RESEARCH COMMUNICATION

Values of Three Different Preoperative Regimens in Comprehensive Treatment For Young Patients with Stage Ib2 Cervical Cancer

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Abstract

Objective: To compare the clinical efficacy of concurrent chemoradiotherapy, neoadjuvant chemotherapy, and intracavity brachytherapy in comprehensive treatment for young patients with stage Ib2 cervical cancer. Methods: One hundred and twelve young patients with stage Ib2 cervical cancer were enrolled retrospectively in our hospital from January 2003 to June 2005. They were categorized into three groups according to preoperative regimens, including the concurrent chemoradiotherapy group (Group 1, n=38), the neoadjuvant chemotherapy (Group 2, n=49), and the intracavity brachytherapy group (Group 3, n=25). Radical hysterectomy was performed following these regimens. Chemotherapy and radiotherapy were given according to pelvic lymph node metastasis, deep cervical stromal invasion, intravascular cancer emboli, histological grading, vaginal stump and positive surgical margin. Results: The cancer disappearance and superficial muscle invasion rates were statistically significantly better in the concurrent chemoradiotherapy group than in the other two groups (P<0.01). No statistically significant difference was noted in the deep muscle invasion rate, surgical time and intraoperative blood loss among three groups, but significantly more postoperative complications occurred in the concurrent chemoradiotherapy group. The 2-year pelvic recurrence was statistically significantly lower in the concurrent chemoradiotherapy group compared to other two groups, while the 5-year survival was higher. Conclusion: Concurrent chemoradiotherapy is efficacious for young patients with stage Ib2 cervical cancer.

Keywords: Concurrent chemoradiotherapy - neoajuvant chemotherapy - brachytherapy - stage Ib2 cervical cancer

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Introduction

Cervical cancer tends to occur at an early age. Treatment for cervical cancer includes surgery, chemotherapy, radiotherapy or their combination. The 2-year survival of early cervical cancer after surgery or chemoradiothearpy reaches over 80%. Stage Ib2 cervical cancer, however, is a high-risk early stage cervical cancer with easy recurrence and metastasis. Its 5-year survival is as low as about 50%. Thus how to increase survival and decreases mortality of stage Ib2 cervical cancer is a hot spot in genealogical cancer research.

Materials and Methods

General data

One hundred and twelve young patients below 35 years with stage Ib2 cervical cancer were enrolled retrospectively in our hospital from January, 2003 to June, 2005. They ranged in age from 20 to 35 years with a median age of 32 years. The cases of cervical cancer were all confirmed as invasive cancer by our Department of Pathology, including 87 cases of squamous cell carcinoma, eighteen cases of adenocarcinoma, 6 cases of adenosquamous carcinoma, and one case of small cell carcinoma.

Treatment

The patients were categorized into three groups according to preoperative regimens, including the concurrent chemoradiotherapy group (Group 1, n=38), the neoadjuvant chemotherapy (Group 2, n=45), and the intracavity brachytherapy group (Group 3, n=29). In Group 1, the patients received chemotherapy after preoperative examination identified no contraindications. All patients in group 1 received the cisplatin, vinblastine, and bleomycin (PVB) regimen. At 2d after chemotherapy, the patients were given 2-4 insertions of intracavitary brachytherapy, 7.5GY/week. After 1-week local radiotherapy, the patients underwent surgical procedure. In Group 2, the patients only received chemotherapy with PVB regimen prior to surgical procedur. In Group 3, the patients were given 2-4 insertions of intracavitary brachytherapy, 7.5GY/week prior to the surgical procedure. Surgical procedure included resection of extensive whole uterus, bilateral

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uterine appendages (bilateral ovaries were retained in 90 patients) as well as pelvic lymph nodes. Biopsies of bilateral ovaries from 90 cases were collected for rapid pathology examination and confirmed to be normal, and these bilateral ovaries marked by silver clip were translocated to bilateral paracolic gutters. The patients with pelvic lymph node metastasis, deep cervical stromal invasion, positive vaginal stump, or positive surgical margin were given external beam radiotherapy 45GY-50GY, and even intracavitary brachytherapy (only for those with positive surgical margin). The patients with intravascular cancer emboli were given 2-4 cycles of original chemotherapy regimen at 7-10d postoperatively.

Statistical analysis

SPSS 13.0 was applied for statistical analyses. Analysis of variance was used for group comparison. A statistically significant difference was considered if P was <0.05.

Results

The proportion of cancer cell disappearance and that of superficial muscle invasion were statistically significantly better in Group 1 than other two groups (P<0.01). No statistically significant difference was noted in the deep muscle invasion rate (Table 1).

No statistically significant differences were noted in surgical time and intraoperative blood loss among three groups, but there were significantly more postoperative complications in Group 1 (Table 2).

The 2-year pelvic recurrence was statistically significantly lower in Group 1 compared to other two groups, while the 5-year survival was statistically significantly higher than the other groups. However, no statistically significant differences were observed between Groups 2 and 3 (Table 3).

Table 1. Postoperative Pathology of Three Groups

Group	Pathology			
	Cancer cell disappearance (%)	Superficial muscle invasion (%)	Deep muscle invasion (%)	Total
1	12[ab] (31.6 %)	14[ab] (36.8 %)	12 (31.5 %)	38
2	8 (17.8 %)	20 (44.4%)	17[c] (37.8%)	45
3	7 (24.1%)	14 (48.2 %)	8 (27.5 %)	29

[a]P<0.05 Vs. Group 2;[b]P<0.05 Vs. Group 3; [c]P<0.05 Vs. Group 3

Table 2. Surgical Time, Intraoperative Bleeding, and Postoperative Complications Between Three Groups

	Group 1	Group 2	Group 3
Surgical time (m)	223±35	254±32	241±22
Intraoperative bleeding (ml)	380±60	350±40	360±60
Postoperative complications (percent)	6 (15.8%)[ab]	5 (11.1%)	3 (10.3%)

[a]P<0.05 Vs. Group 2; [b]P<0.05 Vs. Group 3

Table 3. Pelvic Recurrence Within two Years and Five-year Survival Between Three Groups

	Group 1	Group 2	Group 3
2-year Pelvic recurrence	1 (2.6%)[ab]	3(6.7%)	2(6.9%)
Five-year survival	31(81.5%)[ab]	33(73.3%)	21(72.4%)

[a]P<0.05 Vs. Group 2; [b]P<0.05 Vs. Group 3; [c]P<0.05 Vs. Group 3

Discussion

Cervical cancer increasingly occurs in young females. The average onset age decreases from 56 years between 1955-1964 to 44 years between 1995 and 2004. The proportion of young cervical cancer patients increases from 3.4% to 24.9%. Cervical cancer can be treated by surgery, radiotherapy, chemotherapy and their combination.

Several studies show that radical surgery alone and chemoradiotherapy alone achieve equivalent outcomes in terms of the 5-year survival, mortality and complications for early cervical cancer patients (Rau et al., 2007; Darus et al., 2008). Though early cervical cancer witnesses favorable efficacy, local advanced cervical cancer is still a challenge in clinical treatment. In recent years, gynecologists in China and abroad have practiced multiple preclinical and clinical studies to investigate efficacy of combined treatment for early cervical cancer.

As molecular oncology advances, researchers realize that even early cervical cancer is systemic disease and chemotherapy as a systemic technique may be complimentary in treatment for early cervical cancer. As neoadjuvant chemotherapy achieves favorable efficacy in breast cancer, colon cancer and lung cancer, gynecologists thus consider bringing it into clinical treatment for cervical cancer. Bae J-H, Choi CH confirmed that neoadjuvant chemotherapy could decrease lymph node metastasis and local recurrence (Choi et al., 2007; Bae et al., 2008).

Compared to neoadjuvant chemotherapy, concurrent chemoradiotherapy is widely accepted as it is validated by rationale. Chemotherapy regimens are cell-cycle specific and sensitize radiotherapy in chemoradiotherapy. Complementary effects of chemotherapy and radiotherapy can kill cancer cells in different cell-cycle phases. Chemotherapy also kills anoxic cells, inhibits regeneration of cancer cells, and decreases recurrence of radiotherapy. Accumulated evidence demonstrates that concurrent chemoradiotherapy achieves better survival and decreases mortality than chemotherapy alone (Kuzuya., 2004; Ferrandina et al., 2007). Concurrent chemoradiotherapy is thus a standard regimen for medium-term and advanced cervical cance (Mariagrazia et al., 2005; Ferrandina et al., 2010). It is considered that it may be also applied for early cervical cancer (Goksedef et al., 2009). However, concurrent chemoradiotherapy is rarely compared with neoadjuvant chemotherapy in studies.

In our study, the cancer cell disappearance and superficial muscle invasion rate were statistically significantly better in the concurrent chemoradiotherapy group than other two groups, indicating that chemotherapy may be efficacious for advanced cervical cancer besides intracavity brachytherapy prior to operation. Concurrent chemoradiotherapy reducing tumor micrometastasis and tumor volume creates important chance for total hysterectomy.

No statistically significant differences were noted in the deep muscle invasion rate, surgical time and

intraoperative bleeding among three groups, but there were significantly more postoperative complications in the concurrent chemoradiotherapy group. Consistent with results from Tan et al. (2008), it is suggested that concurrent chemoradiotherapy has severe toxicities and occurrence of complications though it achieves favorable efficacy.

Several studies demonstrate that concurrent chemoradiotherapy is better than chemotherapy alone preoperatively (Eifel et al., 2004; Pearcey et al., 2007; Rose et al., 2007; Stehman et al., 2007), which is also implied in our study.

Compared to neoadjuvant chemotherapy, the pelvic recurrence within two years was statistically significantly lower in the concurrent chemoradiotherapy group, while the 5-year survival was not statistically significantly higher than the other groups, which agrees well with the findings that neoadjuvant chemotherapy achieves high short-term response but does not affect long-term survival much (Eddy et al., 2007).

The study demonstrates that concurrent chemoradiotherapy is better than neoadjuvant chemotherapy and intracavity brachytherapy in stage Ib2 cervical cancer patients. Though toxicities and other complications increase for concurrent chemoradiotherapy, it prolongs survival and decreases pelvic recurrence. There's currently lack of pervasive perspective comparative studies between these three regimens. Thus in clinical practice, gynecologists still need to perform treatments after weighing pros and cons of different regimens based on guidelines of evidence-based medicine.

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