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CME

Analysis of Cervical Cancer in Chinese Patients Treated with Chemoradiation or Radiotherapy Alone

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ABSTRACT

Aim: *A retrospective review was performed to compare chemoradiation and radiotherapy alone for the treatment of carcinoma of the cervix in a Hong Kong Chinese population.*

Patients and Methods: *208 Chinese patients with carcinoma of the cervix stage I to IVA were treated with radical intent between 1994 and 2004. 177 patients (85.1%) received radiotherapy alone and 31 patients (14.9%) received chemoradiation. Radiotherapy consisted of external beam pelvic irradiation followed by low-dose rate brachytherapy and additional parametrial irradiation. Patients in the chemoradiation group received weekly cisplatin during external irradiation.*

Results: *The median age was 65.4 years (range, 32.6 to 90.2 years). The median follow-up time was 5.0 years (range, 0.2 to 12.1 years) for patients in the radiotherapy group and 3.4 years (range, 0.5 to 6.6 years) for patients in the chemoradiation group. At 3 years, the overall survival was 74.7% for the radiotherapy group and 87.5% for the chemoradiation group (p = 0.23). The 3-year disease-free survival was 71.5% for the radiotherapy group and 77.4% for the chemoradiation group (p = 0.23). The overall 3-year actuarial late toxicity was 26.4% (4.3% grade 3 to 4) in the radiotherapy group and 15.2% (0% grade 3 to 4) in the chemoradiation group.*

Conclusions: *Due to the limited number of patients in the chemoradiation group, the survival benefit for chemoradiation for cervical cancer could not be demonstrated. Nevertheless, the treatment was well tolerated by Chinese patients and there was no increase in late toxicities.*

Key Words*: Asian continental ancestry group; Carcinoma, squamous cell; Drug therapy; Radiotherapy; Toxicity*

INTRODUCTION

Radiotherapy is a well-established treatment modality for cervical cancer. Recent randomised trials have suggested superiority for cisplatin-based concomitant chemotherapy and radiotherapy over radiotherapy alone for treating invasive cervical cancer.[1-5] Despite some negative results, 2 subsequent meta-analyses confirmed an overall benefit for concurrent chemoradiation over radiotherapy alone.[6-10] Before these meta-analyses were published, the National Cancer Institute recommended chemoradiation as a standard treatment for patients with locoregional advanced cervical cancer, based on the available data at that time.[11]

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Chemoradiation was adopted by the Department of Clinical Oncology, Pamela Youde Nethersole Eastern Hospital, Hong Kong, for the treatment of cervical cancer in 1999. A clinical audit was performed to review the outcomes for patients with cervical cancer treated from 1994 to 2004, when low-dose rate brachytherapy was used in the Department of Clinical Oncology, with specific interest in the efficacy and toxicities of chemoradiation. Therefore, a retrospective review was performed to assess the outcomes of chemoradiation compared with radiotherapy alone in a Chinese population.

PATIENTS AND METHODS

Patients

This was a retrospective study of 208 Chinese patients with squamous cell carcinoma of the cervix treated at the Pamela Youde Nethersole Eastern Hospital with radical intent between January 1994 and December 2004. All patients had performance status 0 to 1 according to the Eastern Cooperative Oncology Group criteria.

All patients underwent clinical examination, complete blood count, liver and renal function tests, and chest X-ray. Examination under anaesthesia was performed for 95% of patients. Patients treated after 1999 also had routine computed tomography (CT) of the abdomen and pelvis or magnetic resonance imaging (MRI) of the pelvis as part of the staging investigations. All patients were staged according to the International Federation of Gynaecologists and Oncologists (FIGO) staging system.[12] Patients with evidence of para-aortic lymphadenopathy or stage IVB disease were excluded from this analysis. Patients who did not receive brachytherapy were also excluded as the treatment was considered suboptimal.

The selection criteria for chemoradiation were as follows:
- age younger than 65 years
- adequate renal function
- FIGO stage IB2 to IVA.

Forty five patients received chemoradiation during the study period after 1999. After excluding patients who were not Chinese, those who had para-aortic lymph node involvement, and those who did not receive brachytherapy, only 31 patients were included in the chemoradiation group.

External Beam Radiotherapy

Patients from the radiotherapy alone group received whole pelvic irradiation (WPI) of 40 Gy in 20 fractions in 5 fractions per week for 4 weeks, and patients from the chemoradiation group received 40.8 Gy in 24 fractions in 5 fractions per week for 4.5 weeks. External beam radiotherapy (EBRT) was delivered by a 23 MV linear accelerator using anterior-posterior opposing fields before 1999; after 1999, EBRT was given via a 6 MV linear accelerator using a 4-field box technique. The upper border of the pelvic field was set at the L4/L5 junction, and the lower border was at the lower part of the obturator foramen, or 3 cm below the lowest extent of the tumour involvement, which was defined by cervical markers inserted before simulation. The lateral borders were set at 1.5 cm lateral to the widest pelvic brim. For the lateral portals, the upper and lower borders followed those of the anterior-posterior fields. The anterior and posterior borders were set at the pubic symphysis and the S2/S3 junction, respectively. After brachytherapy, all patients received additional parametrial irradiation (API) of 12 to 16 Gy in 6 to 8 fractions for 1.5 weeks. Anterior-posterior opposing fields were used and a median shield 4 cm wide was used to shield the high-dose zone of prior brachytherapy.

Brachytherapy

Low-dose rate brachytherapy was delivered by the Selectron remote-afterloading system (Nucletron, Veenendaal, The Netherlands) using Caesium-137 as a radioactive isotope. The dose at point A varied from approximately 50 cGy/hour in 1994 to 40 cGy/hour in 2004. A single insertion of intracavitary brachytherapy was given 2 to 3 weeks after WPI, with 35 Gy delivered to point A.

Chemotherapy

For the chemoradiation group, single-agent cisplatin was given at a weekly dose of 40 mg/m^2/body surface area, with the maximum dose being 70 mg. Cisplatin was given concurrently with external radiotherapy during WPI and API, and was omitted during the period of brachytherapy. A maximum of 6 cycles of chemotherapy were given, and were commenced within 2 hours of radiotherapy as far as possible. Chemotherapy was administered only if the neutrophil count was $\geq 1.8 \times 10^9$/L (normal range, 1.8-7.8 x 10^9/L) and the platelet count was $\geq 100 \times 10^9$/L (normal range, 150-450 x 10^9/L). The dose was reduced by 20% during subsequent cycles after any grade 3 to 4 myelotoxicity. Chemotherapy was stopped when there was any other grade 4 toxicity.

Statistical Analysis

For overall survival (OS), disease-free survival (DFS) and disease-specific survival (DSS), the time was calculated from the date of biopsy to the time of the event. The Statistical Package for the Social Sciences Version 12.0 was used for statistical analysis. The actuarial survival rate and actuarial complication rate were obtained using the Kaplan-Meier method and were compared between different patient groups using the Log-rank test.

RESULTS

208 patients with carcinoma of the cervix were analysed. 177 patients (85.1%) were included in the radiotherapy group and 31 patients (14.9%) were included in the chemoradiation group. The median age was 65.4 years (range, 32.6 to 90.2 years). The number of patients with FIGO stage I, II, III, and IVA disease was 35 (16.8%), 109 (52.4%), 59 (28.4%), and 5 (2.4%), respectively. The treatment groups are shown in Table 1. There were 2 patients with stage IA2 disease and 23 patients with stage IB1 disease in the radiotherapy group. One patient with clinical FIGO stage IB1 was treated with chemoradiation as parametrial involvement was noted on the MRI scan. As expected, due to the selection criteria for concurrent chemoradiation, the chemoradiation

Table 1. Patients' characteristics.

	Radiotherapy group	Chemoradiation group	p Value
Number of patients (%)	177 (85.1)	31 (14.9)	
Age (years)			
Median (range)	68.4 (32.6-90.2)	54.1 (32.6-68.3)	
Mean	65.2	52.1	<0.01*
Comorbidities (%)			
All comorbidities	80 (45.2)	6 (19.4)	<0.01†
Diabetes mellitus	33 (18.6)	3 (9.7)	
Hypertension	54 (30.5)	1 (3.2)	
Ischaemic heart disease	17 (9.6)	0 (0)	
Chronic obstructive airway disease	11 (6.2)	2 (6.5)	
Cerebrovascular accident	6 (3.4)	0 (0)	
FIGO stage (%)			
I	30 (16.9)	5 (16.1)	0.38†
II	89 (50.3)	20 (64.5)	
III	54 (30.5)	5 (16.1)	
IV	4 (2.3)	1 (3.2)	
Median follow-up (range) [years]	5.0 (0.2-12.1)	3.4 (0.5-6.6)	

* *t* test.
† Chi-squared test.

group was younger with fewer medical comorbidities than the radiotherapy group. Otherwise, there was no significant difference in stage distribution in both groups. The patients' characteristics and the median follow-up times are summarised in Table 1.

Treatment and Compliance

Fifteen of the 208 patients (7.2%) were lost to follow-up and 37 patients (17.8%) died of unrelated causes.

Three patients in the radiotherapy group required premature termination of brachytherapy after delivery of approximately 10 Gy (1 patient had exacerbation of chronic obstructive airway disease, 1 had poorly controlled diabetes, and 1 had premature withdrawal of the brachytherapy applicator). These patients received additional external radiotherapy to maintain the dose at 66 to 70 Gy to point A. The median dose to point A was 75 Gy for the radiotherapy group and 74.8 Gy for the chemoradiation group. The median overall treatment times were 48 days and 51 days for the radiotherapy and chemoradiation groups, respectively. There were no significant differences between the 2 groups for total dose delivered and overall treatment time.

In the chemoradiation group, 93.5% of patients received more than 5 cycles of chemotherapy, and 87.1% of patients received more than 80% of the full dose of chemotherapy (Table 2).

Table 2. Chemotherapy regimen received by patients in the chemoradiation group.

Chemotherapy regimen received	Number of patients (%)
Number of cycles received	
4	2 (6.5)
5	16 (51.6)
6	13 (41.9)
Total	31 (100)
Percent of full dose received	
50%	1 (3.2)
66.6%	1 (3.2)
75%	2 (6.5)
83.3%	16 (51.6)
100%	11 (35.5)
Total	31 (100)

Outcomes

The pelvic control at 3 years was 94.1% for all patients (n = 208), the DFS at 3 years was 73.8%, and the OS at 3 years was 76.5% (Figures 1 to 3). The OS by stage is shown in Figure 4.

A retrospective comparison showed no statistically significant differences in any of the endpoints. The pelvic control rate at 3 years was 93.6% for the radiotherapy group and 96.8% for the chemoradiation group (p = 0.965). The DFS at 3 years was 71.5% for the radiotherapy group and 77.4% for the chemoradiation group (p = 0.23). The DSS at 3 years was 83.5% for the radiotherapy group and 87.5% for the chemoradiation group (p = 0.98) [Figure 5]. The OS at 3 years was 74.7% for the radiotherapy group and 87.5% for the chemoradiation group (p = 0.23) [Figure 6]. The apparent superiority of chemoradiation for OS did not reach statistical significance.

Acute Toxicity

Two patients (6.5%) in the chemoradiation group had grade 3 to 4 haematological toxicity according to the Radiation Therapy Oncology Group (RTOG) criteria.

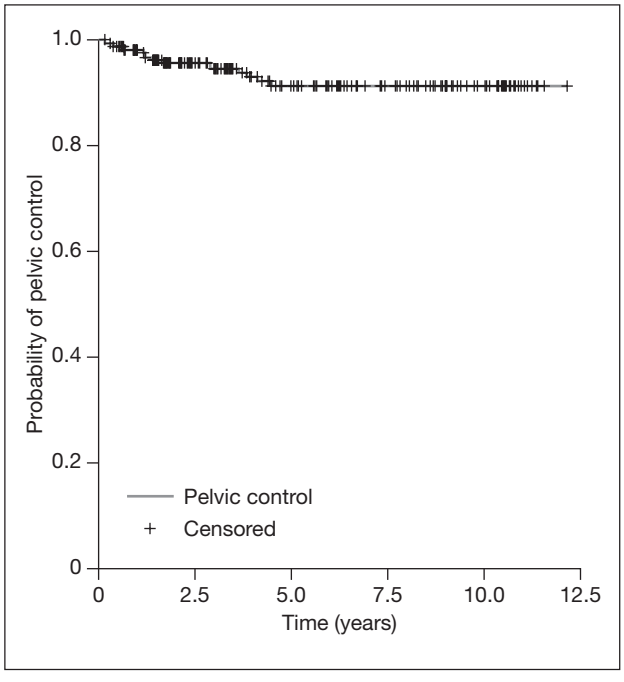

Figure 1. Pelvic control of all patients (n = 208).

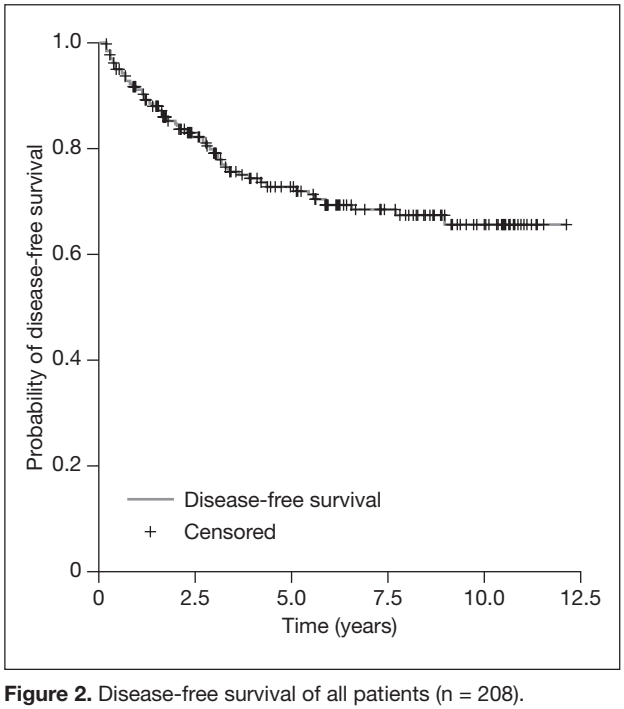

Figure 2. Disease-free survival of all patients (n = 208).

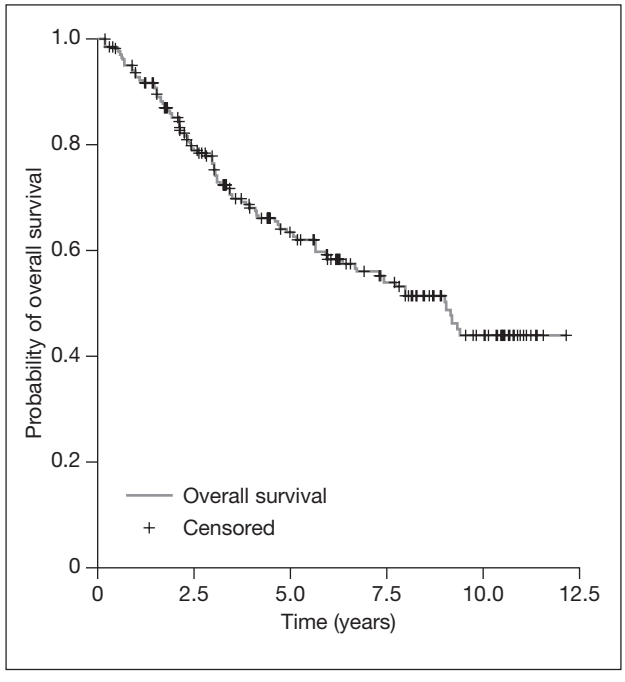

Figure 3. Overall survival of all patients (n = 208).

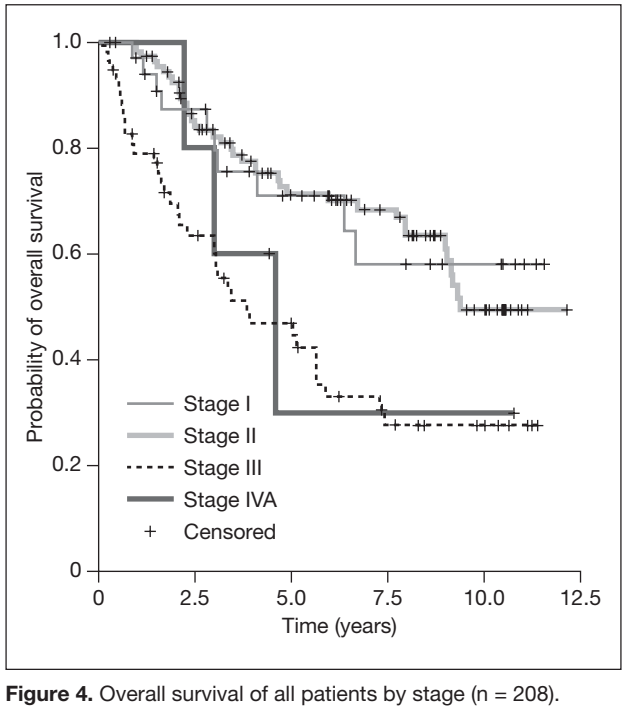

Figure 4. Overall survival of all patients by stage (n = 208).

Three patients (3.7%) experienced grade 3 to 4 renal toxicity, 1 of whom completed 4 cycles of cisplatin with dose reduction and 2 of whom completed 5 cycles with dose reduction.

Late Toxicity

Late toxicities were graded according to the RTOG toxicity criteria. The overall 3-year actuarial toxicities of proctitis, cystitis, vaginal stenosis, vaginal fistulation, and enteritis were 18.5%, 2.8%, 11.6%, 1.1%, and 1.1%, respectively.

A comparison of the late toxicities of the 2 treatment groups was performed. The overall 3-year actuarial late toxicity was 26.4% (4.3% grade 3 to 4) in the radiotherapy group and 15.2% (0% grade 3 to 4) in the chemoradiation group. The corresponding late toxicities of the chemoradiation group were 15.2%, 0%, and

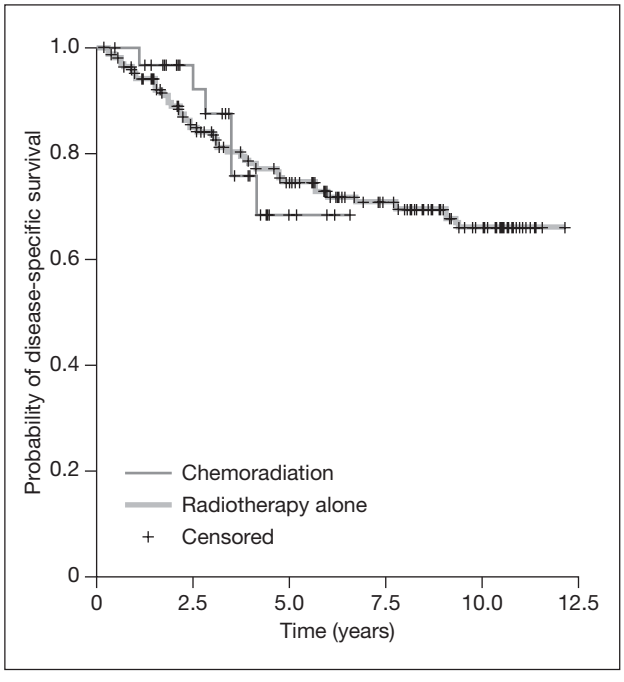

Figure 5. Disease-specific survival (radiotherapy alone versus chemoradiation).

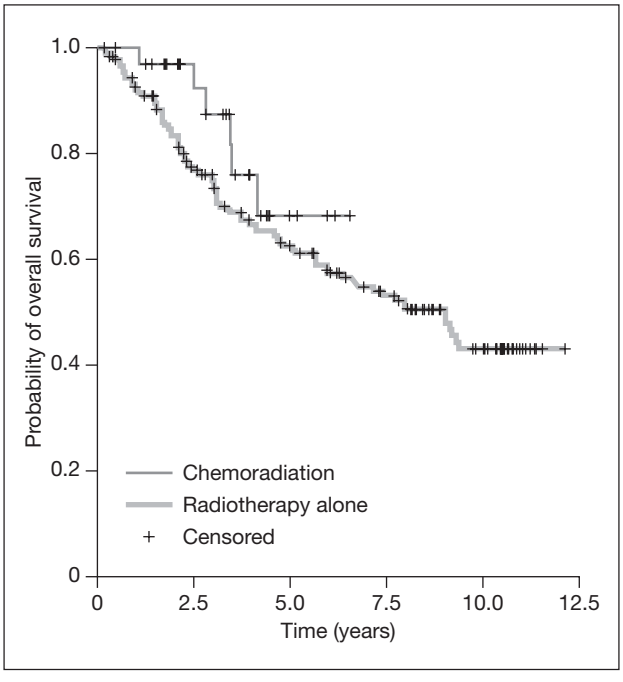

Figure 6. Overall survival (radiotherapy alone versus chemoradiation).

3.3%, respectively, for all grades, and 0% for grade 3 or above. Two patients in the radiotherapy group had grade 4 enteritis requiring bowel resection and permanent colostomy. However, the differences in the actuarial toxicities in different treatment groups did not reach statistical significance (Table 3).

DISCUSSION

Cervical cancer is the fourth commonest female cancer in Hong Kong, with an estimated incidence of 11.4 per 100,000 population in 2003, and accounts for 4.3% of all new cancer cases in women.[13] Cervical cancer is the eighth commonest cause of cancer death in Hong Kong, accounting for 2.8% of all cancer deaths in women.[13] Globally, cervical cancer is the second most common cancer in women and is most prevalent in low-income countries,[14] where the disease frequently presents at later stages. In developed countries, such as Europe and North America, the incidence and mortality of cervical cancer has decreased due to effective screening programmes.[15] In Hong Kong, women of reproductive age are opportunistically screened, resulting in a steady decrease in the incidence of cervical cancer during the past 3 decades.[13]

A major advancement in the treatment of cervical cancer is the use of concurrent chemoradiation. Various studies of concomitant chemoradiation using a variety of different chemotherapy regimens have been performed. Five large randomised trials have shown superiority for cisplatin-based concurrent chemoradiation versus radiotherapy alone.[1-5] These positive trials vary somewhat in terms of disease stage, radiation dose, chemotherapy protocol, and enrolment criteria; the true benefit for chemoradiation may require more detailed stratification of patients' risk.[16]

Whitney et al performed a randomised trial of patients with invasive carcinoma of the cervix, of whom 91%

Table 3. Late toxicity experienced by patients receiving radiotherapy or chemoradiation.

Treatment group	Actuarial toxicity at 3 years Number of patients (%)									
	Proctitis		Cystitis		Vaginal stenosis		Vaginal fistula		Enteritis	
	Total	Grade 3-4	Total	Grade 3-4	Total	Grade 3-4	Total	Grade 3-4	Total	Grade 3-4
All patients	33 (18.5)	3 (1.7)	5 (2.8)	0 (0)	21 (11.6)	0 (0)	2 (1.1)	2 (1.1)	2 (1.1)	2 (1.1)
Radiotherapy	29 (19.2)	3 (2.0)	5 (3.3)	0 (0)	20 (13.2)	0 (0)	2 (1.3)	2 (1.3)	2 (1.3)	2 (1.3)
Chemoradiation	4 (15.2)	0 (0)	0 (0)	0 (0)	1 (3.3)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)

had biopsy-proven squamous cell carcinoma (SCC), and 9% had adenosquamous or adenocarcinoma.[4] The patients had stage IIB to IVA disease, and were surgically staged by para-aortic lymph node sampling. Patients with positive para-aortic lymph nodes were excluded. 177 patients received concurrent chemoradiation with cisplatin and 5-fluorouracil (PF) and 191 patients received hydroxyurea (HU). The OS at 8.7 years was 55% for the PF group and 43% for the HU group (p = 0.018), and the relative mortality rate for the PF group compared with the HU group was 0.74 (90% confidence interval [CI], 0.58-0.95). This study showed that a platinum-containing regimen is superior to an HU-containing regimen for the treatment of cervical cancer by chemoradiation.

Rose et al conducted a randomised study to evaluate the effect of concomitant radiotherapy with 3 different chemotherapy regimens: cisplatin alone (group 1; n = 173), PF + HU (group 2; n = 177), and oral HU alone (group 3; n = 176).[2] Ninety percent of patients had SCC, ranging from stage IIB to IVA. All patients underwent surgical sampling of para-aortic lymph nodes and positive cases were excluded. The 2 groups given a cisplatin-containing regimen had a higher rate of progression-free survival (PFS) than the group receiving HU alone (p < 0.001). The OS was significantly higher in groups 1 and 2 than in group 3, with relative risks for death of 0.61 and 0.58, respectively. Treatment with cisplatin alone was less toxic than the 3-drug regimen, and therefore cisplatin was recommended as the standard drug for chemoradiation for locally advanced cervical cancer. However, in these 2 studies,[2,4] patients given HU with radiotherapy acted as a control group and there was no comparison between chemoradiation with radiotherapy alone.

There are at least 5 randomised studies comparing chemoradiation and radiotherapy alone.[1-8] Morris et al compared the effect of radiotherapy to the pelvic and para-aortic fields with that of pelvic radiation and concomitant chemotherapy with PF in 388 patients with cervical carcinoma.[1] Ninety percent of patients had SCC, ranging from bulky stage IB (≥5 cm) to IVA disease. Seventy five percent of patients underwent lymphangiography and the remaining 25% had retroperitoneal exploration to detect para-aortic lymph nodes. Patients with positive para-aortic lymph nodes were excluded. 193 and 195 patients were assigned to the radiotherapy and chemoradiation groups, respectively. The OS and DFS were 73% and 67%, respectively, in the chemoradiation group, and 58% and 40%, respectively, in the radiotherapy group (p < 0.004). However, this trial used extended field radiation as the control group rather than standard pelvic field.

A trial by Pearcey et al compared chemoradiation with weekly cisplatin (n = 127) with standard pelvic field radiotherapy (n = 126).[6] All patients had SCC, ranging from stage IB2 to IVA disease. Surgical staging was not mandatory for this study. Nevertheless, there were no significant differences in the DFS (chemoradiation, 60%; radiotherapy alone, 56%) and OS (chemoradiation, 66%; radiotherapy alone, 58%) between the groups.

Wong et al performed a randomised study of 64 patients with carcinoma of the cervix (98% SCC), ranging from FIGO clinical stage IIB to IIIB.[8] The patients were divided into 3 groups consisting of chemoradiation with weekly cisplatin; chemoradiation with twice-weekly cisplatin; and radiotherapy alone. No significant difference in long-term survival was demonstrated among the groups. This result might be attributed to the small number of patients and the suboptimal dose of cisplatin (only 25 mg/m^2 for patients receiving weekly cisplatin). Another randomised study by Wong et al demonstrated superiority of chemoradiation to radiotherapy in patients with stage IB2 to IIIB SCC.[17] The 5-year DFS was 83% versus 72% (p = 0.03) in favour of chemoradiation and the overall survival was 80% versus 68% (p=0.04) in favour of chemoradiation. However, epirubicin was used as the chemotherapeutic agent instead of cisplatin in both the concurrent and adjuvant settings. Tseng et al performed a randomised trial in a Chinese population of 122 patients with FIGO stage IB2 to IIIB SCC.[7] Sixty patients were randomised to receive chemoradiation with cisplatin, vincristine, and bleomycin, and 62 patients were randomised to receive radiotherapy alone. The 3-year actuarial survival for the chemoradiation and radiotherapy groups were 61.7% and 64.5%, respectively, with no statistically significant difference between the groups. However, late toxicity was significantly greater for the chemoradiation group.

There are 2 randomised studies of chemoradiation combined with surgery. Keys et al compared radiotherapy and chemoradiation followed by adjuvant extrafascial hysterectomy.[3] All patients had stage IB1 disease with negative pelvic lymph nodes, 81% of which were SCC. After surgical staging, patients were randomised to receive radiotherapy or chemoradiation with cisplatin followed by adjuvant hysterectomy. The 3-year survival

rates were 83% for the chemoradiation group and 74% for the radiotherapy group (p = 0.008), and the relative risk of death for the chemoradiation group compared with the radiotherapy group was 0.54. A study by Peters et al compared the effect of chemoradiation with radiotherapy in the postoperative setting.[5] Patients with clinical stage IA2 to IIA cervical cancer (79% SCC), treated initially with radical hysterectomy and pelvic lymphadenectomy, and who had positive pelvic lymph nodes, with or without positive margins and microscopic involvement of the parametrium, were randomised to receive chemoradiation with 4 cycles of PF or radiotherapy alone. The hazard ratio for OS in the radiotherapy group compared with the chemoradiation group was 1.96 (p = 0.007) and the projected OS at 4 years was 71% for radiotherapy alone and 81% for chemo-radiation. However, it should be noted that chemoradiation was not the definitive treatment in these 2 studies.

Subsequently, 2 meta-analyses have demonstrated the superiority of concurrent chemoradiation over radiotherapy alone for treating cervical carcinoma. The Cochrane Collaboration meta-analysis reviewed 24 randomised controlled trials (21 published, 3 unpublished) involving 4921 patients.[9] This analysis strongly suggested that chemoradiation improves OS and PFS, with absolute benefits of 10% and 13%, respectively. The Canadian meta-analysis reviewed 8 randomised controlled trials involving 2141 patients.[10] This analysis demonstrated a statistically significant effect in favour of cisplatin-based chemoradiation compared with radiotherapy (risk ratio, 0.74; 95%CI, 0.64 to 0.86).

A clinical audit of treatment outcome for cervical cancer between 1994 and 2004 was performed at the Pamela Youde Nethersole Eastern Hospital in 2006. The survival outcomes by stage were similar to the quoted figures (the 5-year survival rate was 80% to 90% for patients with stage IB1 disease, 50% to 80% for those with stage IIB disease, and 25% to 50% for those with stage III disease).[18,19]

Following the promising results of chemoradiation from the randomised studies, these authors performed further exploratory analyses during this audit. Patients with non-squamous histology, who did not undergo brachytherapy, and who were not of Chinese ethnicity were excluded from this study so that the characteristics of patients in the chemoradiation group would be similar to those of patients receiving radiotherapy alone, hence only 31 patients were included in the chemoradiation group.

Due to the non-randomised nature of this trial, patients in the chemoradiotherapy group were younger and had fewer comorbidities than those in the radiotherapy group. Furthermore, as CT and MRI scans were introduced as routine investigations in 1999, there was likely to be a possible staging migration effect in favour of the chemoradiation group. However, despite these favourable factors for the chemoradiotherapy group, no significant differences between the 2 groups were detected for any of the clinically relevant endpoints. The most likely explanations are that there was only a small number of patients in the chemoradiotherapy group, which greatly affected the statistical power, the inequality between the treatment groups, and the retrospective nature of the study. Nevertheless, the 3-year OS of 87.5% achieved in this study for the chemoradiation group is comparable with the international benchmark studies using weekly cisplatin 40 to 50 mg/m^2. The 3-year OS for the weekly cisplatin group was 64%, 69%, and 83% in the studies by Rose et al,[2] Pearcey et al,[6] and Keys et al,[3] respectively. The outcomes for weekly cisplatin in different studies are shown in Table 4.

Importantly, this study demonstrated that this aggressive concurrent treatment was well tolerated in a Chinese population. The grade 3/4 acute haematological toxicity in the chemoradiation group was 6.5% and the late grade 3/4 toxicity was less than 5%, which are comparable with other studies. The acute toxicities were 4%, 13%, 21%, and up to 30% in the studies by Morris et al,[1] Rose et al,[2] Keys et al,[3] and Pearcey et al,[6] respectively. The late toxicities were 11%, 16%, 20%, and up to 35% in the studies by Morris et al,[1] Keys et al,[3] Pearcey et al,[6] and Tseng et al,[7] respectively. Such a low complication rate could be partly due to the routine use of 4-field EBRT technique, and the selection of younger patients without any pretreatment comorbidities might also contribute to this favourable tolerance.

Chemoradiation has become the standard of care for the treatment of carcinoma of the cervix in developed countries. Due to the small number of patients in the chemoradiation group, the limitations of a non-randomised comparison study, and the inequality of the treatment groups, it was not possible to demonstrate a superiority of chemoradiation over radiotherapy alone in this study. Nevertheless, concomitant chemoradiation was well-tolerated among Chinese patients, and there were

Table 4. Comparison of studies using weekly cisplatin regimens.

	This study, 2007	Rose et al,[2] 1999	Pearcey et al,[6] 2002	Keys et al,[3] 1999
Number of patients	31	173	127	183
Disease-free survival at 3 years	77.4%	~60%	65%	~78%
Overall survival at 3 years	87.5%	~64%	69%	~83%
Disease stage	IA2-IVA	IIB-IVA	IB2-IVA	IB (≥4 cm) and lymph node–negative
Histology: squamous cell carcinoma	100%	90%	100%	81%
Treatment groups	Cisplatin + radiotherapy vs radiotherapy alone	Cisplatin + radiotherapy vs hydroxyurea + radiotherapy vs cisplatin + 5-fluorouracil + hydroxyurea + radiotherapy	Cisplatin + radiotherapy vs radiotherapy alone	Cisplatin + radiotherapy + hysterectomy vs radiotherapy + hysterectomy
p Value	0.23	0.004	0.53	0.008

no significant increases in acute toxicities and overall late toxicities compared with other studies.[1-3,6,7] As the combination of 5-flurouracil with cisplatin is also a viable chemotherapeutic regimen for treating carcinoma of the cervix and has been used as an experimental treatment in many studies with positive results, further randomised study may be warranted to delineate the most appropriate platinum-based regimen.

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