GYNECOLOGY

Perioperative morbidity and rate of upstaging after laparoscopic staging for patients with locally advanced cervical cancer: results of a prospective randomized trial

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OBJECTIVE: The International Federation of Gynecology and Obstetrics (FIGO) staging for cervical cancer is based on clinical examination. Previous studies have demonstrated significant upstaging with surgical staging. However, no randomized trial has ever shown a survival benefit when radiation combined with chemoradiation (RCTX) is modified according to surgical staging. The objective of the study was to evaluate the feasibility and outcomes of surgical staging prior to radical RCTX treatment among patients with locally advanced cervical cancer in the setting of a larger, prospective, randomized study (the Uterus-11 study of the German Gynecologic Oncology Group).

STUDY DESIGN: Between 2009 and 2013, 255 patients with advanced cervical cancer (FIGO IIB-IVA) were randomized to surgical staging and RCTX (arm A) or RCTX (arm B). RCTX in both arms included pelvic external beam radiotherapy with weekly cisplatin at 40 mg/m^2 and brachytherapy. Extended-field radiation was performed in cases of confirmed paraaortic metastases.

RESULTS: One hundred thirty patients were randomized to surgical staging; 121 were eligible for this analysis. The mean patient age was 47.2 years, and the mean body mass index was 26.2 kg/m^2; the FIGO stages were IIB, IIIA, IIIB, and IVA in 85 (70.2%), 4 (3.3%), 29 (24%), and 3 (2.5%) patients, respectively. Arm A and arm B were similar with respect to Karnofsky performance status, histology, comorbidities, and lymphovascular space involvement. The surgical approach was transperitoneal laparoscopy in nearly all patients (93.4%), with no operative mortality. One patient (0.8%) had a conversion to laparotomy; 2 patients had more than 500 mL blood loss; the early postoperative complication rate was 7.3%. A mean of 19 pelvic and 17 paraaortic nodes were removed, with means of 2.4 and 1.3 positive nodes, respectively. RCTX began between 7 and 21 days after surgery. Operative staging led to upstaging in 40 of 121 (33%).

CONCLUSION: Surgical staging in patients with locally advanced cervical cancer is safe and does not delay primary RCTX in a randomized study.

Key words: laparoscopic staging, locally advanced cervical cancer, operative morbidity, randomized trial

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Primary radiation combined with chemotherapy (RCTX) has become the standard treatment for patients with locally advanced cervical cancer.[1] Patients with cervical tumors greater than 4 cm in diameter have an increased risk of lymph node metastases at the time of presentation, which have a significant prognostic impact. However, the most recent International Federation of Gynecology and Obstetrics (FIGO) statement reinforced the exclusive use of clinical staging in patients with cervical cancer.[2] Although their sensitivity and specificity are rather disappointing,

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computed tomography (CT) and magnetic resonance imaging (MRI) are often performed as part of clinical staging.[3-5] Furthermore, positron emission tomography (PET)-CT has failed to meet prior expectations because of its relatively high false-negative rates.[6-11]

An alternative to clinical staging is surgical staging, which can evaluate the most important prognostic and therapeutic factors, including lymph node status, adjacent organ involvement, and intraabdominal tumor dissemination.[12,13] The preferred approaches for surgical staging are laparoscopic or robotic transperitoneal or extraperitoneal techniques to minimize the duration of hospitalization and avoid delaying primary RCTX.[8,11,14-17]

Several retrospective studies have demonstrated a significant rate of upstaging, mainly determined by nodal or peritoneal spread, as a confirmation of more extensive disease, in a nontrivial number of patients when comparing the results of clinical standard staging with histological features after surgery.[12,13,16,18-22] However, controversy remains regarding whether adjusting the primary treatment according to the findings of surgical staging is associated with a survival benefit.[23] One randomized trial failed to demonstrate an oncological benefit for surgical staging in patients with locally advanced cervical cancer.[24] The main limitations of that study were its small sample size, its premature termination because of morbidity, and significant problems regarding the radiation technique.

The aim of this study was to evaluate the feasibility and outcomes of surgical staging prior to radical RCTX treatment among patients with locally advanced cervical cancer in the setting of a larger prospective randomized study (the Uterus-11 study of the German Gynecologic Oncology Group [ClinicalTrials.gov, identifier NCT01049100]). The operative data from the surgical arm of this prospective randomized international multicenter study are reported in this first analysis.

Materials and Methods

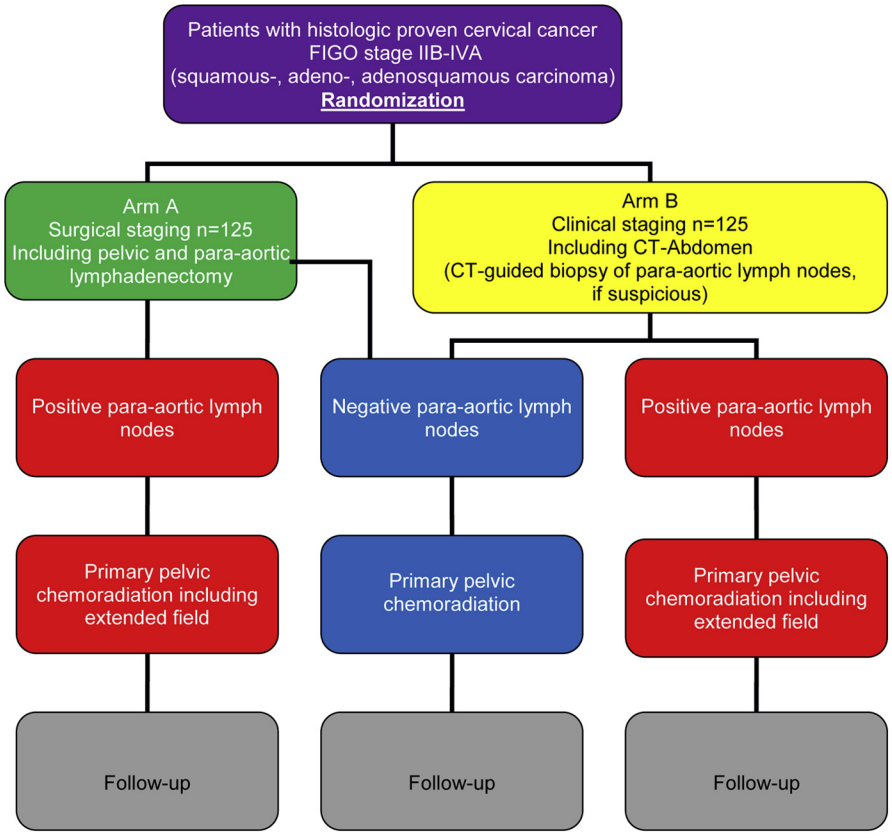
Both informed consent and ethics committee approval for studies on patients, patient records, or volunteers were obtained before the study started (institutional review board approval EA4/148/05, June 28, 2008). Between 2009 and 2013, 255 patients were included. Histological reports confirmed the presence of squamous cell carcinoma, adenocarcinoma, or adenosquamous cervical cancer. The FIGO stage ranged from IIB to IVA. All of the patients underwent a general clinical and gynecological examination. Pretreatment imaging included a whole abdominal CT and/or an abdominal MRI and/or PET-CT as well as chest imaging.

Eligible patients were randomly assigned to either the experimental arm, which incorporated surgical staging (arm A), or to traditional clinical staging (arm B). Patients in arm A underwent surgical staging with a transperitoneal laparoscopic, extraperitoneal laparoscopic, or open transperitoneal approach, followed by primary RCTX. For patients in arm B with suspicious paraaortic lymph nodes, a CT-guided biopsy was performed prior to primary RCTX (Figure 1).

Primary RCTX in both arms consisted of the following 3 steps: (1) external beam radiotherapy to the pelvis; (2) brachytherapy; and (3) concurrent chemotherapy with cisplatin 40 mg/m^2 weekly for 5 cycles. Carboplatinum was substituted for cisplatin in patients with contraindications to the use of cisplatin.

Surgical staging always started with a careful inspection of the abdominal cavity. Biopsies were taken from any suspicious areas and sent for frozen section. If peritoneal spread or a positive supraclavicular lymph node was confirmed, the retroperitoneal lymph node dissection was abandoned, and the patient was referred for palliative chemotherapy.

FIGURE 1
Flowchart design of the Uterus-11 study



CT, computed tomography; *FIGO*, International Federation of Gynecology and Obstetrics.

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