possible carcinosis (Table 1). The inclusion and exclusion criteria are shown in a flow chart (Fig. 1).

The data and variables on patient characteristics were retrieved from electronic patient records, pathology results, paper files and anesthesiology recordings.

Systematic description of operative tumor presence

All data were retrieved and recorded by SK in a standard form, with systematic interpretation of tumor presence at the 36 specific sites. The 36 sites were divided into nine regions.

Scoring system design

Two transverse and two sagittal planes divide the abdomen into nine regions (compartments). Each quadrant is defined by both surface landmarks and the anatomical structures found in each compartment. The upper transverse plane is located at the lowest aspect of the costal margin, and the lower plane is placed at the anterior superior iliac spine. As opposed to the PCI lesion size score, we simply identified the tumor as present or not present at specific sites in each of the nine compartments, including deep organ involvement, as outlined in Fig. 2. The design of the final scoring system shown on the left side of Fig. 2 is explained in the Results Section.

In a few cases, the surgical data allowed no precise interpretation of the different co-variables. In these cases, an experienced surgeon (JB) reviewed the individual case, and the pathology data were used to determine the degree of tumor affliction of the uterus, the ovaries, the lymph nodes and the omentum.

Information regarding pelvic lymph nodes was omitted from the scoring system due to lack of surgical notes as they were routinely removed and therefore not commented upon.

Imaging protocol

The bladder was emptied pre-imaging, and 1 mg of Glucagen® was administered intramuscularly to reduce artifacts due to bowel movement. T2-weighted sequences (5 mm) in the axial and sagittal planes and T1 gradient and T1 gradient FATSAT (fat saturation) (6 mm) sequences in the axial plane were used to scan the small pelvis. The abdomen was scanned with T2-weighted sequences (8 mm) in the axial and sagittal planes. Owing to high tissue contrast, the anatomical structures and prospective pathology are best visualized with T2-weighted sequences. Both of the T1-weighted sequences were used to detect prospective occurrence of blood (e.g. endometrioma) or fat (e.g. teratoma) in the ovarian tumor.

An experienced specialist in gynecologic MRI (EM) reviewed all images. The standard form gave a systematic evaluation of tumor presence in the nine compartments and at 36 sites (Fig. 2).

Surgical procedures

All patients in both studies underwent standard longitudinal laparotomy, and surgical staging according to standard guidelines was performed. Maximal radical surgery (achievement of residual disease $\leq$1 cm in diameter) was intended in all patients. Radical surgery consisted of total abdominal hysterectomy, bilateral salpingo-oophorectomy, total omentectomy, appendectomy, multiple biopsies, radical pelvic and paraaortal lymphadenectomy, and additional surgery if so required (diaphragm stripping; abdominopelvic peritoneal stripping; bladder, liver and pancreatic resection; and splenectomy). In cases in which optimal cytoreduction was not attainable, as assessed at primary laparotomy, the patients were referred to neoadjuvant chemotherapy.

Statistical methods

Data were entered into a standard form and database and were processed in STATA (StataCorp LP, release 12) and all calculations performed by a trained statistician (MD).

We calculated the diagnostic efficiency of MRI for tumor diagnosis in each abdominal location, with findings at surgery as the reference standard. Moreover, we evaluated each finding at each site at surgery and at MRI to assess incomplete cytoreduction. Diagnostic test performances were analyzed in terms of sensitivity, specificity, positive predictive value (PPV), negative predictive values (NPV) and likelihood ratios (LHRs). We created a scoring system based on the diagnostic efficiency of the ASA group, surgical parameters and MRI that could be used to predict optimal cytoreduction. Stepwise logistic regression was performed with three variables in the model.

Area under the curve (AUC) analyses were performed for the compartments involved and for the score model. Sensitivity, specificity and LHRs of optimal cut-off points for scores for

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