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ORIGINAL ARTICLE

Clinical staging and histopathological findings after radical hysterectomy in FIGO stage IIB cervical cancer

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Summary

Purpose: *Advanced cervical cancer still represents a major health care challenge in the developing world. According to standard protocols the treatment of choice for stage IIB cervical cancer is cisplatin-based chemoradiotherapy. However, in some European countries, and especially in Japan, patients with stage IIB cervical cancer are generally treated with radical hysterectomy as initial treatment. The aim of this study was to compare clinical stage with pathological findings, and also to correlate any relationship between parametrial infiltration and nodal status.*

Patients and methods: *From 1997 to 2006, 26 patients with FIGO stage IIB cervical cancer were radically operated (Piver class III operation). Preoperative clinical findings were compared with the pathological findings of the surgical material. The correlation between infiltration of the parametria and lymph node status was also examined. Fisher's exact test was used to examine statistical significance.*

Results: *The patients' median age was 48.3 years (range 36-61). The median number of removed lymph nodes was 16 (range 8-40). The histopathological types of cervical tumors were: squamous cell carcinoma 80%, adenosquamous carcinoma 15% and adenocarcinoma 5%. In 50% of the patients the parametria were infiltrated, suggesting that 50% of the patients were clinically overstaged. Positive lymph nodes were found in 69% of patients with positive parametria and 15% in patients with negative parametria ($p < 0.05$). Patients with positive lymph nodes received adjuvant chemoradiotherapy.*

Conclusion: *Adequate preoperative staging such as clinical examination under anesthesia or nuclear magnetic resonance could help to exclude parametrial involvement in equivocal cases. Parametrial invasion presents an important risk factor for lymph nodes metastases.*

Key words: cervical cancer, clinical stage, nodal disease, parametrial invasion, pathological stage, stage IIB

Introduction

Invasive cervical cancer is the second commonest malignancy in women, with estimated 471,000 new cases diagnosed per year of which 80% occur in the developing countries [1,2]. The decision about treatment depends on the performance status, co-morbidity and general condition of patients, but a most important factor is the clinical stage of disease. Clinical staging is usually performed by a gynecologic oncologist together with a radiotherapist. Locoregional spread and parametrial involvement are crucial in decision-making [3]. Advanced cervical cancer still represents a major health care challenge in the developing world. According to standard protocols the treatment of choice for stage IIB cervical cancer is concurrent cisplatin-based chemoradiotherapy with brachytherapy [4-6].

The most important prognostic factors in cervical cancer are tumor subtype, grade, vascular invasion, pattern and depth of invasion when used individually or as a part of a scoring system [7]. All these factors are histopathological but most of them are not included in the clinical staging of cervical cancer except stage I disease.

Parametrial involvement is another important prognostic factor for cervical cancer and preoperative evalu-

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ation of the parametria is very important. According to recent studies approximately 21-55% of patients with clinical stage IIB have in fact histologically confirmed parametrial invasion [8-10].

The main goal of the present study was to compare clinical stage and operative pathological findings and to see for any relationship between infiltration of the parametria and lymph node involvement.

Fatients and methods

From 1997 to 2006 26 patients with clinical FIGO stage IIB cervical cancer were radically operated.

Cervical cancer was biopsy-confirmed before the operation. All patients were examined by the Oncologic Board for Gynecologic Tumors and after clinical staging they were hospitalized and operated with radical Piver class III operation by a gynecologic oncologist. The surgical material was examined by two pathologists.

The main goal was to compare clinical FIGO stage IIB with histological findings. Correlation between infiltration of the parametria and lymph nodes status was also examined. Patients with lymph node metastases were planned to receive chemoradiotherapy (external beam radiation 45-50 Gy, 180-200 cGy daily fractions, plus cisplatin 40 mg/m^2 weekly during radiotherapy).

Fisher's exact test was used to examine any statistical relation between two categorical variables (with two levels).

Results

The patients' average age was 48.3 years (range 36-61). The final histological types of cervical cancer were: 21 (80%) squamous cell carcinoma, 3 (15%) adenosquamous carcinoma and 2 (5%) adenocarcinoma (Figure 1).

The average number of the removed pelvic lymph nodes was 16 (range 8-40).

Parametrial infiltration was pathologically confirmed in 13 (50%) patients while in the rest of them the parametria were disease-free, indicating a high false positive rate of clinical staging assessment.

Two (15%) patients without parametrial involvement were found to harbor lymph node metastases (Figure 2).

In 9 (69%) patients with positive parametrial involvement nodal metastases were also found (Figure 3). Positive nodal disease was significantly higher in patients with parametrial infiltration ($p<0.05$).

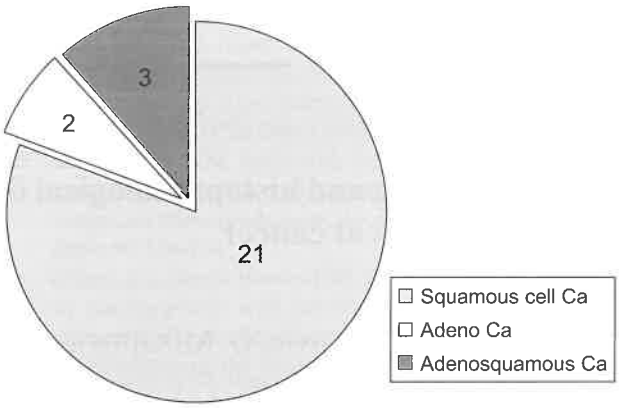


Figure 1. Histopathological subtypes of cervical cancer (number of patients).

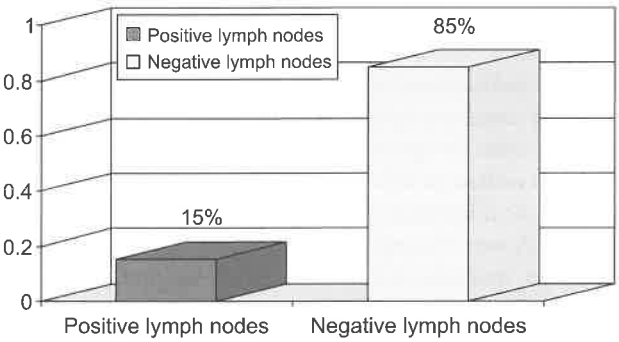


Figure 2. Lymph node status in patients with negative parametrial involvement.

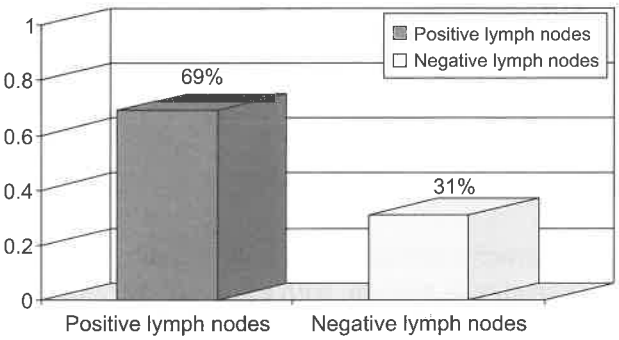


Figure 3. Lymph node status in patients with positive parametrial involvement.

Discussion

Histological identification of parametrial invasion in surgically treated cervical cancer patients is of great importance. Parametrial involvement is a poor prognostic factor in early-stage cervical cancer, regardless of lymph node status [11]. In surgically treated stage II carcinomas, the extent of parametrial involvement is

an important prognostic indicator [12,13]. According to recent studies clinical examination of the parametria has some limitations. About 1/3-1/2 of patients are overstaged [8-10,14]. This clinical and pathological discrepancy is most likely caused by the difficulty in discriminating parametrial invasion from inflammatory changes, endometriosis, adhesions, irregular shape of bulky cervix, etc [4].

Meticulous bilateral examination of the parametria is crucial. In some studies it was not mentioned whether the clinical staging for parametrial evaluation was carried out under anesthesia or not [8,9,15]. Our clinical examination was not carried out under anesthesia.

Kamura et al. performed examination under anesthesia in 82 patients who were operated with FIGO IIB cervical cancer; parametrial infiltration was identified in 42% of them [10].

Magnetic resonance imaging (MRI) can improve the accuracy of parametrial involvement. In some studies the accuracy of MRI was 84-89% [16,17]. The sensitivity of MRI in the diagnosis of parametrial infiltration ranges greatly (46-100%) with specificity ranging from 75 to 96% [18,19].

Postema et al. made a direct comparison between MRI and clinical pelvic examination as a preparative test. The pelvic examination resulted in correct treatment decisions in 89% of the patients. However, the sensitivity for extracervical spread was only 44%. MRI was better at identifying extracervical tumor spread. Still, MRI showed more false positive results and correct treatment decisions were made in 69-84% of the patients. MRI did not bring an improvement but it was better in diagnosing parametrial infiltration, but at the cost of more false positive results [20].

Diagnosis of parametrial infiltration with MRI is not so easy because rich vascularity of the parametrial tissues, peritumoral oedema, inflammatory reactions, endometriosis and some other pelvic tumors can discredit the accuracy of MRI [19].

Nevertheless, in some studies MRI has shown good positive predictive value in the assessment of proximal tumor extension beyond the internal cervical os into the body of the uterus, which is a more important factor for the decision of performing a radical trachelectomy as fertility-sparing operation in young patients with FIGO stage IA2-IB1 cervical carcinoma. Despite the small number of patients in these studies Peppercorn et al. showed that MRI can be used as preoperative diagnostic tool in the evaluation of the spread of early stage cervical cancer beyond the internal os into the body of the uterus which is not included in FIGO staging but it is an important factor to decide performing or not radical trachelectomy [21].

Parametrial involvement is very important as a prognostic factor [13,22,23]. Also infiltration of parametrial tissues correlates with increasing rates of metastasis to the lymph nodes which is one of the most important independent prognostic factors for overall survival, disease free interval, and local recurrence [7, 9,24].

Finally, the main problem in patients diagnosed as clinical FIGO stage IIB is that 35-50% are overstaged, leading thus to erroneous therapeutic decisions.

These data arise a new question, i.e. whether such patients should be operated immediately or a more thorough staging should precede the operation.

Postoperative radiotherapy is usually performed as adjuvant therapy in patients with stage IIB cervical cancer with adverse pathological prognostic factors (parametrial involvement, positive pelvic nodes or positive surgical margins, deep stromal invasion, lymphovascular space involvement) [7-10,13-15].

In Kamura et al. study 72% of patients with stage IIB cervical cancer received adjuvant postoperative radiation therapy [10].

In 2004, the Japanese Patterns of Care Working group presented a study with results obtained from 73 institutions in Japan where only 33% of patients with stage IIB cervical cancer received postoperative radiation therapy [25].

In many centers clinical stage IIB cervical carcinoma is initially treated with radical radiotherapy which gives results similar to surgical treatment concerning overall survival, but postirradiation complications may deteriorate the quality of life, and posttreatment evaluation of these patients is very difficult.

Suprasert et al. have recently reported survival data in patients radically operated with clinical FIGO IIB stage, parametrial involvement and nodal disease [26].

In a French cooperative study from 1970 to 1993 29% of stage IIB patients were treated with radiotherapy alone. In this group of patients the 5-year survival rate was 71% [27]. Yamashita et al. registered a 5-year overall survival rate of 83.5% in 21 stage IIB patients who where treated with external beam radiotherapy and high-dose rate intracavitary brachytherapy [28].

According to these results it is questionable whether to do or not radical operation in patients diagnosed with FIGO stage IIB because of no clear improvement in survival. On the other hand, the posttreatment complications increased among patients who received adjuvant radiotherapy following radical operation.

Meticulous preoperative assessment using clinical and imaging diagnostic tools will assist to choose the best treatment modality because in cervical cancer there exist more than one options with similar out-

comes. Inaccurate preoperative staging and overtreatment could lead to poor outcomes and increase of posttreatment complications which will endanger a patient's posttreatment recovery and quality of life.

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